NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

STUDIES OF

MAGNETIC FIELD PROMOTION
(DMBA INITIATION)

IN FEMALE SPRAGUE-DAWLEY RATS

(WHOLE-BODY EXPOSURE/GAVAGE STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

August 1999

NTP TR 489

NIH Publication No. 99-3979

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

These studies were supported by the EMF Research and Public Information Dissemination (EMF *RAPID*) Program through the United States Department of Energy.

FOREWORD

The National Toxicology Program (NTP) is made up of four charter agencies of the U.S. Department of Health and Human Services (DHHS): the National Cancer Institute (NCI), National Institutes of Health; the National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health; the National Center for Toxicological Research (NCTR), Food and Drug Administration; and the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention. In July 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS. The NTP coordinates the relevant programs, staff, and resources from these Public Health Service agencies relating to basic and applied research and to biological assay development and validation.

The NTP develops, evaluates, and disseminates scientific information about potentially toxic and hazardous chemicals. This knowledge is used for protecting the health of the American people and for the primary prevention of disease.

The studies described in this Technical Report were performed under the direction of the NIEHS and were conducted in compliance with NTP laboratory health and safety requirements and must meet or exceed all applicable federal, state, and local health and safety regulations. Animal care and use were in accordance with the Public Health Service Policy on Humane Care and Use of Animals. The prechronic and chronic studies were conducted in compliance with Food and Drug Administration (FDA) Good Laboratory Practice Regulations, and all aspects of the chronic studies were subjected to retrospective quality assurance audits before being presented for public review.

These studies are designed and conducted to characterize and evaluate the toxicologic potential, including carcinogenic activity, of selected chemicals or physical agents in laboratory animals (usually two species, rats and mice). The interpretive conclusions presented in this Technical Report are based only on the results of these NTP studies. Extrapolation of these results to other species and quantitative risk analyses for humans require wider analyses beyond the purview of these studies. Selection *per se* is not an indicator of carcinogenic potential.

Listings of all published NTP reports and ongoing studies are also available from NTP Central Data Management, NIEHS, P.O. Box 12233, MD E1-02, Research Triangle Park, NC 27709 (919-541-3419). The Abstracts and other study information for 2-year studies are available at the NTP s World Wide Web site: http://ntp-server.niehs.nih.gov.

NTP TECHNICAL REPORT

ON THE

TOXICOLOGY AND CARCINOGENESIS

STUDIES OF

MAGNETIC FIELD PROMOTION
(DMBA INITIATION)

IN FEMALE SPRAGUE-DAWLEY RATS

(WHOLE-BODY EXPOSURE/GAVAGE STUDIES)

NATIONAL TOXICOLOGY PROGRAM
P.O. Box 12233
Research Triangle Park, NC 27709

August 1999

NTP TR 489

NIH Publication No. 99-3979

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

These studies were supported by the EMF Research and Public Information Dissemination (EMF *RAPID*) Program through the United States Department of Energy.

CONTRIBUTORS

National Toxicology Program
Evaluated and interpreted results and reported findings

G.A. Boorman, D.V.M., Ph.D., Study Scientist
D.A. Bridge, B.S.
J.R. Bucher, Ph.D.
R.E. Chapin, Ph.D.
J.R. Hailey, D.V.M.
J.K. Haseman, Ph.D.
R.R. Maronpot, D.V.M.
G.N. Rao, D.V.M., Ph.D.
J.H. Roycroft, Ph.D.
C.S. Smith, Ph.D.
G.S. Travlos, D.V.M.
D.B. Walters, Ph.D.
K.L. Witt, M.S., Integrated Laboratory Systems

Battelle Pacific Northwest Laboratories
Conducted studies, evaluated pathology findings

L.E. Anderson, Ph.D., Principal Investigator
S.L. Grumbein, D.V.M., Ph.D.
S.E. Rowe, D.V.M., M.S.
D.L. Miller, Ph.D.
L.B. Sasser, Ph.D.

Experimental Pathology Laboratories, Inc.
Provided pathology quality assurance

J.F. Hardisty, D.V.M., Principal Investigator
P.C. Mann, D.V.M.

Dynamac Corporation
Prepared quality assurance audits

S. Brecher, Ph.D., Principal Investigator

NTP Pathology Working Group
Evaluated slides, prepared pathology report (11 December 1997)

M.P. Jokinen, D.V.M., Chairperson
Pathology Associates International
G.A. Boorman, D.V.M., Ph.D.
National Toxicology Program
J.H. Everitt, D.V.M.
Chemical Industry Institute of Toxicology
S.L. Grumbein, D.V.M., Ph.D.
Battelle Pacific Northwest Laboratories
P.C. Mann, D.V.M.
Experimental Pathology Laboratories, Inc.
R.R. Maronpot, D.V.M.
National Toxicology Program
R.C. Sills, D.V.M., Ph.D.
National Toxicology Program
J.M. Ward, D.V.M., Ph.D.
National Cancer Institute

Analytical Sciences, Inc.
Provided statistical analyses

R.W. Morris, M.S., Principal Investigator
S.R. Lloyd, M.S.
N.G. Mintz, B.S.

Biotechnical Services, Inc.
Prepared Technical Report

S.R. Gunnels, M.A., Principal Investigator
J.R. Carlton, B.A.
G. Gordon, M.A.
L.M. Harper, B.S.
A.M. Macri-Hanson, M.A., M.F.A.
E.S. Rathman, M.S.
W.D. Sharp, B.A., B.S.

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 in the United States and 50 Hz in Europe) and generally of low intensity. Because some epidemiology studies and initiation/promotion studies in rats have suggested a potential for increased breast cancer rates with increasing magnetic field exposure, the ability of 50- and 60-Hz magnetic fields to promote mammary gland tumors initiated by the administration of 7,12-dimethylbenz(a)anthracene (DMBA) was examined in female Sprague-Dawley rats in 13- and 26-week whole-body exposure studies. Additional animals were evaluated for changes in pineal gland and serum melatonin concentrations.

FIRST 13-WEEK STUDY

Groups of 100 female Sprague-Dawley rats were administered 20 mg DMBA (four weekly gavage doses of 5 mg in sesame oil) and exposed to 1 G 50-Hz, 5 G 50-Hz, or 1 G 60-Hz magnetic fields for 18.5 hours per day, 7 days per week, for 13 weeks. A group of 100 rats administered 20 mg DMBA served as DMBA controls. A group of 100 vehicle control rats was administered only sesame oil on the same schedule. Additional groups of 10 rats receiving similar treatment were evaluated for pineal gland and serum melatonin concentrations at 4, 8, or 12 weeks.

All vehicle control rats survived to the end of the study. Of the animals administered 20 mg DMBA, 6 rats in the DMBA control group, 13 in the DMBA/1 G 50-Hz group, eight in the DMBA/5 G 50-Hz group, and five in the DMBA/1 G 60-Hz group died or were removed from the study prior to the final necropsy. Final mean body weights and body weight gains of the DMBA/1 G 50-Hz and DMBA/1 G 60-Hz groups and the mean body weight gain of the DMBA/5 G 50-Hz group were slightly greater than those of the DMBA control group. Clinical findings including torso masses and ulcers (on the mammary masses) were attributed to DMBA administration.

The numbers of palpable mammary gland tumors, tumor sizes, and total tumor areas in DMBA/magnetic field groups were similar to those in the DMBA control group. Relative to the DMBA control group, exposure to magnetic fields did not significantly affect overall incidences of mammary gland neoplasms or nonneoplastic lesions in the DMBA/magnetic field groups.

SECOND 13-WEEK STUDY

Groups of 100 female Sprague-Dawley rats were administered 8 mg DMBA (four weekly gavage doses of 2 mg in sesame oil) and exposed to 1 G 50-Hz or 5 G 50-Hz magnetic fields for 18.5 hours per day, 7 days per week, for 13 weeks. A group of 100 female rats administered 8 mg DMBA served as DMBA controls. Additional groups of 10 rats receiving similar treatment were evaluated for pineal gland and serum melatonin concentrations at 4, 8, or 12 weeks.

Except for one rat in the DMBA/5 G 50-Hz group, all rats survived until the end of the study. Final mean body weights of DMBA/magnetic field groups were similar to those of the DMBA control group. Clinical findings including torso masses and ulcers were attributed to DMBA administration.

The numbers of palpable mammary gland tumors, tumor sizes, and total tumor areas in DMBA/magnetic field groups were similar to those in the DMBA control group. Relative to the DMBA control group, exposure to magnetic fields did not significantly affect overall incidences of mammary gland neoplasms or nonneoplastic lesions in the DMBA/magnetic field groups.

26-WEEK STUDY

Groups of 100 female Sprague-Dawley rats were administered 10 mg DMBA (in sesame oil) by gavage followed by exposure to 1 G 50-Hz, 5 G 50-Hz, or 1 G 60-Hz magnetic fields for 18.5 hours per day, 7 days per week, for 26 weeks. A group of 100 female rats administered 10 mg DMBA served as DMBA controls. Another 100 vehicle control rats were administered only sesame oil. Additional groups of 10 rats receiving similar treatment were evaluated for pineal gland and serum melatonin concentrations at 4, 8, or 12 weeks.

All rats in the vehicle control group survived until the end of the study. Twelve rats in the DMBA control group, 15 in the DMBA/1 G 50-Hz group, 9 in the DMBA/5 G 50-Hz group, and six in the DMBA/1 G 60-Hz group died or were removed during the study. The final mean body weights and body weight gains of the DMBA/1 G 50-Hz and DMBA/5 G 50-Hz groups were significantly greater than those of the DMBA control group. Clinical findings including torso masses, abscesses, and ulcers were attributed to DMBA administration. The pineal gland melatonin concentrations of DMBA/5 G 50-Hz and DMBA/1 G 60-Hz rats were significantly greater than that of the DMBA controls at week 12; however, these data were highly variable between individual animals within each group.

The numbers of palpable mammary gland tumors, tumor sizes, and total tumor areas in DMBA/magnetic field groups were similar to those in the DMBA controls. The incidences of mammary gland carcinoma (including multiple) in the DMBA/1 G 60-Hz group were significantly decreased relative to the DMBA control group.

CONCLUSIONS

In an initiation/promotion study in which female Sprague-Dawley rats were initiated by four weekly doses of 5 mg DMBA per rat beginning at 50 days of age and exposed to 50-Hz magnetic fields at 1 or 5 G field intensities or to 1 G 60-Hz magnetic fields for 13 weeks, there was no evidence that magnetic fields promoted the development of mammary gland neoplasms. The prevalence and multiplicity of mammary gland carcinomas in all DMBA groups limited the ability of this assay to detect a promoting effect of magnetic fields.

In an initiation/promotion study in which female Sprague-Dawley rats were initiated by four weekly doses of 2 mg DMBA per rat beginning at 50 days of age and exposed to 50-Hz magnetic fields at 1 or 5 G field intensities for 13 weeks, there was no evidence that magnetic fields promoted the development of mammary gland neoplasms.

In an initiation/promotion study in which female Sprague-Dawley rats were initiated by a single 10 mg DMBA dose at 50 days of age and then exposed to 50-Hz magnetic fields at 1 or 5 G field intensities or to 1 G 60-Hz magnetic fields for 26 weeks, there was no evidence that magnetic fields promoted the development of mammary gland neoplasms.

A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on page 9.

Summary of the 13- and 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Studies in Female Sprague-Dawley Rats

	First 13-Week Study	Second 13-Week Study	26-Week Study
Doses/Fields	20 mg DMBA control 20 mg DMBA/1 G 50 Hz 20 mg DMBA/5 G 50 Hz 20 mg DMBA/1 G 60 Hz	8 mg DMBA control 8 mg DMBA/1 G 50 Hz 8 mg DMBA/5 G 50 Hz	10 mg DMBA control 10 mg DMBA/1 G 50 Hz 10 mg DMBA/5 G 50 Hz 10 mg DMBA/1 G 60 Hz
Body weights	DMBA/1 G 50-Hz and DMBA/1 G 60-Hz groups greater than the DMBA control group	DMBA/magnetic field exposed groups similar to the DMBA control group	DMBA/1 G 50-Hz and DMBA/5 G 50-Hz groups greater than the DMBA control group
Survival rates	94/100, 87/100, 92/100, 95/100	100/100, 100/100, 99/100	88/100, 85/100, 91/100, 94/100
Mammary gland carcinoma	92/100, 86/100, 96/100, 96/100	43/100, 48/100, 38/100	96/100, 90/100, 95/100, 85/100
Mammary gland fibroadenoma	3/100, 2/100, 1/100, 1/100	None	71/100, 76/100, 73/100, 68/100
Evidence of promotional ability	No evidence	No evidence	No evidence

NATIONAL TOXICOLOGY PROGRAM BOARD OF SCIENTIFIC COUNSELORS
TECHNICAL REPORTS REVIEW SUBCOMMITTEE

The members of the Technical Reports Review Subcommittee who evaluated the draft NTP Technical Report on 7,12-dimethylbenz(a)anthracene initiation/magnetic field promotion on 11 March 1998 are listed below. Subcommittee members serve as independent scientists, not as representatives of any institution, company, or governmental agency. In this capacity, subcommittee members have five major responsibilities in reviewing the NTP studies:

- to ascertain that all relevant literature data have been adequately cited and interpreted,
- to determine if the design and conditions of the NTP studies were appropriate,
- to ensure that the Technical Report presents the experimental results and conclusions fully and clearly,
- to judge the significance of the experimental results by scientific criteria, and
- to assess the evaluation of the evidence of carcinogenic activity and other observed toxic responses.

Gary P. Carlson, Ph.D., Chairperson
School of Health Sciences
Purdue University
West Lafayette, IN

A. John Bailer, Ph.D.
Department of Mathematics and Statistics
Miami University
Oxford, OH

Steven A. Belinsky, Ph.D.
Inhalation Toxicology Research Institute
Kirkland Air Force Base
Albuquerque, NM

James S. Bus, Ph.D.
Health and Environmental Sciences
Dow Chemical Company
Midland, MI

Linda A. Chatman, D.V.M., Principal Reviewer
Inhalation Toxicology Research Institute.
Pfizer, Inc.
Groton, CT

John M. Cullen, V.M.D., Ph.D.
Department of Microbiology, Parasitology, and Pathology
College of Veterinary Medicine
North Carolina State University
Raleigh, NC

Susan M. Fischer, Ph.D., Principal Reviewer
M.D. Anderson Cancer Center
University of Texas
Smithville, TX

Thomas L. Goldsworthy, Ph.D.
Integrated Laboratory Systems
Research Triangle Park, NC

Stephen S. Hecht, Ph.D.*
University of Minnesota Cancer Centers
Minneapolis, MN

Michele Medinsky, Ph.D.
Chemical Industry Institute of Toxicology
Research Triangle Park, NC

Jose Russo, M.D., Principal Reviewer
Fox Chase Cancer Center
Philadelphia, PA

Expert Consultants

Clinton J. Grubbs, Ph.D.
Nutritional Sciences Department
University of Alabama
Birmingham, AL

Martin Misakian, Ph.D.
National Institute of Standards and Technology
Gaithersburg, MD

Maria Stuchly, Ph.D.
Department of Electrical and Computer Engineering
University of Victoria
Victoria, BC, Canada

* Did not attend

SUMMARY OF TECHNICAL REPORTS REVIEW SUBCOMMITTEE COMMENTS

On 11 March 1998, the draft Technical Report on the toxicology and carcinogenesis studies of 7,12-dimethylbenz(a)anthracene (DMBA) initiation/magnetic field promotion received public review by the National Toxicology Program's Board of Scientific Counselors' Technical Reports Review Subcommittee. The review meeting was held at the National Institute of Environmental Health Sciences, Research Triangle Park, NC.

Dr. G.A. Boorman, NIEHS, introduced the toxicology and carcinogenesis studies by discussing the known and reported effects of DMBA and electromagnetic fields (EMFs) and the rationale for the study, describing the experimental design, reporting on survival and body weight effects, and commenting on the lack of an effect of magnetic fields on chemical-related mammary gland neoplasms and nonneoplastic lesions in female rats. The proposed conclusion for the initiation/promotion studies was no evidence that magnetic fields promoted the development of mammary gland neoplasms in Sprague-Dawley rats.

Dr. Russo, a principal reviewer, agreed with the proposed conclusion. He noted that when the mean number of tumors per tumor-bearing animal was plotted against time, it took four more weeks for animals exposed to magnetic fields to reach the same number of tumors as DMBA control animals. In addition, the increase in the mean size of tumors was delayed in animals exposed to magnetic fields. Dr. Russo said that these data suggest that EMF exposure retarded rather than accelerated growth of these lesions, and that this aspect should be discussed more thoroughly in the report.

Dr. Chatman, the second principal reviewer, agreed with the proposed conclusion. She commented that it was not clear if the distance between the source and the animals was included in the definition of exposure. If it was part of the definition, then it should be so stated, and described consistently. Dr. Boorman said that the exposure conditions would be defined more clearly. He pointed out that the animals were in a field that was uniform, and that there were coils around the field; hence, as the animals moved around in their cages, they stayed within a field. Dr. Chatman asked if there had been any observations made about cancers in pets in homes where cancer was believed to be associated with EMF. Dr. Boorman replied that he was unaware of any such data on companion animals.

Dr. Fischer, the third principal reviewer, agreed with the proposed conclusion. She observed that the experiments by Löscher involved 24-hour exposure times while the present NTP experiments involved 18.5-hour exposure times, and that there was a need to assess the importance of this difference in the outcomes. Dr. Boorman responded that the daily exposure time employed in the NTP studies allowed adequate time for the technicians to conduct animal care without becoming exposed themselves. He noted that the cumulative exposure hours in the 26-week study would have been at least equal to Löscher's 13-week, 24-hours-per-day exposure regimen. Dr. Fischer thought that the differences in tumor sizes should be given more attention, especially since (as noted by Dr. Russo) there was a suggestion of a protective effect of magnetic fields with regard to neoplasm growth rates.

Comments were taken from the *ad hoc* expert consultants. Dr. Stuchly said that initially she had been concerned by the high neoplasm incidences in the first 13-week study, which were higher than in the Löscher study, but thought that the second 13-week and 26-week experiments allowed for better detection of possible promotional effects. She commented that the review of the epidemiology studies was too brief and needed to be expanded to include studies that gave negative results. Dr. Boorman said that he would expand the epidemiology review to provide more complete coverage. Dr. Stuchly said that the statement describing the effects of the Löscher studies as "marginal" was at odds with Löscher's own interpretation, and that these viewpoints might have to be reconciled. Dr. Boorman agreed and said he would let the data speak for themselves. Dr. Grubbs noted that the NTP study was a well-designed study conducted in excellent facilities by a highly qualified and competent staff, and that the data were fairly conclusive. He observed that a certain number of rats

in each group did not survive until the end of the study, said that it would be helpful to know the reasons, and suggested that survival curves would be helpful. Dr. Boorman replied that there was only one death in the second 13-week study. In the other studies, 8 to 12 animals died per group, with about half being classified as moribund deaths and the other half as natural deaths due to ulcerated tumors. Dr. Grubbs argued for presenting the data on tumor size and tumor numbers differently; that is, to obtain the mean tumor size, he suggested dividing the cumulative tumor sizes of all the rats in a group by the number of rats in that group (usually 100), regardless of whether any particular rat had a tumor. The same approach could also be used in estimating mean tumor number.

Dr. Cullen commented that promotion could be defined as the generation of not only an earlier onset of neoplasms (which was not the case with the present study) but also of a higher number or an increased yield of neoplasms. He wondered how an increased yield could be detected when there were such high incidences of neoplasms. Dr. Boorman responded that the neoplasms were counted and confirmed histologically. Drs. Russo and Fischer also emphasized that in typical initiation/promotion studies where incidences of tumor-bearing animals are quite high, multiplicity and the number of tumors become important in discerning an effect. Dr. Boorman agreed, noting that having the tumor multiplicity data, along with time to tumor and tumor size information, enabled the study scientists to confidently conclude that magnetic fields did not have neoplasm-promoting effects.

Dr. Russo moved that the Technical Report on three DMBA initiation/magnetic field promotion studies in female Sprague Dawley rats be accepted with revisions as discussed, and with the conclusion that there was no evidence that magnetic fields promoted the development of mammary gland neoplasms. Dr. Chatman seconded the motion, which was accepted by eight yes votes, with one abstention (Dr. Goldsworthy).

INTRODUCTION

Electric and magnetic fields associated with the production, transmission, and use of electricity are ubiquitous in industrialized society. The electric and magnetic fields associated with alternating current are predominantly of low frequency (50 or 60 Hz) and generally of low intensity. Electric fields exist when there is electric potential (voltage) 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 are referred to as electromagnetic fields, or EMFs. Electric fields are easily shielded by trees, walls, and other material, whereas 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 2 milligauss (mG), although many commonly used household appliances generate fields that exceed this intensity (Gauger, 1985). In some industries, mean workplace magnetic field exposure may exceed 10 mG (Theriault *et al.*, 1994).

Electromagnetic radiation, such as X-rays, ultraviolet light, or other 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 Liimatainen, 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, many had assumed that exposure to low-frequency, low-intensity magnetic fields could not pose a health hazard. This view was challenged by Wertheimer and Leeper (1979), who were supported by a second study by Savitz *et al.* (1988), reporting 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. Other epidemiology studies have failed to find this association, and the relationship between magnetic field exposure and the increased incidence of childhood cancers is not clear (NRC, 1997).

TOXICITY

Experimental Animals

Experimental animal studies to evaluate the potential effects of magnetic fields are difficult to conduct, and the exposure variables are difficult to control. Most reports of animal studies on the effects of magnetic fields do not give sufficient details on the exposure parameters or the local static magnetic fields of the earth to permit assessment of results. Conflicting results have been reported from animal studies on the potential hazard of exposure to electric and magnetic fields (Kavet and Banks, 1986; Kavet, 1996). Laboratory studies have shown that animals can respond behaviorally to electric fields; the evidence for behavioral response to magnetic fields is more tenuous, but in either case, no general adverse behavioral effects have been observed. While neuroendocrinologic effects have been reported in animals, these effects have not been associated with adverse health effects (NRC, 1997). In the NTP studies, no evidence of toxicity was observed in male or female F344/N rats or $B6C3F_1$ mice continuously exposed to 0.02, 2, or 10 G for 18.5 hours per day, 7 days per week for 8 weeks or intermittently exposed (1 hour on, 1 hour off) to 10 G for the same period (NTP, 1996; Boorman *et al.*, 1997).

Humans

The literature on the potential toxicity of 60-Hz magnetic fields includes human (epidemiology) studies and clinical studies. Most of this literature is difficult to evaluate due to the complex nature of the fields and the lack of adequate descriptions of the exposures or the potential confounding factors. Epidemiology studies can provide only an estimate of the exposures, because exposure in the home varies according to the location in the house; the number and type of appliances in use; the current load on outside lines, which varies with electrical demand; and development and changes within a community, which cause variations in the magnetic fields over time. Ambient

levels of 60-Hz magnetic fields in residences and most workplaces are typically in the range from 0.1 to 3 mG (NRC, 1997). Further, residential exposures account for only a portion of a person's total magnetic field exposure because exposures also occur in the school or workplace, during travel, and during outdoor activities (Feychting *et al.*, 1996; Friedman *et al.*, 1996; Kheifets *et al.*, 1997).

Studies of residential exposures have suggested possible increased rates of childhood leukemia (Savitz *et al.*, 1988; Feychting and Ahlbom, 1993, 1995) and brain cancer (Wertheimer and Leeper, 1979; Savitz *et al.*, 1988) in homes expected to have higher magnetic field intensities. Studies of occupational exposure of electricians have suggested possible increased risks of leukemia (Theriault *et al.,* 1994), brain cancer (Savitz and Loomis, 1995), and breast cancer (Matanoski *et al.*, 1991). However, the studies are not always consistent. Savitz and Loomis (1995) reported increased incidences of brain cancer but not leukemia in electricians, while Theriault *et al.* (1994) reported increased incidences of leukemia but not brain cancer. Other reported indicators of toxicity in humans include headaches, depression, impaired neuropsychologic performance, and suicide, but the results were inconsistent and the studies of mixed quality (NRC, 1997). In a series of studies, no effects of 200 mG exposure on nocturnal melatonin concentrations were seen in volunteers (Graham *et al.*, 1996, 1997).

REPRODUCTIVE TOXICITY

A review of the literature concluded that laboratory and epidemiological studies have not yielded conclusive data to suggest that magnetic field exposures induce adverse reproductive effects under the conditions studied (Chernoff *et al.*, 1992). Maffeo *et al.* (1988) and Jauchem (1993) have also suggested that the evidence for any reproductive effects is very weak.

Experimental Animals

There have been over 70 experimental animal and *in vitro* studies that evaluated the effect of low-frequency (30- to 300-kHz) or very low-frequency (30-kHz or less) EMF exposure on some aspect of reproduction or teratology (Delgado *et al.*, 1982; Juutilainen and Saali, 1986; Beers, 1989; Eckert, 1992). Many embryology studies used the chicken 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 retarded development (Juutilainen and Saali, 1986; Martin, 1988), while in other studies, there were no differences in embryos from exposed or control eggs (Maffeo *et al.*, 1984). Medaka fish eggs exposed to a 60-Hz magnetic field showed no gross abnormalities, but the embryonic growth was retarded (Cameron *et al.*, 1985). Magnetic field exposures inhibited proliferation of sea urchins (Cameron *et al.*, 1993). No reproductive or developmental effects were seen in Sprague-Dawley rats exposed to magnetic fields of up to 10 G, 18.5 hours per day for as long as 6 months (NTP, 1996; Ryan *et al.*, 1996; Rommereim *et al.*, 1966).

Humans

Studies of the reproductive effects of EMF exposures in humans include studies of exposures to video display terminals, power lines, and household appliances. The video display terminal studies were generally negative for reproductive effects, while the reproductive risks of power lines and home appliances were less consistent (Brent *et al.*, 1993). The National Research Council (NRC, 1997) concluded that there was no substantial or conclusive evidence for adverse reproductive effects caused by residential exposure to electric and magnetic fields.

NEUROENDOCRINOLOGIC TOXICITY IN EXPERIMENTAL ANIMALS

Several studies have suggested that electric or magnetic field exposures may suppress nocturnal melatonin concentrations in rodents (Wilson *et al.*, 1986, 1989; Lerchl *et al.*, 1991; Reiter, 1992; Stevens *et al.*, 1992; Anderson, 1993; Stevens, 1994). In one study, serum melatonin concentrations but not pineal gland melatonin synthesis were reduced in Sprague-Dawley rats, suggesting that degradation or tissue uptake of melatonin may be stimulated by exposure to electric fields (Grota *et al.*, 1994). Another study reported that serotonin-*N*-acetyltransferase, the rate-limiting enzyme for melatonin production, may be inhibited by magnetic field exposure (Olcese and Reuss, 1986). No alterations occurred in serum or pineal gland melatonin or pineal gland serotonin *N*-acetyltransferase in male or female F344/N rats or $B6C3F_1$ mice exposed to magnetic fields of up to 10 G for 8 weeks (NTP, 1996). In that study, the magnitude of the pineal gland response was evaluated at only one nocturnal time point; consequently, the duration of the melatonin secretion could not be determined. When

this study was repeated in mice, with evaluation of pineal gland response at multiple nocturnal time points, no effect of magnetic field exposures was observed. The NTP studies employed linear magnetic fields, and it has been suggested that circularly polarized magnetic fields will cause decreased melatonin concentrations in rats even though linear fields will not (Kato *et al.*, 1994a,b). Melatonin has been reported to be oncostatic (Kerenyi *et al.*, 1990; Reiter, 1992, 1993). Exposure to extremely low-frequency magnetic fields has been shown to block melatonin's growth inhibition of MCF-7 breast cancer cells (Liburdy *et al.*, 1993), and melatonin suppression may be associated with breast cancer, one of the cancers hypothesized to be increased by magnetic field exposure (Stevens *et al.*, 1992). Furthermore, melatonin treatment in human clinical trials has been reported to be effective in advanced cancers resistant to standard antitumor therapies (Lissoni *et al.*, 1991). It has been suggested that lower nocturnal levels of melatonin resulting from light at night and/or magnetic field exposures may relate to the increasing incidence of human breast cancer (Tynes, 1993; Stevens *et al.*, 1992). More recent studies have not shown consistent alterations in nocturnal melatonin concentrations in hamsters exposed to 60-Hz magnetic fields (Truong *et al.*, 1996), nor was there an effect on reproductive maturation (Yellon, 1996).

CARCINOGENICITY

Experimental Animals

While the animal studies to date have given conflicting results on the potential hazard of exposure to electric and magnetic fields (Kavet and Banks, 1986; Kavet, 1996), results of studies of breast cancer promotion in the rat model have shown an effect more consistently. Beniashvili *et al.* (1991) reported that low-frequency magnetic fields (50 Hz, 0.2 G) enhance the promotion of mammary gland tumors in rats induced with nitrosomethyl urea. Additional studies in which mammary gland tumors were induced by 7,12-dimethylbenz(a)anthracene (DMBA) in female Sprague-Dawley rats have suggested that magnetic field exposure may promote breast cancer (Löscher *et al.*, 1993, 1994; Löscher and Mevissen, 1994; Mevissen *et al.*, 1993, 1994, 1995; Baum *et al.*, 1995), generally limited to 50 Hz at 0.1 and 1 G field intensities.

Several short-term (180-day) rodent carcinogenesis studies of magnetic fields have also been conducted (Anderson, 1993). Static magnetic fields did not enhance the development of spontaneous lymphoblastic leukemia in female AKR mice (Bellossi, 1986). 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 the neoplasm rate (Rannug *et al.*, 1993a). In SENCAR mice, intermittent magnetic field exposure was associated with a marginal increase in the accumulated number of skin tumors per tumor-bearing animal (Rannug *et al.*, 1994). In one copromotion study, where mice were exposed to fields of 60 Hz at 20 G intensity, more mice with tumors and more tumors per mouse were seen at 12 and 18 weeks. However, by week 23 at the end of the study, no differences between control and exposed animals were found (Stuchly *et al.*, 1992). In three independent studies in SENCAR mice, the results were variable and did not support an effect of magnetic fields on skin tumor promotion in this model (McLean *et al.*, 1997). In Sprague-Dawley rats, there was no increase in the incidence of liver foci following magnetic field exposure (Rannug *et al.*, 1993b); following partial hepatectomy and treatment with the tumor initiator diethylnitrosamine, magnetic field exposure was associated with a slight reduction in the size and number of liver foci compared to unexposed controls (Rannug *et al.*, 1993c).

Humans

The potential of magnetic field exposure to promote breast cancer has been suggested by several epidemiology studies, but the data are far from conclusive. Magnetic field exposure may affect the rates of breast cancer in men (Matanoski *et al.*, 1991; Tynes, 1993). Loomis *et al.* (1994) indicated a modest increase (odds ratio 1.38, 95% confidence interval = 1.04 to 1.82) in the incidence of breast cancer in female electrical workers exposed to magnetic fields. There was no excess of breast cancer in seven other predominantly female occupations that also involve potentially elevated magnetic field exposures, such as computer operations (Loomis *et al.*, 1994).

GENETIC TOXICITY

The potential genotoxic effects of low-frequency EMFs have been investigated in a variety of studies covering a broad range of test types and endpoints; thorough reviews of these studies were presented by McCann *et al.* (1993) and Murphy *et al.* (1993). With few exceptions, the data from laboratory experiments support the conclusion that low-frequency EMFs, as well as electric and magnetic fields separately, present little if any risk of induced genetic damage under the conditions of investigation. It is generally accepted that the energy from low-frequency electromagnetic radiation is insufficient to produce direct DNA damage (Kavet, 1996). However, electric field exposures 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; Murphy *et al.*, 1993). Reports of 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 workplace environment (Nordenson *et al.*, 1984, 1988) and of dose-related increases in micronuclei in bone marrow cells of mice exposed to 50-Hz sinusoidal electrical fields of varying intensities (170 to 290 kV/m) (El Nahas and Oraby, 1989) raised a concern about the genetic effects of these exposures. However, neither of these studies has been independently duplicated, and numerous *in vitro* investigations of chromosomal or mutational effects conducted under carefully controlled and defined laboratory conditions with human cells (Nordenson *et al.*, 1984; Cohen *et al.*, 1986a,b; Rosenthal and Obe, 1989; Livingston *et al.*, 1991; Scarfi *et al.*, 1991) and rodent cells (Wolff *et al.*, 1980; Livingston *et al.*, 1991; Fiorio *et al.*, 1993; Suri *et al.*, 1996) have not confirmed the potential for EMF-induced genetic damage. Also, results from DNA repair studies (Pino *et al.*, 1985; Whitson *et al.*, 1986; Reese *et al.*, 1988; Frazier *et al.*, 1990) and DNA damage studies (Fairbairn and O'Neill, 1994; Antonopoulos *et al.*, 1995) with mammalian cells exposed to EMFs were negative, as were results from bacterial mutagenicity assays (Moore, 1979; Thomas and Morris, 1981; Juutilainen and Liimatainen, 1986; Shimizu *et al.*, 1989; Morandi *et al.*, 1996).

Effects of electric and magnetic fields on biological systems that might potentially be related to cancer induction may include enhancement of cell proliferation, and earlier studies have been reviewed (McCann *et al.*, 1993; Murphy *et al.*, 1993). Investigations of the effects of EMF exposure on cell cycle progression have yielded mixed results, and possible modes of action whereby EMFs might enhance cell proliferation have not been determined (Murphy *et al.*, 1993; Kavet, 1996). Livingston *et al.* (1991) and Miyakoshi *et al.* (1996) found no exposure-related changes in clonogenicity and/or cell cycle time of Chinese hamster ovary cells cultured for at least 96 hours in the presence of 60-Hz electromagnetic or magnetic fields, and Cridland *et al.* (1996) detected no effects on the rate of DNA synthesis, a measure of cell proliferation, in normal human fibroblasts exposed to 50-Hz magnetic fields for up to 30 hours. Other investigators have reported stimulation of human peripheral blood lymphocyte proliferation *in vitro* after exposure to 50 G, 50-Hz EMFs (Rosenthal and Obe, 1989; Antonopoulos *et al.*, 1995) or 50-Hz pulsed magnetic fields (Scarfi *et al.*, 1994).

The possible effects of EMF exposure on epigenetic endpoints, such as transcriptional activation or modulation of gene expression, have been investigated at a number of laboratories with conflicting results (Blank *et al.*, 1992; Phillips, 1993; Gold *et al.*, 1994; Goodman *et al.*, 1992, 1994a,b; Libertin *et al.*, 1994; Saffer and Thurston, 1995). For example, exposure to extremely low-frequency EMFs was reported to stimulate transcription of c-*fos*, c-*jun*, c-*myc* and/or protein kinase C genes in various cell types, including human HL60, mouse myeloma, and yeast cells (Wei *et al.*, 1990; Phillips, 1993; Goodman *et al.*, 1992, 1994a,b; Lin *et al.*, 1994). However, Lacy-Hulbert *et al.* (1995) were unable to duplicate the c-*myc* transcriptional stimulation in HL60 human leukemic cells, despite the use of carefully controlled experimental protocols and a variety of sophisticated analytical methods capable of detecting very small alterations in transcriptional activation. In addition, Saffer and Thurston (1995) used ribonuclease protection assays as another sensitive means of measuring transcriptional activation in HL60 cells exposed to extremely low-frequency EMFs and found no alterations in gene expression. Furthermore, Miyakoshi *et al.* (1996) reported that similar exposure of cultured Chinese hamster ovary cells to 60-Hz EMFs did not alter cell growth rate or expression of c-*myc*. Several reviews of the controversial reports of transcriptional modulation following EMF exposures are found in the literature (Adair, 1992; Florig, 1992; Phillips, 1993; Lacy-Hulbert *et al.*, 1995; Blank and Goodman, 1997), and the current consensus among investigators

in the field is that observations of transcriptional stimulation resulted from unique experimental conditions that could not be duplicated in any of several independent laboratories under carefully monitored conditions.

In summary, although a number of well-designed and conducted genotoxicity experiments with EMFs have been published, not all types of exposures nor all of the commonly employed assays have been used, and many studies are deficient in design, conduct, or reporting format (McCann *et al.*, 1993; Murphy *et al.*, 1993). However, the accumulated evidence implies little risk of direct genetic damage from EMF exposure.

STUDY RATIONALE AND DESIGN

In response to a series of epidemiology studies suggesting that some human cancers may be associated with either residential (Savitz *et al.*, 1988) or occupational (Gilman *et al.*, 1985) magnetic field exposures, the NIEHS began a standard rodent study through the NTP to determine whether 2-year exposure to 60-Hz magnetic fields would increase rodent neoplasia (NTP, 1999). In addition, the Electric Power Research Institute (EPRI) initiated a large initiation/promotion study to determine whether 60-Hz magnetic fields could promote leukemia in a mouse model.

In the 1992 Energy Policy Act (Section 2118), the United States Congress established an accelerated EMF Research and Public Information Dissemination (EMF *RAPID*) Program to address public concerns about exposure to 60-Hz (power-line frequency) electric and magnetic fields. This program is supported by matching private funds, with the Department of Energy responsible for program management and engineering and mitigation research and the NIEHS responsible for health research. The EMF *RAPID* Program advisory groups suggested that the NIEHS conduct magnetic field studies on breast cancer initiation/promotion.

Many scientists had concluded that it was unlikely that magnetic fields alone could initiate the carcinogenic process; however, the role of magnetic field exposures in the promotion of a carcinogenic process that has already been initiated was still open to question. Animal studies also offered the opportunity to control many variables that cannot be controlled in human studies. NIEHS proposed that previous studies be replicated and extended using the standard DMBA initiation/promotion mammary gland tumor model of Löscher and associates (Löscher *et al.*, 1993, 1994; Löscher and Mevissen, 1994; Mevissen *et al.*, 1993, 1994, 1995; Baum *et al.*, 1995). The National EMF Advisory Committee and the EMF Interagency Committee, two advisory committees established under the 1992 Energy Policy Act, supported the additional proposed studies to be funded under the EMF *RAPID* Program.

The first 13-week DMBA initiation study used four weekly doses of 5 mg DMBA, as in the Löscher protocol (Mevissen *et al.*, 1993, 1994, 1995; Löscher and Mevissen, 1994; Löscher *et al.*, 1994). A 26-week study using a single DMBA dose concentration was also conducted to evaluate a lower DMBA dose concentration with extended magnetic field exposure. All DMBA groups in the first 13-week study had mammary gland neoplasm incidences, determined by gross palpation, that were greater than 80%; therefore, a second 13-week study was conducted with four weekly doses of 2 mg DMBA. The results of these 13- and 26-week initiation/promotion studies in female Sprague-Dawley rats exposed to 50- or 60-Hz magnetic fields are presented in this Technical Report.

These studies used 100 animals per group (rather than the usual 50) to increase the chance of detecting a marginal promotional effect on the cancer rates. The Löscher and Beniashvili studies were conducted at 50 Hz, the European power frequency (Beniashvili *et al.*, 1991). However, because the predominant magnetic field frequency in United States homes is 60 Hz, exposures at both 50 and 60 Hz were used in this study, with field intensities similar to those used by Löscher and associates. They reported a greater promotional effect with 1 G fields than with fields of lower intensity. After discussions with Dr. Löscher, one higher field intensity was also included in the NTP study. As field intensities increase, noise, heat, vibration, and stray fields may become confounding factors. A manageable maximum field intensity was 5 G, which is approximately 1,000-fold greater than what was considered high intensity for homes in the epidemiology studies. In addition to 50 Hz at 1 or 5 G, a third group was exposed to 60 Hz

at 1 G. Because the Löscher studies evaluated sine wave fields, the NTP studies were also restricted to pure sine wave exposures.

In summary, the NTP initiation/promotion mammary gland tumor studies evaluated the potential for 1 G (50 and 60 Hz) and 5 G (50 Hz) magnetic fields to promote DMBA-induced mammary gland tumors in female Sprague-Dawley rats. Pineal gland and serum melatonin concentrations in rats exposed to 50- or 60-Hz magnetic fields were also evaluated because these parameters have been reported to be altered by magnetic field exposure in rats (Löscher *et al.*, 1994; Mevissen *et al.*, 1993). The incidences of the mammary gland neoplasms in the standard 2-year NTP study, reported separately (NTP, 1999), also have obvious implications for the interpretation of this initiation/promotion study.

MATERIALS AND METHODS

PROCUREMENT AND CHARACTERIZATION

7,12-Dimethylbenz(a)anthracene

7,12-Dimethylbenz(a)anthracene (DMBA) was purchased by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO) from TCI America (Portland, OR) in one lot (FID01) which was used during the 13-week studies and the 26-week study. Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory. Reports on analyses performed in support of the DMBA initiation/magnetic field promotion studies are on file at the National Institute of Environmental Health Sciences (NIEHS).

The chemical, a light-yellow, crystalline powder with a melting point of 121° to 122° C, was identified as DMBA by infrared and nuclear magnetic resonance spectrometry. All spectra were consistent with those expected for the structure and with the literature spectra. The purity of lot FID01 was determined by high-performance liquid chromatography. Three impurities with a combined area of approximately 1.4% relative to the major peak area were detected. The purity of lot FID01 was determined to be approximately 99%. These results were in agreement with the purity information supplied by the manufacturer, which indicated a purity of 98.6%.

Bulk chemical stability studies of lot M111384 of DMBA, not used in the current studies, were performed by gas chromatography. Results indicated that DMBA did not degrade compared to a frozen reference sample over a 2-week period when stored refrigerated, at room temperature, or warmed to 60° C when protected from light. The bulk chemical was stored at room temperature throughout the studies. Lot FID01 was also evaluated for purity and stability at the end of the last study.

Sesame Oil

Sesame oil was obtained by MRI from Welch, Holme, and Clark Company, Inc. (Newark, NJ), in one lot (39-252), which was used during the 13-week studies and the 26-week study. Identity and peroxide content determinations were performed by the analytical chemistry laboratory. The chemical, a slightly yellow oil, was identified as sesame oil by infrared spectrometry; the spectrum was consistent with that expected for sesame oil. The peroxide content was determined by titration. The peroxide content of the first shipment of sesame oil (used during the first 13-week study and the 26-week study) received by the study laboratory was 0.87 $\pm$ 0.10 mEq peroxide/kg. Approximately 10 months later, a peroxide determination was performed on samples from a second shipment of sesame oil (used in the second 13-week study); the peroxide content was determined to be 6.89 $\pm$ 0.07 mEq/kg. Both peroxide levels are considered within acceptable levels. Bulk sesame oil was stored refrigerated at the study lab.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The dose formulations were prepared on the day of dosing by mixing DMBA with sesame oil to give the desired concentration (Table F1). Samples of the 5 and 10 mg/mL formulations prepared on 7 June 1996 were shipped to Midwest Research Institute (MRI) for analysis to determine dose formulation proficiency. Samples were analyzed by high-performance liquid chromatography and all samples examined (6/6) were within 2% of the target concentration (Table F2).

Stability studies of 2 and 15 mg/mL formulations were performed by the analytical chemistry laboratory. Samples were analyzed by high-performance

liquid chromatography and stability of the formulations was confirmed for up to 35 days when stored at room temperature or refrigerated at approximately 5° C. Formulations were also stable when stored for 3 hours open to air and light.

MAGNETIC FIELD PRODUCTION AND MONITORING

In all three studies, rats were exposed to either 0, 1, or 5 G 50-Hz magnetic fields because a German study and a Russian study had suggested a promotion effect of 50 Hz (European power-line frequency) on DMBA-induced breast cancer in rats. In the first of two 13-week studies and in a 26-week study presented here, a 1 G 60-Hz (United States power-line frequency) group was also included. The original protocol called for the highest magnetic field intensity to be 10 G, but at this intensity the overlap of magnetic fields (stray fields) from separate exposure areas was excessive. Thus, the protocol was modified, and the highest magnetic field intensity was set at 5 G 50 Hz. Exposed rats were housed in one room (Room 122/126) while the control rats were housed in a separate room (Room 135) (Figure G1).

The magnetic field exposure system consisted of three identical field-generating coil sets, each associated with three animal exposure racks in a single exposure room. Each coil set consisted of four pairs of 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 horizontal linear magnetic field (50 or 60 Hz) in one direction while the top coils produced a similar field in the opposite direction. The opposing fields produced by coil pairs functioned to cancel one another outside the area of the exposure rack. Coil wires were embedded in plastic and coils rested on vibration damping feet to reduce vibration and hum; copper cooling tubes were included to control coil temperature.

Electrical power to the coils was supplied by Techron Model 7570 (Crown International, Elkhart, IN) power amplifiers via condensers that served as power-factor correctors. This arrangement "tuned" the coils to the proper frequency (50 or 60 Hz) and provided for a highly pure sinusoidal exposure field with a total harmonic distortion of 0.2%.

Regulation and monitoring of magnetic fields and data acquisition were controlled by a computer housed in a separate control room (Room 130; Figure G1). The control/monitoring computer was equipped with a measurement coprocessor board and a tape drive for system backup. Multifunction synthesizer units attached to the control/monitoring computer supplied signals to the power amplifiers to produce 50- or 60-Hz fields. Emdex II data logging units were used to monitor field intensities. Field data were collected by the control computer every 6 minutes, at which time the computer adjusted fields by varying the voltage supplied to the power amplifier. The fields were turned on and off automatically under computer control to provide access to animals for husbandry and observation; exposure was 18.5 hours per day, 7 days per week during the studies. When fields were turned on or off they were increased or decreased gradually over 7 to 9 cycles (0.11 to 0.15 seconds) to prevent transients. In addition to the collection of field data, temperature, relative humidity (Omega Engineers, Stamford, CT), and sound (CEL Instruments, Severna Park, MD) sensors provided data to the control/monitoring computer every 6 minutes (Tables G1 and G2).

In the first 13-week study and the 26-week study, the stray 60-Hz magnetic fields did not exceed 3 mG in the 1 or 5 G 50-Hz animal exposure areas; however, the stray 50-Hz magnetic fields in the 1 G 60-Hz animal exposure area varied from 5 to 30 mG (11.4 ± 6.4 mG). The 11.4 mG stray 50-Hz magnetic fields represented only 1.1 % of the induced 1 G 60-Hz fields. In the second 13-week study, only 50-Hz magnetic fields were used, and there were no stray fields of other frequencies. The mean magnetic field intensity during the 13-week and 26-week studies was within 10% of the target at all time points. The mean stray magnetic fields for the control area were less than 1 mG in all three studies.

FACILITY VALIDATION

Prior to and after the end of the animal studies, studies were performed to characterize magnetic field intensities, audible sound, electric fields, coil heating, and earth static magnetic fields in exposure rooms. Magnetic fields were assessed with Emdex field meters (Enertech Consultants) placed at the approximate center position of each cage. Magnetic field data are presented in Table G3. Electric field levels

were low (< 10 V/m) because cage racks were connected to an electrical ground. Coil heating was negligible at the field levels used in these studies. At 5 G, coils heated less than 1° C and any resulting cage heating was undetectable. Magnetic field characterizations were verified by a representative of the National Institute of Standards and Technology (NIST) (Table G4). Earth static magnetic fields were also characterized by the NIST (Table G4); all were within acceptable ranges. The static magnetic field component parallel to the alternating fields was between 150 and 200 mG.

FIRST 13-WEEK STUDY

Female Sprague-Dawley rats were obtained from Charles River Laboratory (Raleigh, NC). On receipt, the rats were 35 ± 2 days old. Rats were quarantined for 15 days and were 50 ± 2 days old on the first day of the study. Before initiation of the study, 10 rats were randomly selected for parasite evaluation and gross observation for evidence of disease. Sera from 10 rats were evaluated 3 weeks after arrival for *Mycoplasma pulmonis*, Toolan's H-1 virus, Kilham rat virus, pneumonia virus of mice, rat coronavirus/sialodacryoadenitis virus, and Sendai virus. At the end of the study, serologic analyses were performed on five rats from each of two exposure rooms using the protocols of the NTP Sentinel Animal Program (Appendix H).

DMBA Initiation: Four groups of 130 female Sprague-Dawley rats (100 core and 30 special study) were administered 5 mg DMBA dissolved in 1 mL of sesame oil by gavage at the beginning of weeks 1, 2, 3, and 4. Of the four groups administered DMBA, one group received no magnetic field exposure and served as a DMBA control group. An additional 130 female rats were administered 1 mL of sesame oil by gavage at the beginning of weeks 1, 2, 3, and 4. These rats received no magnetic field exposure and served as a vehicle control group.

Magnetic Field Promotion: Three groups administered DMBA were also exposed to magnetic field intensities/frequencies of 1 G 50 Hz, 5 G 50 Hz, or 1 G 60 Hz for 18.5 hours per day, 7 days per week, for 13 weeks.

Feed (NIH-07 rat and mouse ration) and water were available *ad libitum*. Rats were housed four per cage. Clinical findings were recorded weekly; animals were weighed on day 1 of the study and weekly thereafter. Rats administered DMBA (control and magnetic field-exposed) or sesame oil (vehicle control) were palpated weekly for the detection of mammary gland tumors. Details of the study design and animal maintenance are summarized in Table 1.

The core study rats were palpated once a week for the detection of mammary gland tumors. Two individuals each palpated half the rats and alternated the groups that they examined each week. Specific mammary glands were identified by site as L(left)1 through L6 and R(right)1 through R6, with 1 being the most cranial and 6 the most caudal gland. Masses were located by gland and those occurring anterior to position 1 or posterior to 6 were identified as "pre 1" and "post 6." The size of each mammary gland tumor was noted by comparison to wooden spheres of various diameters. Each person palpating noted the presence, location, and size of the masses. If there was a discrepancy with the previous observation, the person who palpated the rat the previous week was consulted, and the issue was resolved. In this manner, each rat was palpated on alternate weeks by two investigators with the opportunity to verify each other's results. The high incidence of tumors in the first 13-week study and the 26-week study required the training of two additional people to help with the tumor palpations toward the end of these studies.

Ten special study rats per group were killed by decapitation at 4, 8, or 12 weeks, 6 hours into the dark cycle (between 11 p.m. and 12 a.m.), under dim red filter light (60 W and < 1 lux). Trunk blood was collected and allowed to clot. Pineal glands were removed, frozen on dry ice, and stored at -70° C until analysis. Animals were then discarded without further analysis. The sera and pineal glands were analyzed for melatonin by the LC-MS-MS method.

A necropsy was performed on all core study rats. The liver and right kidney were weighed. Mammary glands and associated skin were transilluminated to identify all potential tumors. Palpation data were available to the pathologist, and these tumors and additional mammary gland lesions were found at necropsy. Mammary gland and other gross lesions were measured (length and width) to the nearest 0.1 cm, and these measurements were used to calculate the area of the mammary gland tumors for each group. Mammary gland lesions were logged according to gland of occurrence (trace gross lesion

identifier). Tissues for microscopic examination were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 5 to 6 μm, and stained with hematoxylin and eosin. Table 1 lists the tissues and organs examined. Neoplasm types were identified histopathologically. Histologic diagnoses of mammary gland lesions were correlated with trace gross lesion identifiers.

SECOND 13-WEEK STUDY

Female Sprague-Dawley rats were obtained from Charles River Laboratory (Raleigh, NC). On receipt, the rats were 36 $\pm$ 2 days old. The rats were quarantined for 14 days and were 50 $\pm$ 2 days old on the first day of the study. Before initiation of the study, 10 rats were randomly selected for parasite evaluation and gross observation for evidence of disease. Sera from 10 rats were evaluated 3 weeks after arrival for the same pathogens as in the first 13-week study. At the end of the study, serologic analyses were performed on five rats from each of two exposure rooms using the protocols of the NTP Sentinel Animal Program (Appendix H).

DMBA Initiation: Three groups of 130 female Sprague-Dawley rats (100 core and 30 special study) were administered 2 mg DMBA dissolved in 1 mL of sesame oil by gavage at the beginning of weeks 1, 2, 3, and 4. One group administered DMBA received no magnetic field exposure and served as a DMBA control group. No vehicle control group was included in the protocol because no tumors were observed in the vehicle control group from the first 13-week study.

Magnetic Field Promotion: Two of the three groups administered DMBA were also exposed to magnetic fields of 50 Hz at intensities of 1 or 5 G for 18.5 hours per day, 7 days per week, for 13 weeks.

Feed (NIH-07 rat and mouse ration) and water were available *ad libitum*. Rats were housed five per cage. Clinical findings were recorded weekly; rats were weighed on day 1 of the study and weekly thereafter. The core study rats were palpated for the identification of mammary gland tumors as described in the first 13-week study. Details of the study design and animal maintenance are summarized in Table 1.

As described for the first 13-week study, 10 special study rats per group were killed by decapitation at 4, 8, or 12 weeks for the collection of sera and pineal glands for melatonin analyses.

A necropsy was performed on all core study rats. Mammary glands and associated skin were transilluminated to identify all potential tumors. Palpation data were available to the pathologist, and these tumors and additional mammary gland lesions were found at necropsy. Mammary gland and other gross lesions were measured (length and width) to the nearest 0.1 cm, and these measurements were used to calculate the area of the mammary gland carcinomas for each group. Mammary gland lesions were logged according to gland of occurrence (trace gross lesion identifier). Tissues for microscopic examination were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 5 to 6 μm, and stained with hematoxylin and eosin. Table 1 lists the tissues and organs examined. Neoplasm types were identified histopathologically. Histologic diagnoses of mammary gland lesions were correlated with trace gross lesion identifiers.

26-WEEK STUDY

Female Sprague-Dawley rats were obtained from Charles River Laboratory (Raleigh, NC). On receipt, the rats were 37 $\pm$ 2 days old. Rats were quarantined for 13 days and were 50 $\pm$ 2 days old on the first day of the study. Before initiation of the study, 10 rats were randomly selected for parasite evaluation and gross observation for evidence of disease. Sera from 10 rats were evaluated 3 weeks after arrival for the same pathogens as in the 13-week studies. At the end of the study, serologic analyses were performed on five rats from each of two exposure rooms using the protocols of the NTP Sentinel Animal Program (Appendix H).

DMBA Initiation: Four groups of 130 female Sprague-Dawley rats (100 core and 30 special study) were administered 10 mg DMBA dissolved in 1 mL of sesame oil by gavage on day 1 of the study. Of the four groups administered DMBA, one group received no magnetic field exposure and served as a DMBA control group. An additional 130 female rats were administered 1 mL of sesame oil by gavage on day 1

of the study. These rats received no magnetic field exposure and served as a vehicle control group.

Magnetic Field Promotion: Three groups administered DMBA were also exposed to magnetic fields at intensities/frequencies of 1 G 50 Hz, 5 G 50 Hz, or 1 G 60 Hz for 18.5 hours per day, 7 days per week, for 26 weeks.

Feed (NIH-07 rat and mouse ration) and water were available *ad libitum*. Rats were housed five per cage. Clinical findings were recorded weekly; rats were weighed on day 1 of the study and weekly thereafter. The core study rats were palpated for the identification of mammary gland tumors as described in the first 13-week study. Details of the study design and animal maintenance are summarized in Table 1.

As described for the first 13-week study, 10 special study rats per group were killed by decapitation at 4, 8, or 12 weeks to collect sera and pineal glands for melatonin analyses.

A necropsy was performed on all core study rats. The liver and right kidney were weighed. Mammary glands and associated skin were transilluminated to identify all potential tumors. Palpation data were available to the pathologist, and these tumors and additional mammary gland lesions were found at necropsy. Mammary gland and other gross lesions were measured (length and width) to the nearest 0.1 cm, and these measurements were used to calculate the area of the mammary gland carcinomas for each group. Mammary gland lesions were logged according to gland of occurrence (trace gross lesion identifier). Tissues for microscopic examination were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in paraffin, sectioned to a thickness of 5 to 6 μm, and stained with hematoxylin and eosin. Table 1 lists the tissues and organs examined. Neoplasm types were identified histopathologically. Histologic diagnoses of mammary gland lesions were correlated with trace gross lesion identifiers.

PATHOLOGY

Microscopic evaluations were completed by the study laboratory pathologist, and the pathology data were entered into the Toxicology Data Management System. 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 evaluated by an independent quality assessment laboratory. The individual animal records and tables were compared for accuracy, the slide and tissue counts were verified, and the histotechnique was evaluated. For all studies, a quality assessment pathologist reviewed the mammary glands.

The quality assessment report and the reviewed slides were submitted to the NTP Pathology Working Group (PWG) chairperson, who reviewed the selected tissues and addressed any inconsistencies in the diagnoses made by the laboratory and quality assessment pathologists. Representative histopathology slides containing mammary gland hyperplasia, fibroadenoma, and carcinoma, examples of disagreements in diagnoses between the laboratory and quality assessment pathologists, or lesions of general interest were presented by the chairperson to the PWG for review. The PWG consisted of the quality assessment pathologist and other pathologists experienced in rodent toxicologic pathology. This group examined the tissues without any knowledge of dose groups or previously rendered diagnoses. When the PWG consensus differed from the opinion of the laboratory pathologist, the diagnosis was changed. Final diagnoses for reviewed lesions represent a consensus between the laboratory pathologist, reviewing pathologist(s), and the PWG. Details of these review procedures have been described, in part, by Maronpot and Boorman (1982) and Boorman *et al*. (1985). For subsequent analyses of the pathology data, the decision of whether to evaluate the diagnosed lesions for each tissue type separately or combined was generally based on the guidelines of McConnell *et al*. (1986).

TABLE 1
Experimental Design and Materials and Methods in the 7,12-Dimethylbenz(a)anthracene Initiation/Magnetic Field Promotion Studies

First 13-Week Study	Second 13-Week Study	26-Week Study
Study Laboratory Battelle Pacific Northwest Laboratories (Richland, WA)	Battelle Pacific Northwest Laboratories (Richland, WA)	Battelle Pacific Northwest Laboratories (Richland, WA)
Strain and Species Sprague-Dawley rats	Sprague-Dawley rats	Sprague-Dawley rats
Animal Source Charles River Laboratory (Raleigh, NC)	Charles River Laboratory (Raleigh, NC)	Charles River Laboratory (Raleigh, NC)
Time Held Before Studies 15 days	14 days	13 days
Average Age When Studies Began 50 ± 2 days	50 ± 2 days	50 ± 2 days
Date of First Exposure 14 August 1996	4 March 1997	29 July 1996
Duration of Exposure 13 weeks	13 weeks	26 weeks
Dates of Last Exposure 11-15 November 1996	3-5 June 1997	27-31 January 1997
Necropsy Dates 11-15 November 1996	3-5 June 1997	27-31 January 1997
Average Age at Necropsy 20-21 weeks	20-21 weeks	33-34 weeks
Size of Study Groups Core study - 100 females Special study - 30 females	Core study - 100 females Special study - 30 females	Core study - 100 females Special study - 30 females
Method of Distribution Animals were distributed randomly into groups of approximately equal initial mean body weights.	Same as in the first 13-week study	Same as in the first 13-week study
Animals Per Cage 4	5	5
Method of Animal Identification Tail tattoo	Tail tattoo	Tail tattoo
Diet NIH-07 open formula pelleted diet (Zeigler Brothers, Inc., Gardners, PA), available *ad libitum*	Same as in the first 13-week study	Same as in the first 13-week study
Water Tap water (City of Richland municipal supply) available *ad libitum* from polycarbonate bottles (Nalgene VWR, Brisbane, CA), changed twice weekly	Same as in the first 13-week study	Same as in the first 13-week study

TABLE 1
Experimental Design and Materials and Methods in the 7,12-Dimethylbenz(a)anthracene Initiation/Magnetic Field Promotion Studies

First 13-Week Study	Second 13-Week Study	26-Week Study
Cages		
Polycarbonate (Nalgene VWR, Brisbane, CA), changed twice weekly and rotated in the racks once weekly	Same as in the first 13-week study	Same as in the first 13-week study
Bedding		
Sani-Chips® (P.J. Murphy Forest Products Corp., Montville, NJ), changed twice weekly	Same as in the first 13-week study	Same as in the first 13-week study
Racks		
Aluminum (Lab Products, Inc, Rochelle Park, NJ)	Same as in the first 13-week study	Same as in the first 13-week study
Animal Room Environment		
Temperature: 20.1°-27.3° C Relative humidity: 25%- 74% Light: 12 hours fluorescent light/day followed by 12 hours dim red light/day Room air changes: 17-20/hour	Temperature: 20.8°-25.3° C Relative humidity: 33%- 80% Light: 12 hours fluorescent light/day followed by 12 hours dim red light/day Room air changes: 18/hour	Temperature: 20.1°-27.3° C Relative humidity: 23%- 85% Light: 12 hours fluorescent light /day followed by 12 hours dim red light/day Room air changes: 17-20/hour
Initiation/Promotion		
Vehicle control: vehicle control group received 1 mL sesame oil by gavage at the beginning of weeks 1, 2, 3, and 4.	*Vehicle control:* None	*Vehicle control:* vehicle control group received 1 mL sesame oil by gavage on day 1 of the study.
DMBA control: DMBA control rats were administered 5 mg DMBA in 1 mL sesame oil by gavage at the beginning of weeks 1, 2, 3, and 4.	*DMBA control:* DMBA control rats were administered 2 mg DMBA in 1 mL sesame oil by gavage at the beginning of weeks 1, 2, 3, and 4.	*DMBA control:* DMBA control rats were administered 10 mg DMBA in 1 mL sesame oil by gavage on day 1 of the study.
Initiation: groups to be promoted with magnetic field exposure were administered initiation doses of 5 mg DMBA in 1 mL sesame oil by gavage at the beginning of weeks 1, 2, 3, and 4.	*Initiation:* groups to be promoted with magnetic field exposure were administered initiation doses of 2 mg DMBA in 1 mL sesame oil by gavage at the beginning of weeks 1, 2, 3, and 4.	*Initiation:* groups to be promoted with magnetic field exposure were administered initiation doses of 10 mg DMBA in 1 mL sesame oil by gavage on day 1 of the study.
Promotion: groups initiated with DMBA were exposed to 1 G 50 Hz, 5 G 50 Hz, or 1 G 60 Hz magnetic fields 18.5 hours per day, 7 days per week, for 13 weeks.	*Promotion:* groups initiated with DMBA were exposed to 1 G 50 Hz or 5 G 50 Hz magnetic field 18.5 hours per day, 7 days per week, for 13 weeks.	*Promotion:* groups initiated with DMBA were exposed to 1 G 50 Hz, 5 G 50 Hz, or 1 G 60 Hz magnetic field 18.5 hours per day, 7 days per week, for 26 weeks.
Type and Frequency of Observation		
Observed twice daily; rats were weighed on day 1 of the study and weekly thereafter; clinical findings were recorded weekly. Core study rats were palpated weekly for the detection of mammary gland tumors.	Same as in the first 13-week study	Same as in the first 13-week study
Method of Sacrifice		
CO_2 asphyxiation	Same as in the first 13-week study	Same as in the first 13-week study

TABLE 1
Experimental Design and Materials and Methods in the 7,12-Dimethylbenz(a)anthracene Initiation/Magnetic Field Promotion Studies

First 13-Week Study	Second 13-Week Study	26-Week Study
Melatonin Analyses Pineal glands and trunk blood were collected from 10 rats per group at 4, 8, and 12 weeks, 6 hours into the dark cycle (between 11 p.m. and 12 p.m.). Analyses included pineal gland and serum melatonin concentrations.	Same as in the first 13-week study	Same as in the first 13-week study
Necropsy A necropsy was performed on all core study rats. Liver and right kidney were weighed and mammary gland and gross neoplasms were measured	A necropsy was performed on all core study rats; mammary gland and gross neoplasms were measured.	Same as in the first 13-week study
Histopathology Histopathology was performed on all core study rats. In addition to gross lesions and tissue masses, the kidney, liver, lung and mainstem bronchi, and mammary gland and adjacent skin were examined microscopically.	Histopathology was performed on all core study rats. In addition to gross lesions and tissue masses, the mammary gland and adjacent skin were examined microscopically.	Same as in the first 13-week study

STATISTICAL METHODS

Calculation of Incidence

The incidences of neoplasms or nonneoplastic lesions are presented in Tables A1, A4, B1, B4, C1, and C4 as the numbers of animals bearing such lesions at a specific anatomic site and the numbers of animals with that site examined microscopically. For calculation of statistical significance, the incidences of most neoplasms (Tables A3, B3, and C3) and all nonneoplastic lesions are given as the numbers of animals affected at each site examined microscopically. However, when macroscopic examination was required to detect neoplasms in certain tissues (e.g., mammary gland and skin) before microscopic evaluation, or when neoplasms had multiple potential sites of occurrence (e.g., leukemia or lymphoma), the denominators consist of the number of animals on which a necropsy was performed. Tables A3, B3, and C3 also give the survival-adjusted neoplasm rate for each group and each site-specific neoplasm. This survival-adjusted rate (based on the Poly-3 method described below) accounts for differential mortality by assigning a reduced risk of neoplasm, proportional to the third power of the fraction of time on study, to animals that do not reach terminal sacrifice.

Analysis of Neoplasm and Nonneoplastic Lesion Incidences

The Poly-k test (Bailer and Portier, 1988; Portier and Bailer, 1989; Piegorsch and Bailer, 1997) was used to assess neoplasm and nonneoplastic lesion prevalence. This test is a survival-adjusted quantal-response procedure that modifies the Cochran-Armitage linear trend test to take survival differences into account. More specifically, this method modifies the denominator in the quantal estimate of lesion incidence to approximate more closely the total number of animal years at risk. For analysis of a given site, each animal is assigned a risk weight. This value is one if the animal had a lesion at that site or if it survived until terminal sacrifice; if the animal died prior to terminal sacrifice and did not have a lesion at that site, its risk weight is the fraction of the entire study time that it survived, raised to the kth power.

This method yields a lesion prevalence rate that depends only upon the choice of a shape parameter for a Weibull hazard function describing cumulative lesion incidence over time (Bailer and Portier, 1988). Unless otherwise specified, a value of $k=3$ was used in the analysis of site-specific lesions. This value was

recommended by Bailer and Portier (1988) following an evaluation of neoplasm onset time distributions for a variety of site-specific neoplasms in control F344 rats and B6C3F$_1$ mice (Portier *et al.*, 1986). Bailer and Portier (1988) showed that the Poly-3 test gave valid results if the true value of k was anywhere in the range from 1 to 5. A further advantage of the Poly-3 method is that it does not require lesion lethality assumptions. Variation introduced by the use of risk weights, which reflect differential mortality, was accommodated by adjusting the variance of the Poly-3 statistic as recommended by Bieler and Williams (1993).

Life table tests were used to compare the time of first detection of palpable mammary gland masses between magnetic-field exposed animals and DMBA controls (Cox, 1972; Tarone, 1975).

Tests of significance included pairwise comparisons of each exposed group with controls and a test for an overall exposure-related trend. Continuity-corrected tests were used in the analysis of lesion incidence, and reported P values are one-sided. Values of P greater than 0.5 are presented as 1–P with the letter N added to indicate a lower incidence or negative trend in neoplasm occurrence relative to the control group (e.g., P=0.99 is presented as P=0.01N).

Analysis of Continuous Variables

Organ and body weight data and serum and pineal gland melatonin concentrations, which have approximately normal distributions, were analyzed with the parametric multiple comparison procedures of Dunnett (1955) and Williams (1971, 1972). For some variables, the variance-stabilizing logarithmic transformation was applied prior to statistical analysis. Dunnetts's test was also used to assess differences in the numbers and sizes of mammary gland tumors. Average severity values were analyzed for significance with the Mann-Whitney U test (Hollander and Wolfe, 1973).

QUALITY ASSURANCE METHODS

The 13- and 26-week studies were conducted in compliance with Food and Drug Administration Good Laboratory Practice Regulations (21 CFR, Part 58). In addition, as records from the 13- and 26-week studies were submitted to the NTP Archives, these studies were audited retrospectively by an independent quality assurance contractor. Separate audits covered completeness and accuracy of the pathology data, pathology specimens, final pathology tables, and a draft of this NTP Technical Report. Audit procedures and findings are presented in the reports and are on file at NIEHS. The audit findings were reviewed and assessed by NTP staff, and all comments were resolved or were otherwise addressed during the preparation of this Technical Report.

RESULTS

FIRST 13-WEEK STUDY

Survival

All vehicle control rats survived to the end of the study (Table 2). Of the animals administered 20 mg DMBA, six rats in the DMBA control group, 13 in the DMBA/1 G 50-Hz group, eight in the DMBA/5 G 50-Hz group, and five in the DMBA/1 G 60-Hz group died or were removed from the study prior to the end of the study. The majority of these animals died or were removed from the study as the result of mammary gland neoplasms; however, one DMBA control, five 1 G 50-Hz rats, and one 5 G 50-Hz rat exhibited no masses at death or at moribund sacrifice.

Body Weights and Clinical Findings

Final mean body weights and body weight gains of the DMBA/1 G 50-Hz and DMBA/1 G 60-Hz groups and the mean body weight gain of the DMBA/5 G 50-Hz group were slightly, but significantly, greater than those of the DMBA control group (Table 2 and Figure 1). Clinical findings attributed to DMBA administration included torso masses and ulcers. Magnetic field exposure neither enhanced nor suppressed these effects.

TABLE 2
Survival and Body Weights of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study

Treatment[a]	Survival[b]	Mean Body Weight[c] (g)			Final Weight Relative to Controls (%)
		Initial	Final	Change	
Vehicle Control	100/100	187 ± 1	357 ± 4	170 ± 3	
20 mg DMBA Control	94/100[d]	188 ± 1	327 ± 4	139 ± 3	
20 mg DMBA/1 G 50 Hz	87/100[e]	186 ± 1	340 ± 4*	154 ± 3**	104
20 mg DMBA/5 G 50 Hz	92/100[f]	184 ± 1	333 ± 3	150 ± 3*	102
20 mg DMBA/1 G 60 Hz	95/100[g]	186 ± 1	339 ± 4*	152 ± 3**	104

* Significantly different ($P \leq 0.05$) from the DMBA control group by Dunnett's test
** $P \leq 0.01$
[a] Animals administered DMBA were given 5 mg at the beginning of weeks 1, 2, 3, and 4.
[b] Number of animals surviving at 13 weeks/number initially in group
[c] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study.
[d] Week of death: 9, 11, 11, 11, 11, 13
[e] Week of death: 7, 10, 10, 11, 11, 11, 12, 12, 12, 12, 12, 12, 12
[f] Week of death: 9, 10, 10, 11, 11, 12, 12, 12
[g] Week of death: 10, 10, 12, 12, 13

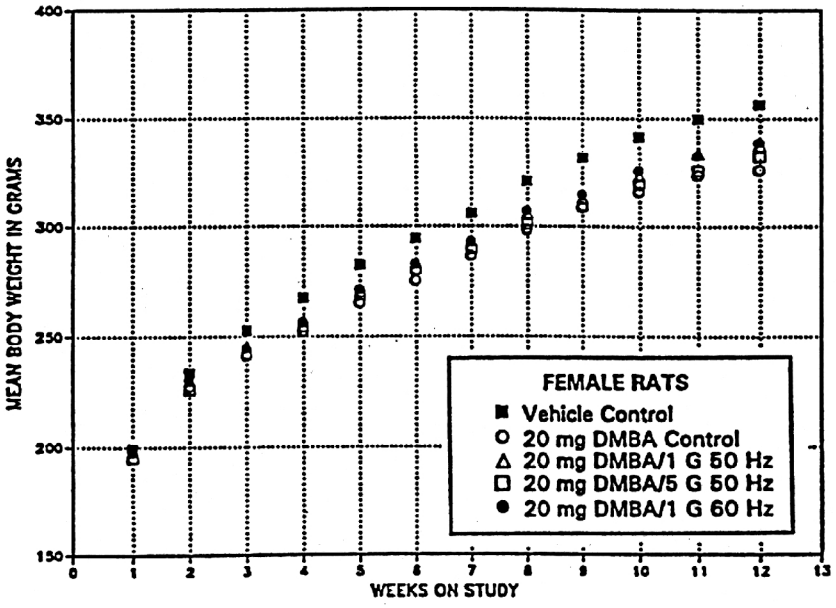


FIGURE 1
Growth Curves for Female Rats
in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/
Magnetic Field Promotion Study

Melatonin Analyses

At all time points, pineal gland melatonin and serum melatonin concentrations were similar among DMBA controls and DMBA/magnetic field groups (Tables D1 and D2). These data were highly variable, which may preclude detection of small differences in melatonin concentrations.

Mammary Gland Tumor Palpation

Except for one tumor at week 2 (DMBA/1 G 60-Hz group), the first mammary gland tumors were detected by palpation at week 6. The cumulative percentage of rats with palpable mammary gland tumors increased steadily throughout the study and was similar in the DMBA/magnetic field groups and the DMBA control group (Figure 2). Mammary gland tumors were not detected in the vehicle control group. The majority of palpated tumors were diagnosed histologically at necropsy as mammary gland carcinomas; additional mammary gland tumors were found at necropsy. Compared to DMBA control incidences, exposure to magnetic fields did not increase the mean number of mammary gland tumors per tumor-bearing rat (Figure 3). Whereas additional mammary gland tumors were found at necropsy and confirmed histologically, the number of animals with tumors was similar to that observed by palpation. The tumor sizes for in-life data were based on the estimates derived by palpation and refer to tumor volumes.

Mammary Gland Tumor Measurement

Mammary gland masses were measured in two directions at gross necropsy and assigned trace gross lesion identifiers so that the masses could be correlated with histologic diagnoses. Mean tumor sizes were similar among DMBA/magnetic field groups and the DMBA control group (Figure 4). The average area of the carcinomas varied from 1.98 cm^2 in the DMBA/5 G 50-Hz group to 2.44 cm^2 in the DMBA/1 G 50-Hz group (Table 3). The tumor sizes at necropsy were based on two-dimensional measurements that were used to calculate tumor area as $\pi[Diameter_1/2 \times Diameter_2/2]$. Neither the total carcinoma areas nor the mean areas per carcinoma differed significantly between DMBA/magnetic field and DMBA control groups.

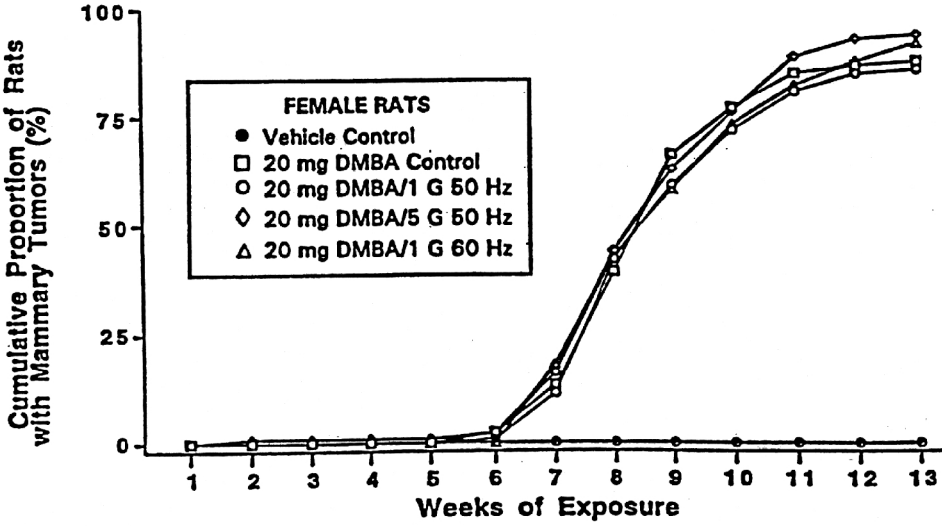


FIGURE 2
Cumulative Proportion of Rats with Palpable Mammary Gland Tumors During the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study

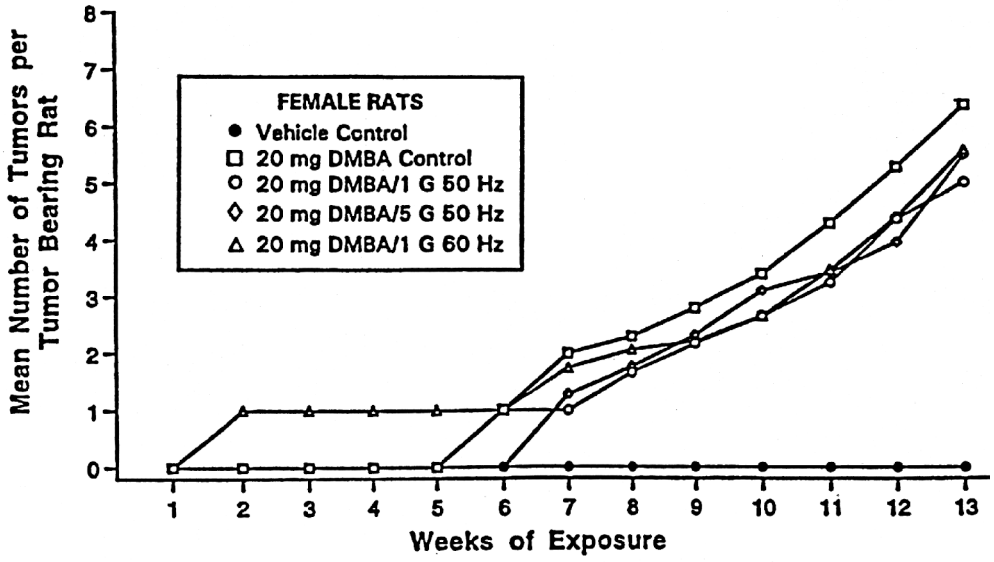


FIGURE 3
Mean Mammary Gland Tumors per Tumor-Bearing Rat During the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study

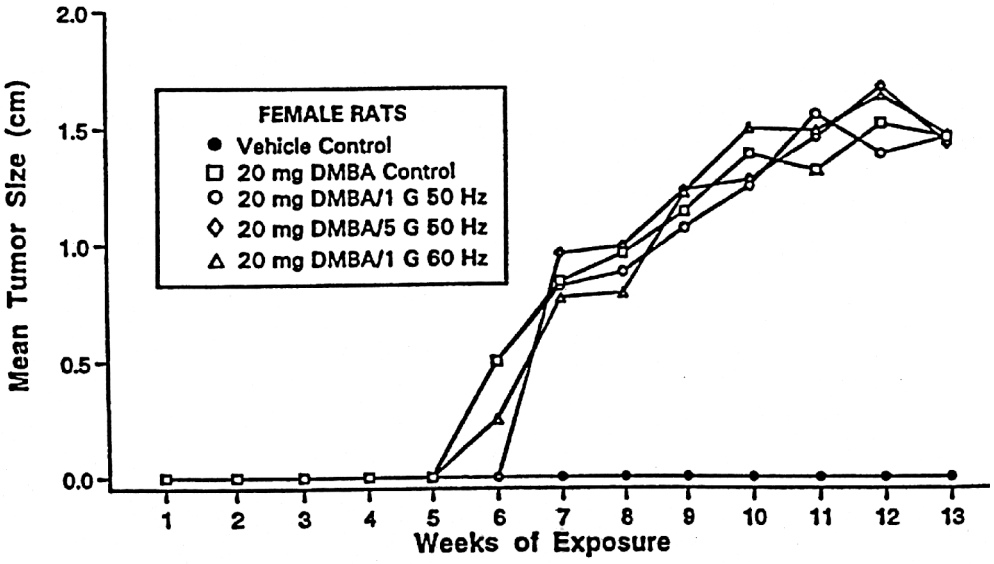


FIGURE 4
Mean Mammary Gland Tumor Size Estimated by Palpation During the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study

TABLE 3
Measurement of Mammary Gland Carcinomas Observed Grossly at Necropsy in Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
Number of carcinomas[b]	691	528	651	692
Carcinomas per animal[c]	6.91 ± 4.85	5.28[d] ± 4.37	6.51 ± 4.92	6.92 ± 4.82
Total carcinoma area (cm^2)	1,502.56	1,287.42	1,289.30	1,444.14
Mean area/carcinoma (cm^2)	2.17	2.44	1.98	2.09
Carcinoma area/animal[c]	15.03 ± 13.87	12.87 ± 12.51	12.89 ± 12.49	14.44 ± 10.68

[a] Animals were administered 5 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] Carcinomas observed at necropsy and confirmed histopathologically
[c] Data are presented as the mean ± standard deviation.
[d] $P < 0.05$ versus DMBA control by Dunnett's test

Organ Weights

Compared to the DMBA control group, no biologically significant differences in kidney or liver weights were observed in the DMBA/magnetic field groups (Table E1).

Pathology and Statistical Analyses

This section describes the incidences of neoplasms at sites of biological interest. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, and statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group are presented in Appendix A.

Mammary Gland: Compared to the vehicle controls (data not shown), markedly increased incidences of multiple mammary gland carcinomas were observed in all groups administered DMBA (Table 4). The incidences of multiple mammary gland carcinoma in the DMBA/magnetic field groups were similar to those in the DMBA control group. Fibroadenoma was observed in rats from each group, but the incidences in DMBA/magnetic field groups were similar to those in the DMBA control group. A small number of rats in groups administered DMBA developed hyperplasia of the mammary gland; however, the incidences in DMBA/magnetic field groups were similar to that in the DMBA control group. The carcinomas were often multiple, and in some animals more than 10 carcinomas were present. The carcinomas were solid to glandular neoplasms composed of deeply basophilic pleomorphic cells. There was usually nuclear crowding, and mitotic figures were often frequent. Even with very small lesions, the malignant nature was obvious. Distant metastases were rarely seen, even in advanced neoplasia. There was no evidence of a different pattern or occurrence of carcinomas in the DMBA/magnetic field groups relative to the DMBA controls. Fibroadenomas were similar to those forming spontaneously. They consisted of ductular or alveolar epithelium separated by dense collagen tissue. A few benign glandular tumors with scant tissue stroma were found and classified as adenoma. Hyperplasia of the glandular epithelium, found in a few rats, usually consisted of epithelium with some atypia, but not enough for the diagnosis of carcinoma.

The lung, liver, and kidney were examined for the presence of neoplasms, especially for the presence of metastatic mammary gland carcinoma. In each of the DMBA groups, a single animal was found with metastatic mammary gland carcinoma (Table A1). Single metastatic mammary gland carcinomas were found in the lung in the 1 G and 5 G 50-Hz groups, while the one found in the 1 G 60-Hz group was located in the liver. Two metastatic mammary gland carcinomas were found in the DMBA control group, one in the lung and one in the liver.

TABLE 4
Incidences of Neoplasms of the Mammary Gland in Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
Number Examined Microscopically	100	100	100	100
Hyperplasia[b]	4 (2.0)[c]	0	3 (1.7)	7 (2.3)
Adenoma	2	1	0	1
Carcinoma, Single	4	8	9	5
Carcinoma, Multiple	88	78	87	91
Carcinoma, Total	92	86	96	96
Fibroadenoma	3	2	1	1

[a] Animals were administered 5 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] Number of animals with lesion
[c] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

SECOND 13-WEEK STUDY

Survival

Except for one rat in the DMBA/5 G 50-Hz group, all rats survived until the end of the study (Table 5).

Body Weights and Clinical Findings

Mean body weights of DMBA/magnetic field groups were similar to those of the DMBA control group (Table 5 and Figure 5). Clinical findings attributed to DMBA administration included torso masses and ulcers. Magnetic field exposure neither enhanced nor suppressed these effects.

Melatonin Analyses

Pineal gland and serum melatonin concentrations of DMBA/magnetic field groups were similar to those of the DMBA control group at all time points (Tables D3 and D4). These data were highly variable, which hindered interpretation.

TABLE 5
Survival and Body Weights of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study

Treatment	Survival[a]	Mean Body Weight[b] (g)			Final Weight Relative to Controls (%)
		Initial	Final	Change	
8 mg DMBA Control[c]	100/100	179 ± 1	337 ± 3	159 ± 3	
8 mg DMBA/1 G 50 Hz	100/100	178 ± 1	336 ± 3	158 ± 3	100
8 mg DMBA/5 G 50 Hz	99/100[d]	178 ± 1	338 ± 4	160 ± 3	100

[a] Number of animals surviving at 13 weeks/number initially in group
[b] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study. Differences from the DMBA control group were not significant by Williams' or Dunnett's test.
[c] Animals were administered 2 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[d] Week of death: 12

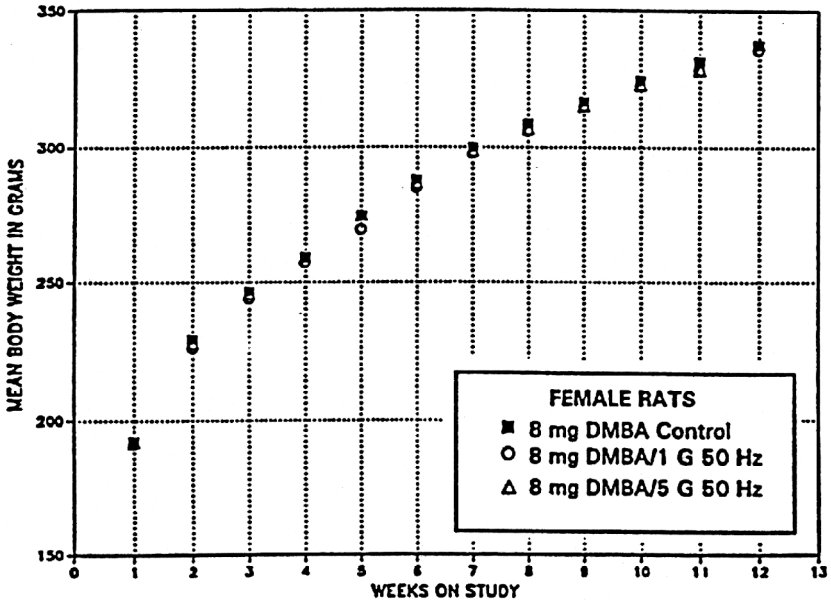


FIGURE 5
Growth Curves for Female Rats
in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/
Magnetic Field Promotion Study

Mammary Gland Tumor Palpation

Except for one tumor at week 2 in the DMBA control group, the first mammary gland tumors were detected by palpation at 5 to 6 weeks. The cumulative percentage of rats with palpable mammary gland tumors increased steadily between weeks 6 and 13 (Figure 6). Magnetic field exposure did not increase the number of animals with palpable mammary gland tumors compared to the DMBA control group. At necropsy, most palpated tumors were shown histologically to be mammary gland carcinomas, and additional tumors were found.

In DMBA/magnetic field groups, magnetic field exposure did not increase the number of mammary gland tumors per tumor-bearing rat relative to the DMBA control group (Figure 7), which averaged between 1.7 and 2 tumors per tumor-bearing rat. While additional mammary gland tumors were found at necropsy and confirmed histologically, the number of rats with tumors was similar to that found by palpation.

Mammary Gland Tumor Measurement

Mammary gland masses were measured in two directions at gross necropsy and assigned trace gross lesion identifiers so that the masses could be correlated with histologic diagnoses. The mean sizes of tumors in the DMBA/magnetic field groups were similar to those in the DMBA control group (Figure 8). The average areas of the carcinomas varied from 1.89 cm^2 in the DMBA control to 2.19 cm^2 in the DMBA/5 G 50-Hz group (Table 6). Neither the total carcinoma areas nor the mean areas per carcinoma differed significantly between DMBA/magnetic field and DMBA control groups.

Pathology and Statistical Analyses

This section describes the incidences of neoplasms and/or nonneoplastic lesions of the mammary gland; only the mammary gland and gross lesions were examined for the presence of neoplastic disease. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, and statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group are presented in Appendix B.

Mammary Gland: Mammary gland carcinomas and multiple carcinomas were observed in all groups of rats; however, the incidences in the DMBA/magnetic field groups were similar to those in the DMBA controls (Tables 7 and B3). None of the mammary gland carcinomas were metastatic. One DMBA/5 G 50-Hz rat was diagnosed with hyperplasia. These lesions were morphologically similar to those observed in the first 13-week study.

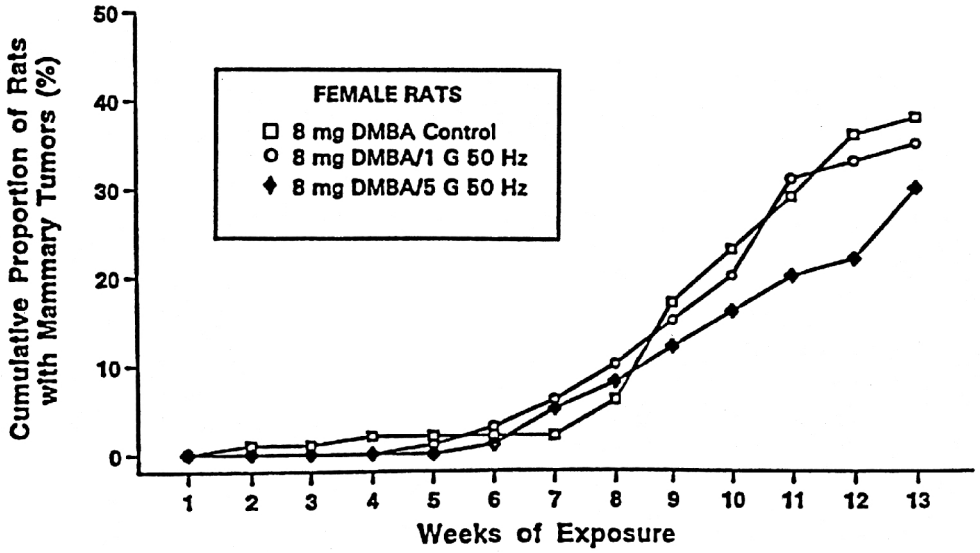


FIGURE 6
Cumulative Proportion of Rats with Palpable Mammary Gland Tumors During the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study

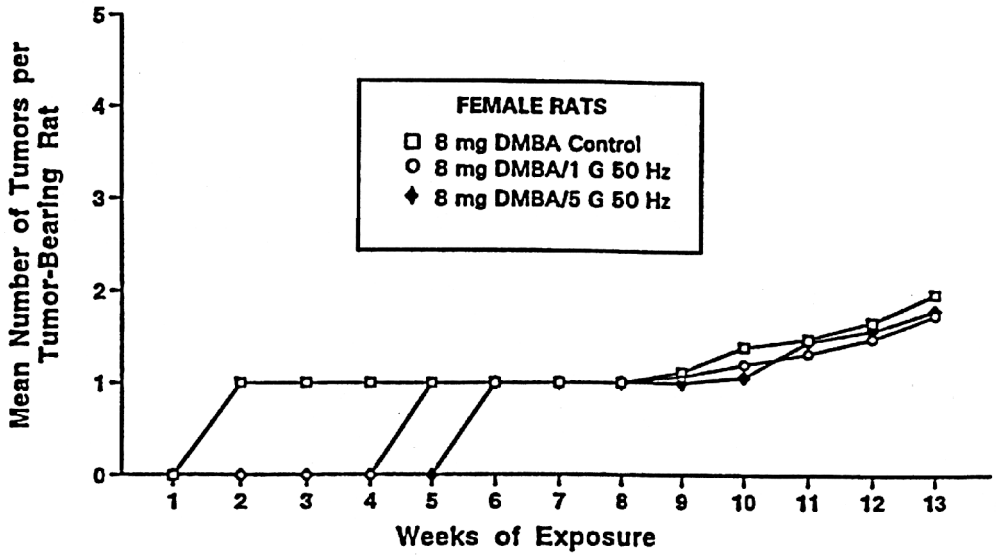


FIGURE 7
Mean Number of Mammary Gland Tumors per Tumor-Bearing Rat During the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study

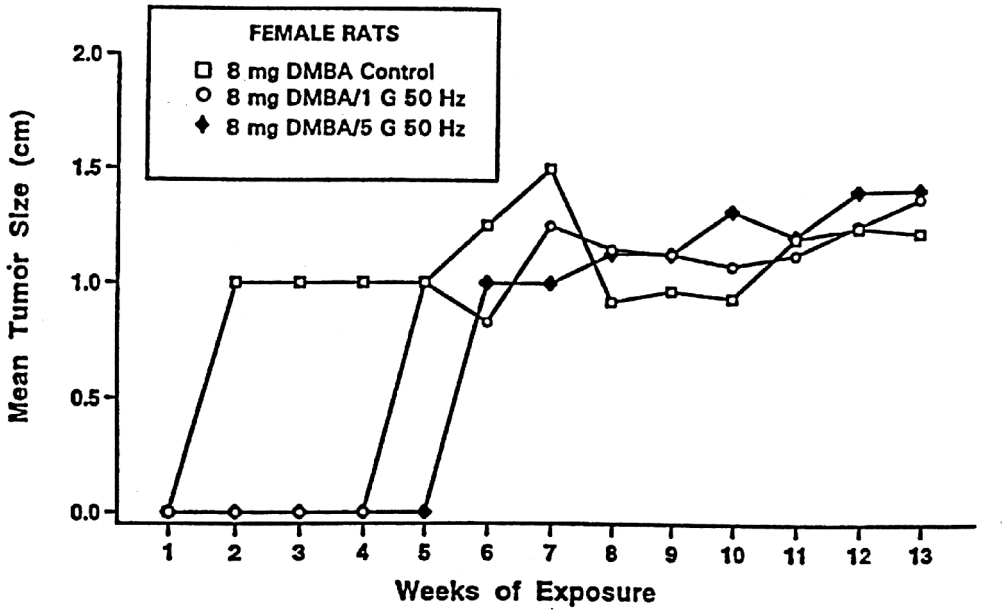


FIGURE 8
Mean Mammary Gland Tumor Size Estimated by Palpation During the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study

TABLE 6
Measurement of Mammary Gland Carcinomas Observed Grossly at Necropsy in Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study[a]

	8 mg DMBA Control	8 mg DMBA/ 1 G 50 Hz	8 mg DMBA/ 5 G 50 Hz
Number of carcinomas[b]	102	90	79
Carcinomas per animal[c]	1.02 ± 1.86	0.90 ± 1.27	0.79 ± 1.29
Total carcinoma area (cm^2)	192.53	184.53	173.06
Mean area/carcinoma (cm^2)	1.89	2.05	2.19
Carcinoma area/animal (cm^2)[c]	1.93 ± 4.68	1.85 ± 4.61	1.73 ± 4.77

[a] Animals were administered 2 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] Carcinomas observed at necropsy and confirmed histopathologically
[c] Data are presented as the mean ± standard deviation.

TABLE 7
Incidences of Neoplasms of the Mammary Gland in Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene Initiation (DMBA)/ Magnetic Field Promotion Study[a]

	8 mg DMBA Control	8 mg DMBA/ 1 G 50 Hz	8 mg DMBA/ 5 G 50 Hz
Number Examined Microscopically	100	100	100
Hyperplasia[b]	0	0	1 (2.0)[c]
Adenoma	0	0	1
Carcinoma, Single	20	24	15
Carcinoma, Multiple	23	24	23
Carcinoma, Total	43	48	38

[a] Animals were administered 2 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] Number of animals with lesion
[c] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

26-WEEK STUDY

Survival

All rats in the vehicle control group survived until the end of the study (Table 8). Twelve rats in the DMBA control group, 15 in the DMBA/1 G 50-Hz group, nine in the DMBA/5 G 50-Hz group, and six in the DMBA/1 G 60-Hz group died or were removed during the study mainly due to mammary gland tumors. Of these animals, one rat each in the DMBA control, DMBA/1 G 50 Hz, and DMBA/5 G 50-Hz groups and two DMBA/1 G 60-Hz rats had no masses at the time of death or moribund sacrifice.

Body Weights and Clinical Findings

The final mean body weights and body weight gains of the DMBA/1 G 50-Hz and DMBA/5 G 50-Hz groups were slightly, but significantly, greater than those of the DMBA control group (Table 8 and Figure 9). Clinical findings attributed to DMBA treatment included ruffled fur, torso masses, and torso ulcers or abscesses. Consistent differences between DMBA/magnetic field groups and the DMBA controls were not observed. There were no clinical findings in the vehicle control group except for one rat observed with tremors.

Melatonin Analyses

The pineal gland melatonin concentrations of DMBA/5 G 50-Hz and DMBA/1 G 60-Hz rats were significantly greater than those of the DMBA controls at week 12 (Table D5). Serum melatonin concentrations of DMBA/magnetic field groups were similar to those of the DMBA control group (Table D6). These data were highly variable within each group, which may preclude interpretation.

Mammary Gland Tumor Palpation

The first mammary gland tumors were detected by palpation at week 5. The cumulative percentage of rats with palpable mammary gland tumors increased steadily throughout the study (Figure 10). Mammary gland tumors were not detected in the vehicle control group except for one animal at week 22 (not noted on subsequent palpation) and two animals at week 26. Tumor incidences were similar among groups at all time points. At necropsy, the majority of palpated tumors were shown histologically to be mammary gland carcinomas and fibroadenomas; additional mammary gland tumors were found at necropsy. Magnetic field exposure had no effect on the mean number of mammary gland tumors per tumor-bearing rat relative to the DMBA controls (Figure 11). While additional mammary gland tumors were found at necropsy and confirmed histologically, the numbers of rats with tumors were similar to those found by palpation.

Mammary Gland Tumor Measurement

Mammary gland masses were measured in two directions at gross necropsy and assigned trace gross lesion identifiers so that the masses could be correlated with histologic diagnoses. Tumor sizes of DMBA/magnetic field groups were similar to those of the DMBA control group (Figure 12). The average areas of the carcinomas varied from 2.67 cm^2 in the DMBA control group to 3.32 cm^2 in the DMBA/5 G 50-Hz group (Table 9). The areas of the fibroadenomas varied from 1.14 cm^2 in the DMBA/1 G 50-Hz group to 1.34 cm^2 in the DMBA/5 G 50-Hz group. Neither the total carcinoma areas nor the mean areas per carcinoma differed significantly between DMBA/magnetic field and DMBA control groups.

TABLE 8
Survival and Body Weights of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Fields Promotion Study

Treatment[a]	Survival[b]	Mean Body Weight[c] (g)			Final Weight Relative to Controls (%)
		Initial	Final	Change	
Vehicle Control	100/100	177 ± 1	417 ± 6	241 ± 5	
10 mg DMBA Control	88/100[d]	176 ± 1	379 ± 5	203 ± 4	
10 mg DMBA/1 G 50 Hz	85/100[e]	175 ± 1	396 ± 5*	218 ± 5*	104
10 mg DMBA/5 G 50 Hz	91/100[f]	173 ± 1	400 ± 6**	228 ± 5**	106
10 mg DMBA/1 G 60 Hz	94/100[g]	173 ± 1	385 ± 5	212 ± 4	102

* Significantly different ($P \leq 0.05$) from the DMBA control group by Williams' or Dunnett's test
** $P \leq 0.01$
[a] Animals administered DMBA were given 10 mg on day 1 of the study.
[b] Number of animals surviving at 26 weeks/number initially in group
[c] Weights and weight changes are given as mean ± standard error. Subsequent calculations are based on animals surviving to the end of the study.
[d] Week of death: 13, 16, 17, 17, 20, 21, 22, 24, 25, 26, 26, 26
[e] Week of death: 13, 17, 17, 17, 19, 19, 19, 20, 23, 23, 24, 24, 24, 25, 26
[f] Week of death: 11, 13, 16, 20, 20, 24, 24, 25, 26
[g] Week of death: 11, 13, 22, 24, 24, 25

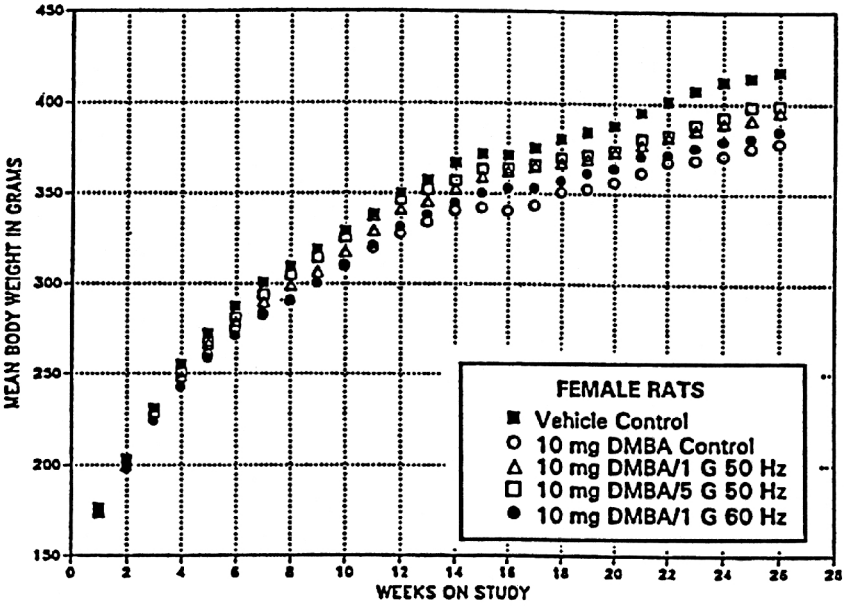


FIGURE 9
Growth Curves for Female Rats
in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/
Magnetic Field Promotion Study

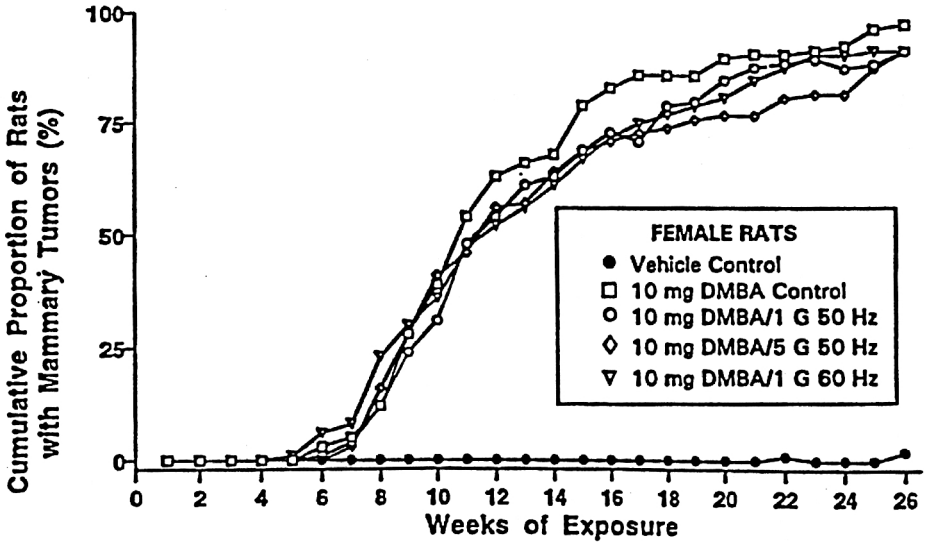


FIGURE 10
Cumulative Proportion of Rats with Palpable Mammary Gland Tumors During the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study

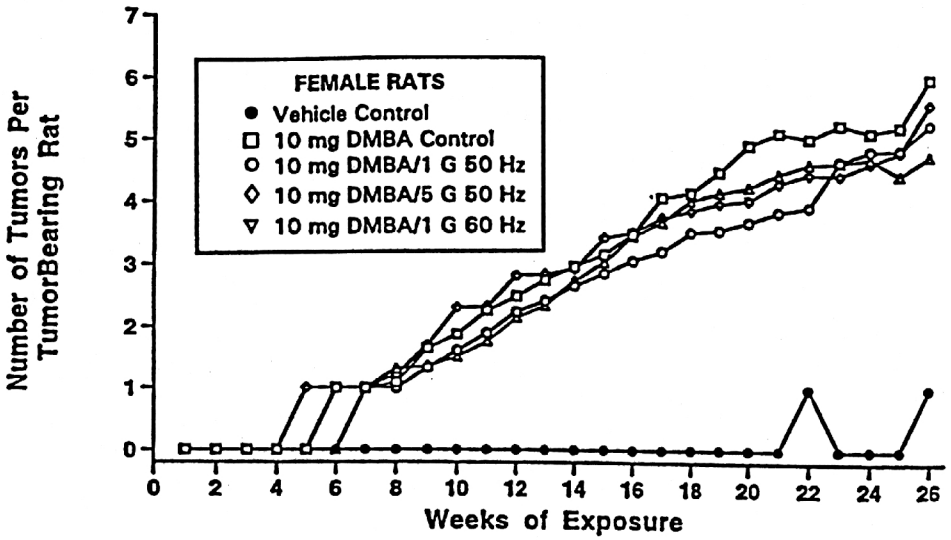


FIGURE 11
Mean Number of Mammary Gland Tumors per Tumor Bearing Rat During the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study

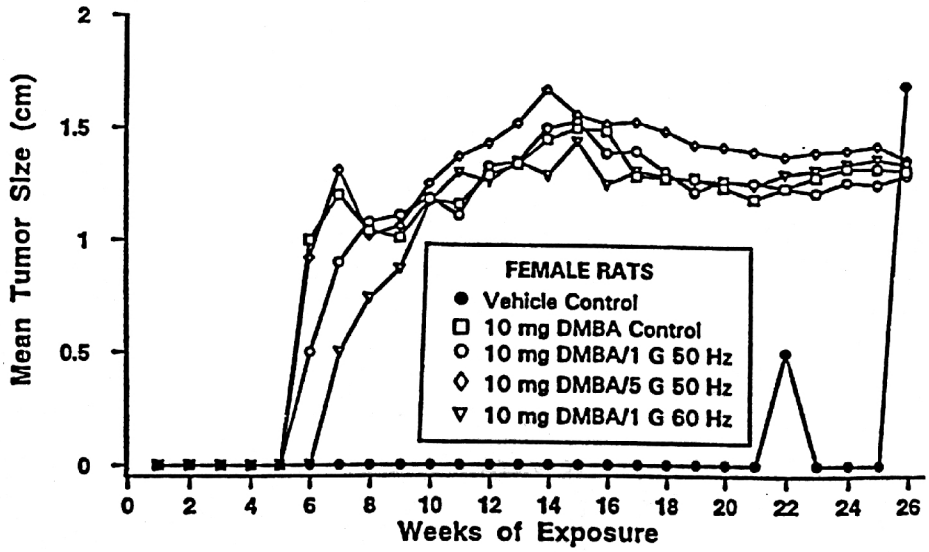


FIGURE 12
Mean Mammary Gland Tumor Size Estimated by Palpation During the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study

TABLE 9
Measurement of Mammary Gland Carcinomas and Fibroadenomas Observed Grossly at Necropsy in Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study[a]

	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
Number of carcinomas[b]	649	494	547	433
Carcinomas per animal[c]	6.49 ± 4.78	4.94[d] ± 4.19	5.47 ± 3.89	4.33[d] ± 3.89
Total carcinoma area (cm^2)	1,731.56	1,435.50	1,815.02	1,366.05
Mean area/carcinoma (cm^2)	2.67	2.91	3.32	3.15
Carcinoma area/animal (cm^2)[c]	17.32 ± 16.31	14.36 ± 16.58	18.15 ± 18.03	13.66 ± 18.13
Number of fibroadenomas	315	317	319	276
Total fibroadenoma area (cm^2)	391.07	361.60	426.57	321.21
Mean area/fibroadenoma (cm^2)	1.24	1.14	1.34	1.16

[a] Animals were administered 10 mg DMBA on day 1 of the study.
[b] Carcinomas observed at necropsy and confirmed histopathologically
[c] Data are presented as the mean ± standard deviation.
[d] $P < 0.05$ versus DMBA control by Dunnett's test

Organ Weights

Compared to the DMBA control group, no biologically significant differences in kidney or liver weights were observed in DMBA/magnetic field groups (Table E2).

Pathology and Statistical Analyses

This section describes the incidences of neoplasms and/or nonneoplastic lesions of the mammary gland and other organs. Summaries of the incidences of neoplasms and nonneoplastic lesions, individual animal tumor diagnoses, and statistical analyses of primary neoplasms that occurred with an incidence of at least 5% in at least one animal group are presented in Appendix C.

Mammary Gland: Mammary gland carcinomas and multiple carcinomas were observed in all groups, but the DMBA/magnetic field groups had consistently fewer mammary gland tumors than the DMBA controls (Tables 9 and 10). The incidences of carcinoma (including multiple) in the DMBA/1 G 60-Hz group were significantly decreased relative to the DMBA control group (Tables 10 and C3). Benign tumors included fibroadenoma and adenoma of the mammary gland. One DMBA control rat, one DMBA/1 G 50-Hz rat, and one DMBA/1 G 60-Hz rat had hyperplasia of the mammary gland.

The lung, liver and kidney were examined for the presence of neoplastic disease, especially for the presence of metastatic mammary gland carcinoma. Four DMBA control rats, four DMBA/1 G 50-Hz rats, one DMBA/5 G 50-Hz rat, and four DMBA/1 G 60-Hz rats had metastatic mammary gland carcinoma in the lung (Table C1). These lesions were morphologically similar to those observed in the 13-week studies.

TABLE 10
Incidences of Neoplasms of the Mammary Gland in Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
Number Examined Microscopically	100	100	100	100
Hyperplasia[b]	1 (1.0)[c]	1 (2.0)	0	1 (2.0)
Adenoma	2	0	0	0
Carcinoma, Single	7	16	16	15
Carcinoma, Multiple	89	74	79	70
Carcinoma, Total	96	90	95	85*
Fibroadenoma, Single	21	24	15	24
Fibroadenoma, Multiple	50	52	58	44
Fibroadenoma, Total	71	76	73	68

* Significantly different ($P \leq 0.05$) from the DMBA control group by the Poly-3 test
[a] Animals were administered 10 mg DMBA on day 1 of the study.
[b] Number of animals with lesion
[c] Average severity grade of lesions in affected animals: 1=minimal, 2=mild, 3=moderate, 4=marked

DISCUSSION AND CONCLUSIONS

These studies were undertaken as part of the Electromagnetic Fields Research and Public Information Dissemination (EMF *RAPID*) Program mandated by the United States Congress to determine if exposure to electric and magnetic fields poses a human health risk. Low-frequency magnetic fields have been reported to be associated with the promotion of chemically induced breast cancer in rats (Beniashvili *et al.*, 1991). Animals were exposed to nitrosomethyl urea to induce tumor growth and then to either static or 50-Hz alternating fields at a 200 mG field intensity for 0.5 or 3 hours per day for 2 years. Nitrosomethyl urea controls and rats exposed to magnetic fields for 30 minutes per day showed similar tumor rates. However, rats exposed for 3 hours per day either to 50-Hz fields or to static magnetic fields showed increased incidences of mammary gland tumors. In a series of studies, it was reported that magnetic field exposure enhanced tumor growth in female Sprague-Dawley rats initiated with 7,12-dimethylbenz(a)anthracene (DMBA) (Mevissen *et al.*, 1993; Löscher *et al.*, 1993, 1994; Löscher and Mevissen, 1994; Baum *et al.*, 1995); however, rats exposed to 3 or 10 mG magnetic fields failed to show the same tumor response (Mevissen *et al.*, 1993). Given the potential significance of even a small influence on the rate of breast cancer in women and the uncertain findings in rats, the NTP attempted to replicate this effect in the present studies.

Löscher *et al.* (1993, 1994) used a modified DMBA protocol whereby rats received a series of four weekly doses of 5 mg DMBA by gavage starting at 50 days of age, with magnetic field exposure starting after the first DMBA dose. This differs from the standard DMBA breast cancer protocols in which rats receive a single initiating dose of DMBA, usually 5 mg per rat (Welsch *et al.*, 1983, 1988), 10 mg per rat (Nakayama *et al.*, 1993), or 15 mg per rat (Tamarkin *et al.*, 1981). Many of the DMBA initiation/promotion protocols use a single initiating dose with a longer exposure time to demonstrate the promoting effect of the compound in question (Russo *et al.*, 1990); however, the goal was to replicate the studies of Löscher *et al.* (1993, 1994) as closely as possible.

The animals were continuously exposed to a dim red light at night, so this light exposure was included as part of the NTP study protocol. The intensities of the earth's static fields were also similar at the Löscher and NTP facilities. One difference between the two studies and the NTP studies was that the NTP studies were interrupted twice a day for animal care procedures; this resulted in 18.5 hours of magnetic field exposure per day instead of a continuous 24-hour exposure. Thus the total magnetic field exposure in the 13-week NTP studies was less than that of the Löscher studies, but the total exposure in the 26-week study exceeded that of Löscher.

In the first of two 13-week NTP studies, as expected, vehicle control rats survived for 13 weeks with no evidence of neoplasia. In contrast, in the DMBA-dosed animals, mammary gland tumors began to appear at 5 weeks and increased rapidly in incidence until approximately 90% of the rats in all groups had palpable mammary gland tumors, usually five to six tumors per tumor-bearing rat. This result is in contrast to the studies of Löscher and colleagues in which the first tumors appeared after 6 weeks of exposure and the DMBA controls had tumor incidences ranging from 34% to 60% (Mevissen *et al.*, 1993; Löscher *et al.*, 1993, 1994; Löscher and Mevissen, 1994; Baum *et al.*, 1995).

In the first 13-week NTP study, mammary gland carcinomas were found in 92/100 controls, in 86/100 rats exposed to 1 G 50-Hz magnetic fields, and in 96/100 rats exposed to 5 G 50-Hz magnetic fields. There were no significant differences in incidences between the DMBA/magnetic field groups and DMBA control group. There was also no evidence of earlier occurrence of mammary gland tumors, which was monitored by weekly palpations. The total number of tumors palpated per tumor-bearing rat was similar between exposure groups.

Thus, there was no evidence that magnetic field exposure was associated with an earlier onset of mammary gland carcinomas or an increased multiplicity of carcinomas. Magnetic field exposure did not affect the size of the carcinomas.

The very high incidences and multiplicity of mammary gland neoplasms in the first 13-week NTP study limited the sensitivity for detecting a promoting effect of magnetic fields. There is no obvious explanation for the difference in tumor incidence between the first 13-week study and the Löscher *et al.* (1993, 1994) studies. Although the strain of rat was the same, the outbred Sprague-Dawley rat from Exertal, Germany, may differ somewhat from Sprague-Dawley rats obtained from colonies held in Raleigh, North Carolina. The NTP used NIH-07 diet, a standard rodent chow, and the rats in the Löscher studies were fed Altromin, a standard rodent diet. While efforts were taken to replicate the Löscher studies as exactly as possible, the cancer rates were much higher in the NTP study. However, this effect was not entirely unanticipated because the results of many DMBA initiation/promotion studies in Sprague-Dawley rats suggest that 20 mg DMBA per rat was a large dose that might cause high tumor rates.

In light of these findings, the Department of Energy, a cooperating agency in this project, sponsored a dose-response study in which rats were administered weekly doses of 2 to 4 mg DMBA for four weeks starting at 50 days of age. From this study, it was predicted that 2 mg given weekly for four doses would replicate the 40% tumor incidence in DMBA controls (Dr. Imry Gyuk, Department of Energy, personal communication). Therefore, a second 13-week NTP study was conducted with a total dose of 8 mg DMBA per rat.

In the second 13-week study, the mammary gland carcinoma incidences were indeed much closer to 40%, with incidences of 43/100 in the DMBA control group, 48/100 in the 1 G 50-Hz group, and 38/100 in the 5 G 50-Hz group. Again, there was no difference in the time of appearance of tumors, in mean number of tumors, or in the overall tumor mass between groups.

A third mammary gland tumor study more similar to standard studies was conducted with a single initiating gavage dose of DMBA (10 mg) followed by 26 weeks of exposure to magnetic fields. The 26-week exposure allowed a greater period of time to detect any potential promotional effects of magnetic field exposure. There was no evidence of early onset of mammary gland tumors as a result of magnetic field exposure.

Throughout the NTP studies, there was a tendency for the various DMBA/magnetic field groups to have fewer, but slightly larger, mammary gland carcinomas than the DMBA controls (Tables 3, 6, and 9); however, none of the pairwise comparisons of total carcinoma area or mean area per carcinoma were statistically significant. The biological significance of this pattern of tumor response is unknown.

In mammary gland tumor initiation/promotion studies, tumor latency, tumor incidence, tumor size, and tumor multiplicity are all considered valid endpoints for the promotion process. In these three breast cancer promotion studies of magnetic fields at up to 5 G at both European (50-Hz) and United States (60-Hz) frequencies, no promotional effect by magnetic fields was found on any of the tumor parameters. If any trend was seen, it was for an increased number of tumors in the controls. This is in contrast to the studies by Löscher *et al.* (1993, 1994), who reported an earlier onset and larger size of tumors in animals exposed to magnetic fields.

In another DMBA initiation/promotion study, groups of 60 female Sprague-Dawley rats were administered a single gavage dose of 7 mg DMBA followed by exposure to 50-Hz magnetic fields at 0, 2.5, or 5 G for up to 25 weeks (Ekström *et al.*, 1998). One-hundred and eleven mammary gland tumors were found in the controls, 102 in the 2.5 G group, and 90 in the 5 G group. The number of tumors per tumor-bearing animal was 2.6 in the controls, 2.4 at 2.5 G, and 2.1 at 5 G. The total tumor weight was 150.4, 164.1, and 107.7 in the control, 2.5 G, and 5 G groups, respectively. The authors concluded that magnetic fields had no promotional effect on DMBA-induced tumors in the Sprague-Dawley rat.

If magnetic field exposures have some promotional effect on mammary gland tumors, these effects might also be seen in standard rodent studies. Therefore, the mammary gland data from three recent 2-year magnetic field studies were reviewed. In one study, groups of female F344 rats were exposed to 0, 0.02, 0.2, 2, or 20 G 60-Hz fields from day 20 of gestation through 2 years of life, and complete histology was

performed (Mandeville *et al.*, 1997). No mammary gland carcinomas were diagnosed. Incidences of fibroadenoma were 24/50, 22/50, 19/50, 19/50, and 17/50 in the control, 0.02, 0.2, 2, and 20 G 60-Hz groups of rats, respectively. The authors concluded that magnetic field exposure did not increase the incidence of mammary gland tumors in this study.

In a standard rodent study, male and female F344 rats were exposed to 50-Hz magnetic fields at 0, 5, or 50 G field intensities for up to 2 years beginning at 5 weeks at age (Yasui *et al.*, 1997). In male rats, the incidences of fibroadenoma were 3/48, 3/48, and 6/48 in the control, 5 G, and 50 G groups, respectively. No carcinomas were diagnosed in male rats, two mammary gland adenomas occurred in the control group, no neoplasms occurred in the 5 G 50-Hz group, and one mammary gland adenoma occurred in the 50 G 50-Hz group. In female rats, the incidences of fibroadenoma were 8/48, 6/48, and 6/48 in the control, 5 G, and 50 G groups, respectively. Two mammary gland carcinomas occurred in the 5 G group, two mammary gland adenomas were found in the control group, four mammary gland adenomas occurred in the 5 G group, and two mammary gland adenomas occurred in the 50 G female group. The authors concluded that there were no significant differences in mammary gland tumor incidences between the exposure groups.

The NTP also performed 2-year studies in which male and female F344/N rats and B6C3F$_1$ mice were exposed to continuous 0.02, 2, or 10 G or intermittent 10 G magnetic fields (NTP, 1999). In male mice, mammary gland tumors were not found in the 100 controls or in the 400 mice exposed to magnetic fields. In female mice, the incidences of mammary gland adenoma or carcinoma (combined) were 1/100, 0/100, 1/100, 2/100, and 2/100 for the control, continuous 0.02, 2, or 10 G, or 10 G intermittent groups, respectively. In male rats, the incidences of mammary gland fibroadenoma were 6/100, 6/100, 11/100, 9/100, and 8/100 for the same groups. Only one male rat (0.02 G group) was diagnosed with mammary gland carcinoma. In female rats, the incidences of mammary gland fibroadenoma (including multiple) were 56/100, 62/100, 54/100, 64/100, and 51/100, and the combined incidences of mammary gland adenoma or carcinoma were 3/100, 8/100, 6/100, 3/100, and 4/100.

Thus, the data from the NTP studies (NTP, 1999), the Mandeville *et al.* (1997) study, and the Yasui *et al.* (1997) study provide no support that magnetic fields can increase the incidence of mammary gland tumors in standard rodent studies.

CONCLUSIONS

In an initiation/promotion study in which female Sprague-Dawley rats were initiated by four weekly doses of 5 mg DMBA per rat beginning at 50 days of age and exposed to 50-Hz magnetic fields at 1 or 5 G field intensities or to 1 G 60-Hz magnetic fields for 13 weeks, there was no evidence that magnetic fields promoted the development of mammary gland neoplasms. The prevalence and multiplicity of mammary gland carcinomas in all DMBA groups limited the ability of this assay to detect a promoting effect of magnetic fields.

In an initiation/promotion study in which female Sprague-Dawley rats were initiated by four weekly doses of 2 mg DMBA per rat beginning at 50 days of age and exposed to 50-Hz magnetic fields at 1 or 5 G field intensities for 13 weeks, there was no evidence that magnetic fields promoted the development of mammary gland neoplasms.

In an initiation/promotion study in which female Sprague-Dawley rats were initiated by a single 10 mg DMBA dose at 50 days of age and then exposed to 50-Hz magnetic fields at 1 or 5 G field intensities or to 1 G 60-Hz magnetic fields for 26 weeks, there was no evidence that magnetic fields promoted the development of mammary gland neoplasms.

A summary of the Technical Reports Review Subcommittee comments and the public discussion on this Technical Report appears on pages 9.

REFERENCES

Adair, R.K. (1992). EMF research. *Science* **258**, 1868-1869.

The Aldrich Library of FT-IR Spectra (1985). 1st ed. (C.J. Pouchert, Ed.), Vol. 1., p. 966., Aldrich Chemical Company, Inc., Milwaukee, WI.

The Aldrich Library of ^{13}C and ^{1}H FT-NMR Spectra (1993). 1st ed., p. 54., Aldrich Chemical Company, Inc., Milwaukee, WI.

Anderson, L.E. (1993). Biological effects of extremely low-frequency electromagnetic fields: In vivo studies. *Am. Ind. Hyg. Assoc. J.* **54**, 186-196.

Antonopoulos, A., Yang, B., Stamm, A., Heller, W.-D., and Obe, G. (1995). Cytological effects of 50 Hz electromagnetic fields on human lymphocytes in vitro. *Mutat. Res.* **346**, 151-157.

Bailer, A.J., and Portier, C.J. (1988). Effects of treatment-induced mortality and tumor-induced mortality on tests for carcinogenicity in small samples. *Biometrics* **44**, 417-431.

Baum, A., Mevissen, M., Kamino, K., Mohr, U., and Löscher, W. (1995). A histopathological study on alterations in DMBA-induced mammary carcinogenesis in rats with 50 Hz, 100 μT magnetic field exposure. *Carcinogenesis* **16**, 119-125.

Beers, G.J. (1989). Biological effects of weak electromagnetic fields from 0 Hz to 200 Mhz: A survey of the literature with special emphasis on possible magnetic resonance effects. *Magn. Reson. Imaging* **7**, 309-331.

Bellossi, A. (1986). Effect of static magnetic fields on survival of leukaemia-prone AKR mice. *Radiat. Environ. Biophys.* **25**, 75-80.

Beniashvili, D.Sh., Bilanishvili, V.G., and Menabde, M.Z. (1991). Low-frequency electromagnetic radiation enhances the induction of rat mammary tumors by nitrosomethyl urea. *Cancer Lett.* **61**, 75-79.

Bieler, G.S., and Williams, R.L. (1993). Ratio estimates, the delta method, and quantal response tests for increased carcinogenicity. *Biometrics* **49**, 793-801.

Blank, M., and Goodman, R. (1997). Do electromagnetic fields interact directly with DNA? *Bioelectromagnetics* **18**, 111-115.

Blank, M., Soo, L., Lin, H., Henderson, A.S., and Goodman, R. (1992). Changes in transcription in HL-60 cells following exposure to alternating current from electric fields. *Bioelectrochem. Bioenerget.* **28**, 3001-3009.

Boorman, G.A., Montgomery, C.A., Jr., Eustis, S.L., Wolfe, M.J., McConnell, E.E., and Hardisty, J.F. (1985). Quality assurance in pathology for rodent carcinogenicity studies. In *Handbook of Carcinogen Testing* (H.A. Milman and E.K. Weisburger, Eds.), pp. 345-357. Noyes Publications, Park Ridge, NJ.

Boorman, G.A., Gauger, J.R., Johnson, T.R., Tomlinson, M.J., Findlay, J.C., Travlos, G.S., and McCormick, D.L. (1997). Eight-week toxicity study of 60 Hz magnetic fields in F344 rats and B6C3F1 mice. *Fundam. Appl. Toxicol.* **35**, 55-63.

Brent, R.L., Gordon, W.E., Bennett, W.R., and Beckman, D.A. (1993). Reproductive and teratologic effects of electromagnetic fields. *Reprod. Toxicol.* **7**, 535-580.

Cameron, I.L., Hunter, K.E., and Winters, W.D. (1985). Retardation of embryogenesis by extremely low frequency 60 Hz electromagnetic fields. *Physiol. Chem. Phys. Med. N.M.R.* **17**, 135-138.

Cameron, I.L., Hardman, W.E., Winters, W.D., Zimmerman, S., and Zimmerman, A.M. (1993). Environmental magnetic fields: Influences on early embryogenesis. *J. Cell. Biochem.* **51**, 417-425.

Chernoff, N., Rogers, J.M., and Kavet, R. (1992). A review of the literature on potential reproductive and developmental toxicity of electric and magnetic fields. *Toxicology* **74**, 91-126.

Code of Federal Regulations (CFR) **21**, Part 58.

Cohen, M.M., Kunska, A., Astemborski, J.A., and McCulloch, D. (1986a). The effect of low-level 60-Hz electromagnetic fields on human lymphoid cells. II. Sister-chromatid exchanges in peripheral lymphocytes and lymphoblastoid cell lines. *Mutat. Res*. **172**, 177-184.

Cohen, M.M., Kunska, A., Astemborski, J.A., McCulloch, D., and Paskewitz, D.A. (1986b). Effect of low-level 60-Hz electromagnetic fields on human lymphoid cells: I. Mitotic rate and chromosome breakage in human peripheral lymphocytes. *Bioelectromagnetics* **7**, 415-423.

Cox, D.R. (1972). Regression models and life-tables. *J. R. Stat. Soc.* **B34**, 187-220.

Cridland, N.A., Cragg, T.A., Haylock, R.G.E., and Saunders, R.D. (1996). Effects of 50 Hz magnetic field exposure on the rate of DNA synthesis by normal human fibroblasts. *Int. J. Radiat. Biol.* **69**, 503-511.

Delgado, J.M.R., Leal, J., Monteagudo, J.L., and Gracia, M.G. (1982). Embryological changes induced by weak, extremely low frequency electromagnetic fields. *J. Anat*. **134**, 533-551.

Dunnett, C.W. (1955). A multiple comparison procedure for comparing several treatments with a control. *J. Am. Stat. Assoc.* **50**, 1096-1121.

Eckert, E.E. (1992). Magnetic influences on fetus and infant as reason for sudden infant death syndrome: A new testable hypothesis. *Med. Hypotheses* **38**, 66-69.

Ekström, T., Mild, K.H., and Holmberg, B. (1998). Mammary tumours in Sprague-Dawley rats after initiation with DMBA followed by exposure to 50 Hz electromagnetic fields in a promotional scheme. *Cancer Lett.* **123**, 107-111.

Fairbairn, D.W., and O'Neill, K.L. (1994). The effect of electromagnetic field exposure on the formation of DNA single strand breaks in human cells. *Cell. Mol. Biol.* **40**, 561-567.

Feychting, M., and Ahlbom, A. (1993). Magnetic fields and cancer in children residing near Swedish high-voltage power lines. *Am. J. Epidemiol.* **138**, 467-481.

Feychting, M., and Ahlbom, A. (1995). Childhood leukemia and residential exposure to weak extremely low frequency magnetic fields. *Environ. Health Perspect.* **103**, 59-62.

Feychting, M., Kaune, W.T., Savitz, D.A., and Ahlbom, A. (1996). Estimating exposure in studies of residential magnetic fields and cancer: Importance of short-term variability, time interval between diagnosis and measurement, and distance to power line. *Epidemiology* **7**, 220-224.

Fiorio, R., Morichetti, E., Vellosi, R., and Bronzetti, G. (1993). Mutagenicity and toxicity of electromagnetic fields. *J. Environ. Pathol. Toxicol. Oncol*. **12**, 139-142.

Florig, H.K. (1992). EMF research: A response. *Science* **258**, 1869, 1960.

Frazier, M.E., Reese, J.A., Morris, J.E., Jostes, R.F., and Miller, D.L. (1990). Exposure of mammalian cells to 60-Hz magnetic or electric fields: Analysis of DNA repair of induced, single-strand breaks. *Bioelectromagnetics* **11**, 229-234.

Friedman, D.R., Hatch, E.E., Tarone, R., Kaune, W.T., Kleinerman, R.A., Wacholder, S., Boice, J.D., Jr., and Linet, M.S. (1996). Childhood exposure to magnetic fields: Residential area measurements compared to personal dosimetry. *Epidemiology* **7**, 151-155.

Gauger, J.R. (1985). Household appliance magnetic field survey. *IEEE Trans. Power Apparatus Syst.* **104**, 2436-2445.

Gilman, P.A., Ames, R.G., and McCawley, M.A. (1985). Leukemia risk among U.S. white male coal miners. A case-control study. *J. Occup. Med.* **27**, 669-671.

Gold, S., Goodman, R., and Shirley-Henderson, A. (1994). Exposure of simian virus-40-transformed human cells to magnetic fields results in increased levels of T-antigen mRNA and protein. *Bioelectromagnetics* **15**, 329-336.

Goodman, R., Wei, L.X., Bumann, J., and Shirley-Henderson, A. (1992). Exposure to electric and magnetic fields increases transcripts in HL-60 cells: Does adaptation to EM fields occur? *Bioelectrochem. Bioenerget*. **29**, 185-192.

Goodman, R., Bassett, C.A.L., and Henderson, A.S. (1994a). Pulsing electromagnetic fields induce cellular transcription. *Science* **220**, 1283-1285.

Goodman, R., Blank, M., Lin, H., Dai, R., Khorkova, O., Soo, L., Weisbrot, D., and Henderson, A. (1994b). Increased levels of hsp70 transcripts are induced when cells are exposed to low frequency electromagnetic fields. *Bioelectrochem. Bioenerget*. **33**, 115-120.

Graham, C., Cook, M.R., Riffle, D.W., Gerkovich, M.M., and Cohen, H.D. (1996). Nocturnal melatonin levels in human volunteers exposed to intermittent 60 Hz magnetic fields. *Bioelectromagnetics* **17**, 263-273.

Graham, C., Cook, M.R., and Riffle, D.W. (1997). Human melatonin during continuous magnetic field exposure. *Bioelectromagnetics* **18**, 166-171.

Grota, L.J., Reiter, R.J., Keng, P., and Michaelson, S. (1994). Electric field exposure alters serum melatonin but not pineal melatonin synthesis in male rats. *Bioelectromagnetics* **15**, 427-437.

Hollander, M., and Wolfe, D.A. (1973). *Nonparametric Statistical Methods*, pp. 120-123. John Wiley and Sons, New York.

Jauchem, J. (1993). Alleged health effects of electric or magnetic fields: Additional misconceptions in the literature. *J. Microw. Power Electromagn. Energy* **28**, 140-155.

Juutilainen, J., and Liimatainen, A. (1986). Mutation frequency in Salmonella exposed to weak 100-Hz magnetic fields. *Hereditas* **104**, 145-147.

Juutilainen, J., and Saali, K. (1986). Development of chick embryos in 1 Hz to 100 kHz magnetic fields. *Radiat. Environ. Biophys*. **25**, 135-140.

Kato, M., Honma, K., Shigemitsu, T., and Shiga, Y. (1994a). Circularly polarized 50-Hz magnetic field exposure reduces pineal gland and blood melatonin concentrations of Long-Evans rats. *Neurosci. Lett*. **166**, 59-62.

Kato, M., Honma, K., Shigemitsu, T., and Shiga, Y. (1994b). Horizontal or vertical 50-Hz, 1-μT magnetic fields have no effect on pineal gland or plasma melatonin concentration of albino rats. *Neurosci. Lett*. **168**, 205-208.

Kavet, R. (1996). EMF and current cancer concepts. *Bioelectromagnetics* **17**, 339-357.

Kavet, R.I., and Banks, R.S. (1986). Emerging issues in extremely-low-frequency electric and magnetic field health research. *Environ. Res*. **39**, 386-404.

Kerenyi, N.A., Pandula, E., and Feuer, G.M. (1990). Oncostatic effects of the pineal gland. *Drug Metabol. Drug Interact*. **8**, 313-319.

Kheifets, L.I., Kavet, R., and Sussman, S.S. (1997). Wire codes, magnetic fields, and childhood cancer. *Bioelectromagnetics* **18**, 99-110.

Koch, W.E., Koch, B.A., Martin, A.H., and Moses, G.C. (1993). Examination of the development of chicken embryos following exposure to magnetic fields. *Comp. Biochem. Physiol*. **105A**, 617-624.

Lacy-Hulbert, A., Wilkins, R.C., Hesketh, T.R., and Metcalfe, J.C. (1995). No effect of 60 Hz electromagnetic fields on *MYC* or ß-actin expression in human leukemic cells. *Radiat. Res*. **144**, 9-17.

Lerchl, A., Honaka, K.O., and Reiter, R.J. (1991). Pineal gland magnetosensitivity to static magnetic fields is a consequence of induced electric currents (eddy currents). *J. Pineal Res.* **10**, 109-116.

Libertin, C.R., Panozzo, J., Groh, K.R., Chang-Liu, C.M., Schreck, S., and Woloschak, G.E. (1994). Effects of gamma rays, ultraviolet radiation, sunlight, microwaves and electromagnetic fields on gene expression mediated by human immunodeficiency virus promoter. *Radiat. Res.* **140**, 91-96.

Liburdy, R.P., Sloma, T.R., Sokolic, R., and Yaswen, P. (1993). ELF magnetic fields, breast cancer, and melatonin: 60 Hz fields block melatonin's oncostatic action on ER^+ breast cancer cell proliferation. *J. Pineal Res.* **14**, 89-97.

Lin, H., Goodman, R., and Shirley-Henderson, A. (1994). Specific region of the c-*myc* promoter is responsive to electric and magnetic fields. *J. Cell. Biochem.* **54**, 281-288.

Lissoni, P., Barni, S., Cattaneo, G., Tancini, G., Esposti, G., Esposti, D., and Fraschini, F. (1991). Clinical results with the pineal hormone melatonin in advanced cancer resistant to standard antitumor therapies. *Oncology* **48**, 448-450.

Livingston, G.K., Witt, K.L., Gandhi, O.P., Chatterjee, I., and Roti Roti, J.L. (1991). Reproductive integrity of mammalian cells exposed to power frequency electromagnetic fields. *Environ. Mol. Mutagen.* **17**, 49-58.

Loomis, D.P., Savitz, D.A., and Ananth, C.V. (1994). Breast cancer mortality among female electrical workers in the United States. *J. Natl. Cancer Inst.* **86**, 921-925.

Löscher, W., and Mevissen, M. (1994). Animal studies on the role of 50/60-Hertz magnetic fields in carcinogenesis. *Life Sci.* **54**, 1531-1543.

Löscher, W., Mevissen, M., Lehmacher, W., and Stamm, A. (1993). Tumor promotion in a breast cancer model by exposure to a weak alternating magnetic field. *Cancer Lett.* **71**, 75-81.

Löscher, W., Wahnschaffe, U., Mevissen, M., Lerchl, A., and Stamm, A. (1994). Effects of weak alternating magnetic fields on nocturnal melatonin production and mammary carcinogenesis in rats. *Oncology* **51**, 288-295.

McCann, J., Dietrich, F., Rafferty, C., and Martin, A.O. (1993). A critical review of the genotoxic potential of electric and magnetic fields. *Mutat. Res.* **297**, 61-95.

McConnell, E.E., Solleveld, H.A., Swenberg, J.A., and Boorman, G.A. (1986). Guidelines for combining neoplasms for evaluation of rodent carcinogenesis studies. *JNCI* **76**, 283-289.

McLean, J.R.N., Stuchly, M.A., Mitchel, R.E.J., Wilkinson, D., Yang, H., Goddard, M., Lecuyer, D.W., Schunk, M., Callary, E., and Morrison, D. (1991). Cancer promotion in a mouse-skin model by a 60-Hz magnetic field: II. Tumor development and immune response. *Bioelectromagnetics* **12**, 273-287.

McLean, J.R.N., Thansandote, A., Lecuyer, D., and Goddard, M. (1997). The effect of 60-Hz magnetic fields on co-promotion of chemically induced skin tumors on SENCAR mice: A discussion of three studies. *Environ. Health Perspect.* **105**, 94-96.

Maffeo, S., Miller, M.W., and Carstensen, E.L. (1984). Lack of effect of weak low frequency electromagnetic fields on chick embryogenesis. *J. Anat.* **139**, 613-618.

Maffeo, S., Brayman, A.A., Miller, M.W., Carstensen, E.L., Ciaravino, V., and Cox, C. (1988). Weak low frequency electromagnetic fields and chick embryogenesis: Failure to reproduce positive findings. *J. Anat.* **157**, 101-104.

Mandeville, R., Franco, E., Sidrac-Ghali, S., Paris-Nadon, L., Rocheleau, N., Mercier, G., Desy, M., and Gaboury, L. (1997). Evaluation of the potential carcinogenicity of 60 Hz linear sinusoidal continuous-wave magnetic fields in Fischer F344 rats. *FASEB J.* **11**, 1127-1136.

Maronpot, R.R., and Boorman, G.A. (1982). Interpretation of rodent hepatocellular proliferative alterations and hepatocellular tumors in chemical safety assessment. *Toxicol. Pathol.* **10**, 71-80.

Martin, A.H. (1988). Magnetic fields and time dependent effects on development. *Bioelectromagnetics* **9**, 393-396.

Martin, A.H. (1992). Development of chicken embryos following exposure to 60-Hz magnetic fields with differing waveforms. *Bioelectromagnetics* **13**, 223-230.

Matanoski, G.M., Breysse, P.N., and Elliot, E.A. (1991). Electromagnetic field exposure and male breast cancer. *Lancet* **337**, 737.

Mevissen, M., Stamm, A., Buntenkötter, S., Zwingelberg, R., Wahnschaffe, U., and Löscher, W. (1993). Effects of magnetic fields on mammary tumor development induced by 7,12-dimethylbenz(a)anthracene in rats. *Bioelectromagnetics* **14**, 131-143.

Mevissen, M., Buntenkötter, S., and Löscher, W. (1994). Effects of static and time-varying (50-Hz) magnetic fields on reproduction and fetal development in rats. *Teratology* **50**, 229-237.

Mevissen, M., Kietzmann, M., and Löscher, W. (1995). In vivo exposure of rats to a weak alternating magnetic field increases ornithine decarboxylase activity in the mammary gland by a similar extent as the carcinogen DMBA. *Cancer Lett.* **90**, 207-214.

Miller, F., Jr., and Schroeer, D., Eds. (1987). *College Physics*, 6th ed. Harcourt Brace Jovanovich, San Diego.

Miyakoshi, J., Ohtsu, S., Shibata, T., and Takebe, H. (1996). Exposure to magnetic field (5 mT at 60 Hz) does not affect cell growth and c-myc gene expression. *J. Radiat. Res.* **37**, 185-191.

Moore, R.L. (1979). Biological effects of magnetic fields: Studies with microorganisms. *Can. J. Microbiol.* **25**, 1145-1151.

Morandi, M.A., Pak, C.M., Caren, R.P., and Caren, L.D. (1996). Lack of an EMF-induced genotoxic effect in the Ames assay. *Life Sci.* **59**, 263-271.

Murphy, J.C., Kaden, D.A., Warren, J., and Sivak, A. (1993). Power frequency electric and magnetic fields: A review of genetic toxicology. *Mutat. Res.* **296**, 221-240.

El Nahas, S.M., and Oraby, H.A. (1989). Micronuclei formation in somatic cells of mice exposed to 50-Hz electric fields. *Environ. Mol. Mutagen.* **13**, 107-111.

Nakayama, M., Ju, H.R., Sugano, M., Hirose, N., Ueki, T., Doi, F., and Eynard, A.R. (1993). Effect of dietary fat and cholesterol on dimethylbenz[a]-anthracene-induced mammary tumorigenesis in Sprague-Dawley rats. *Anticancer Res.* **13**, 691-698.

National Research Council (NRC) (1997). Possible health effects of exposure to residential electric and magnetic fields. 1st ed., National Academy Press, Washington, DC.

National Toxicology Program (NTP) (1996). 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. Toxicity Report Series No. 58. NIH Publication No. 96-3939. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Research Triangle Park, NC.

National Toxicology Program (NTP) (1999). Toxicology and Carcinogenesis Studies of 60-Hz Magnetic Fields in F344/N Rats and B6C3F$_1$ Mice (Whole-Body Exposure Studies). Technical Report Series No. 488. NIH Publication No. 99-3978. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Research Triangle Park, NC.

Nordenson, I., Hansson Mild, K., Nordström, S., Sweins, A., and Birke, E. (1984). Clastogenic effects in human lymphocytes of power frequency electric fields: In vivo and in vitro studies. *Radiat. Environ. Biophys.* **23**, 191-201.

Nordenson, I., Hansson Mild, K., Ostman, U., and Ljungberg, H. (1988). Chromosomal effects in lymphocytes of 400 kV-substation workers. *Radiat. Environ. Biophys.* **27**, 39-47.

Olcese, J., and Reuss, S. (1986). Magnetic field effects on pineal gland melatonin synthesis: Comparative studies on albino and pigmented rodents. *Brain Res.* **369**, 365-368.

Phillips, J.L. (1993). Effects of electromagnetic field exposure on gene transcription. *J. Cell. Biochem.* **51**, 381-386.

Piegorsch, W.W., and Bailer, A.J. (1997). *Statistics for Environmental Biology and Toxicology*, Section 6.3.2. Chapman and Hall, London.

Pino, A., Ricci, R., and Piombo, G. (1985). Absence of DNA damage in liver, spleen and kidney of rats after exposure to therapeutic magnetic fields. *IRCS Med. Sci*. **13**, 257-258.

Portier, C.J., and Bailer, A.J. (1989). Testing for increased carcinogenicity using a survival-adjusted quantal response test. *Fundam. Appl. Toxicol.* **12**, 731-737.

Portier, C.J., Hedges, J.C., and Hoel, D.G. (1986). Age-specific models of mortality and tumor onset for historical control animals in the National Toxicology Program's carcinogenicity experiments. *Cancer Res.* **46**, 4372-4378.

Rannug, A., Ekström, T., Hansson Mild, K., Holmberg, B., Gimenez-Conti, I., and Slaga, T.J. (1993a). A study on skin tumour formation in mice with 50 Hz magnetic field exposure. *Carcinogenesis* **14**, 573-578.

Rannug, A., Holmberg, B., Ekström, T., and Hansson Mild, K. (1993b). A rat liver foci study on coexposure with 50 Hz magnetic fields and known carcinogens. *Bioelectromagnetics* **14**, 17-27.

Rannug, A., Holmberg, B., and Hansson Mild, K. (1993c). A rat liver foci promotion study with 50-Hz magnetic fields. *Environ. Res.* **62**, 223-229.

Rannug, A., Holmberg, B., Ekström, T., Hansson Mild, K., Gimenez-Conti, I., and Slaga, T.J. (1994). Intermittent 50 Hz magnetic field and skin tumour promotion in SENCAR mice. *Carcinogenesis* **15**, 153-157.

Reese, J.A., Jostes, R.F., and Frazier, M.E. (1988). Exposure of mammalian cells to 60-Hz magnetic or electric fields: Analysis for DNA single-strand breaks. *Bioelectromagnetics* **9**, 237-247.

Reiter, R.J. (1992). Alterations of the circadian melatonin rhythm by the electromagnetic spectrum: A study in environmental toxicology. *Regul. Toxicol. Pharmacol*. **15**, 226-244.

Reiter, R.J. (1993). Electromagnetic fields and melatonin production. *Biomed. Pharmacother.* **47**, 439-444.

Rommereim, D.N., Rommereim, R.L., Miller, D.L., Buschbom, R.L., and Anderson, L.E.. (1996). Developmental toxicology evaluation of 60-Hz horizontal magnetic fields in rats. *Appl. Environ. Hyg*. **11**, 307-312.

Rosenthal, M., and Obe, G. (1989). Effects of 50-hertz electromagnetic fields on proliferation and on chromosomal alterations in human peripheral lymphocytes untreated or pretreated with chemical mutagens. *Mutat. Res.* **210**, 329-335.

Russo, J., Gusterson, B.A., Rogers, A.E., Russo, I.H., Wellings, S.R., and van Zweiten, M.J. (1990). Comparative study of human and rat mammary tumorigenesis. *Lab. Invest.* **62**, 244-278.

Ryan, B.M., Mallett, E., Jr., Johnson, T.R., Gauger, J.R., and McCormick, D.L. (1996). Developmental toxicity study of 60 Hz (power frequency) magnetic fields in rats. *Teratology* **54**, 73-83.

Saffer, J.D., and Thurston, S.J. (1995). Short exposures to 60 Hz magnetic fields do not alter *MYC* expression in HL60 or Daudi cells. *Radiat. Res*. **144**, 18-25.

Savitz, D.A., and Loomis, D.P. (1995). Magnetic field exposure in relation to leukemia and brain cancer mortality among electric utility workers. *Am. J. Epidemiol.* **141**, 123-134.

Savitz, D.A., Wachtel, H., Barnes, F.A., John, E.M., and Tvrdik, J.G. (1988). Case-control study of childhood cancer and exposure to 60-Hz magnetic fields. *Am. J. Epidemiol.* **128**, 21-38.

Scarfi, M.R., Bersani, F., Cossarizza, A., Monti, D., Castellani, G., Cadossi, R., Franceschetti, G., and Franceschi, C. (1991). Spontaneous and mitomycin-C-induced micronuclei in human lymphocytes exposed to extremely low frequency pulsed magnetic fields. *Biochem. Biophys. Res. Commun.* **176**, 194-200.

Scarfi, M.R., Lioi, M.B., Zeni, O., Franceschetti, G., Franceschi, C., and Bersani, F. (1994). Lack of chromosomal aberration and micronucleus induction in human lymphocytes exposed to pulsed magnetic fields. *Mutat. Res*. **306**, 129-133.

Shimizu, H., Akiyama, M., Suzuki, Y., and Hayashi, K. (1989). The effects of magnetic field on mutagenic activity. *Mutat. Res*. **216**, 377.

Stevens, R.G. (1994). Re: Magnetic fields and cancer in children residing near Swedish high-voltage power lines. *Am. J. Epidemiol*. **140**, 75.

Stevens, R.G., Davis, S., Thomas, D.B., Anderson, L.E., and Wilson, B.W. (1992). Electric power, pineal function, and the risk of breast cancer. *FASEB J*. **6**, 853-860.

Stuchly, M.A., McLean, J.R.N., Burnett, R., Goddard, M., Lecuyer, D.W., and Mitchel, R.E.J. (1992). Modification of tumor promotion in the mouse skin by exposure to an alternating magnetic field. *Cancer Lett*. **65**, 1-7.

Suri, A., deBoer, J., Kusser, W., and Glickman, B.W. (1996). A 3 milliTesla 60 Hz magnetic field is neither mutagenic nor co-mutagenic in the presence of menadione and MNU in a transgenic rat cell line. *Mutat. Res*. **372**, 23-31.

Tamarkin, L., Cohen, M., Roselle, D., Reichert, C., Lippman, M., and Chabner, B. (1981). Melatonin inhibition and pinealectomy enhancement of 7,12-diemthylbenz(a)anthracene-induced mammary tumors in the rat. *Cancer Res*. **41**, 4432-4436.

Tarone, R.E. (1975). Tests for trend in life table analysis. *Biometrika* **62**, 679-682.

Thériault, G., Goldberg, M., Miller, A.B., Armstrong, B., Guénel, P., Deadman, J., Imbernon, E., To, T., Chevalier, A., Cyr, D., and Wall, C. (1994). Cancer risks associated with occupational exposure to magnetic fields among electric utility workers in Ontario and Quebec, Canada, and France: 1970-1989. *Am. J. Epidemiol*. **139**, 550-572.

Thomas, A., and Morris, P.G. (1981). The effects of NMR exposure on living organisms. I. A microbial assay. *Br. J. Radiol*. **54**, 615-621.

Truong, H., Smith, J.C., and Yellon, S.M. (1996). Photoperiod control of the melatonin rhythm and reproductive maturation in the juvenile Djungarian hamster: 60-Hz magnetic field exposure effects. *Biol. Reprod*. **55**, 455-460.

Tynes, T. (1993). Electromagnetic fields and male breast cancer. *Biomed. Pharmacother*. **47**, 425-427.

Wei, L.-X., Goodman, R., and Henderson, A. (1990). Changes in levels of c-*myc* and histone H2B following exposure of cells to low-frequency sinusoidal electromagnetic fields: Evidence for a window effect. *Bioelectromagnetics* **11**, 269-272.

Welsch, C.W., Scieszka, K.M., Senn, E.R., and DeHoog, J.V. (1983). Caffeine (1,3,7-trimethylxanthine), a temperature promoter of DMBA-induced rat mammary gland carcinogenesis. *Int. J. Cancer* **32**, 479-484.

Welsch, C.W., DeHoog, J.V., and O'Conner, D.H. (1988). Influence of caffeine and/or coffee consumption on the initiation and promotion phases of 7,12-dimethylbenz(a)anthracene-induced rat mammary gland tumorigenesis. *Cancer Res*. **48**, 2068-2073.

Wertheimer, N., and Leeper, E. (1979). Electrical wiring configurations and childhood cancer. *Am. J. Epidemiol*. **109**, 273-284.

Whitson, G.L., Carrier, W.L., Francis, A.A., Shih, C.C., Georghiou, S., and Regan, J.D. (1986). Effects of extremely low frequency (ELF) electric fields on cell growth and DNA repair in human skin fibroblasts. *Cell Tissue Kinet*. **19**, 39-47.

Williams, D.A. (1971). A test for differences between treatment means when several dose levels are compared with a zero dose control. *Biometrics* **27**, 103-117.

Williams, D.A. (1972). The comparison of several dose levels with a zero dose control. *Biometrics* **28**, 519-531.

Wilson, B.W., Chess, E.K., and Anderson, L.E. (1986). 60-Hz electric-field effects on pineal melatonin rhythms: Time course for onset and recovery. *Bioelectromagnetics* **7**, 239-242.

Wilson, B.W., Stevens, R.G., and Anderson, L.E. (1989). Neuroendocrine mediated effects of electromagnetic-field exposure: Possible role of the pineal gland. *Life Sci.* **45**, 1319-1332.

Wolff, S., Crooks, L.E., Brown, P., Howard, R., and Painter, R.B. (1980). Tests for DNA and chromosomal damage induced by nuclear magnetic resonance imaging. *Radiology* **136**, 707-710.

Yasui, M., Kikuchi, T., Ogawa, M., Otaka, Y., Tsuchitani, M., and Iwata, H. (1997). Carcinogenicity test of 50 Hz sinusoidal magnetic fields in rats. *Bioelectromagnetics* **18**, 531-540.

Yellon, S.M. (1996). 60-Hz magnetic field exposure effects on the melatonin rhythm and photoperiod control of reproduction. *Am. J. Physiol.* **270**, E816-E821.

APPENDIX A
SUMMARY OF LESIONS IN FEMALE RATS IN THE FIRST 13-WEEK 7,12-DIMETHYLBENZ(A)ANTHRACENE INITIATION/ MAGNETIC FIELD PROMOTION STUDY

TABLE A1
Summary of the Incidence of Neoplasms in Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
Disposition Summary				
Animals initially in study	100	100	100	100
Early deaths				
Moribund	3	7	4	3
Natural deaths	3	6	4	2
Survivors				
Died last week of study	1	1		1
Terminal sacrifice	93	86	92	94
Animals examined microscopically	100	100	100	100
Alimentary System				
Liver	(100)	(100)	(100)	(100)
Carcinoma, metastatic, mammary gland	1 (1%)			1 (1%)
Cardiovascular System				
None				
Endocrine System				
None				
General Body System				
None				
Genital System				
None				
Hematopoietic System				
Lymph node	(2)	(2)		
Integumentary System				
Mammary gland	(100)	(100)	(100)	(100)
Adenoma	2 (2%)	1 (1%)		1 (1%)
Carcinoma	4 (4%)	8 (8%)	9 (9%)	5 (5%)
Carcinoma, multiple	88 (88%)	78 (78%)	87 (87%)	91 (91%)
Carcinoma, metastatic, Zymbal's gland				1 (1%)
Fibroadenoma	3 (3%)	2 (2%)	1 (1%)	1 (1%)
Musculoskeletal System				
None				
Nervous System				
None				

TABLE A1
Summary of the Incidence of Neoplasms in Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study

	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
Respiratory System				
Lung	(100)	(100)	(100)	(100)
Carcinoma, metastatic, mammary gland	1 (1%)	1 (1%)	1 (1%)	
Special Senses System				
None				
Urinary System				
Kidney	(100)	(100)	(100)	(100)
Systemic Lesions				
Multiple organs[b]	(100)	(100)	(100)	(100)
Leukemia mononuclear	15 (15%)	16 (16%)	10 (10%)	12 (12%)
Neoplasm Summary				
Total animals with primary neoplasms[c]	94	92	96	96
Total primary neoplasms	120	109	114	115
Total animals with benign neoplasms	5	3	1	2
Total benign neoplasms	5	3	1	2
Total animals with malignant neoplasms	93	92	96	96
Total malignant neoplasms	115	106	113	113
Total animals with metastatic neoplasms	1	1	1	2
Total metastatic neoplasms	2	1	1	2

[a] Number of animals examined microscopically at the site and the number of animals with neoplasm; animals were administered 5 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]: 20 mg DMBA Control

Number of Days on Study	058	072	072	073	075	089	090	090	090	090	090	090	090	090	090	090	090	090	090	090	090	090	090	090	090
Carcass ID Number	579	538	580	518	541	503	509	510	511	512	542	543	544	553	554	555	556	560	589	590	591	592	593	594	595
Alimentary System																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland									X																
Cardiovascular System																									
None																									
Endocrine System																									
Adrenal cortex																									
General Body System																									
None																									
Genital System																									
None																									
Hematopoietic System																									
Lymph node																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma					X																				
Carcinoma, multiple		X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Fibroadenoma																									X
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland									X																
Trachea		+																							
Special Senses System																									
None																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X		X	X	X			X	X							X		X							

[a] Animals were administered 5 mg DMBA at the beginning of weeks 1, 2, 3, and 4.

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA Control

Number of Days on Study	0 9 0	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 2	0 9 2	0 9 2	0 9 2
Carcass ID Number	5 5 9 6	5 0 5	5 0 0 6	5 0 0 7	5 0 0 8	5 2 1	5 2 2 2	5 2 2 3	5 2 2 4	5 2 2 5	5 2 2 6	5 2 2 7	5 2 2 8	5 8 1	5 8 2	5 8 3	5 8 4	5 9 7	5 9 8	5 9 9	6 0 0	5 3 7	5 3 9	5 4 0	5 4 9
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																										
Cardiovascular System																										
None																										
Endocrine System																										
Adrenal cortex																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
Lymph node																					+					
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																					X					
Carcinoma					X																					
Carcinoma, multiple	X	X	X	X		X	X	X	X	X	X		X	X	X	X	X	X			X	X	X	X	X	
Fibroadenoma									X																	
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																										
Trachea																										
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																		X			X				X	

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA Control

Number of Days on Study	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3
Carcass ID Number	5 5 0	5 5 1	5 5 2	5 6 1	5 6 2	5 6 3	5 6 4	5 6 5	5 6 6	5 6 7	5 6 8	5 7 3	5 7 4	5 7 5	5 7 6	5 0 1	5 0 2	5 0 4	5 2 9	5 3 0	5 3 1	5 3 2	5 3 3	5 3 4	5 3 5
Alimentary System																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																									
Cardiovascular System																									
None																									
Endocrine System																									
Adrenal cortex																									
General Body System																									
None																									
Genital System																									
None																									
Hematopoietic System																									
Lymph node					+																				
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma								X																	
Carcinoma, multiple		X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X	X		X	X
Fibroadenoma													X												
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																									
Trachea																									
Special Senses System																									
None																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear		X			X													X							

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA Control

Number of Days on Study	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	
Carcass ID Number	5 3 6	5 6 9	5 7 0	5 7 1	5 7 2	5 7 7	5 7 8	5 1 3	5 1 4	5 1 5	5 1 6	5 1 7	5 1 9	5 2 0	5 4 5	5 4 6	5 4 7	5 4 8	5 5 7	5 5 8	5 5 9	5 8 5	5 8 6	5 8 7	5 8 8	Total Tissues/ Tumors
Alimentary System																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma, metastatic, mammary gland																											1
Cardiovascular System																											
None																											
Endocrine System																											
Adrenal cortex			+																								1
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
Lymph node																											2
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Adenoma																			X								2
Carcinoma								X																			4
Carcinoma, multiple	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	88
Fibroadenoma																											3
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma, metastatic, mammary gland																											1
Trachea																											1
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Leukemia mononuclear					X																						15

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA Control/1 G 50 Hz

Number of Days on Study	0 4 9	0 6 6	0 6 6	0 7 2	0 7 3	0 7 5	0 8 1	0 8 1	0 8 1	0 8 2	0 8 2	0 8 4	0 8 4	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0
Carcass ID Number	7 2 7	7 2 5	7 9 1	7 9 8	7 6 4	7 0 3	7 3 6	7 4 0	7 4 4	7 1 6	7 6 9	7 1 7	7 9 2	7 0 9	7 1 0	7 1 1	7 1 2	7 1 8	7 1 9	7 2 0	7 2 9	7 3 0	7 3 1	7 3 2	7 3 3		
Alimentary System																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
Lymph node						+						+															
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma																											
Carcinoma														X	X	X											
Carcinoma, multiple					X	X	X	X	X	X	X								X	X	X	X	X	X	X		
Fibroadenoma																											
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, metastatic, mammary gland																											
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leukemia mononuclear	X	X	X	X	X	X	X				X	X	X														

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA Control/1 G 50 Hz

Number of Days on Study	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 2	0 9 2
Carcass ID Number	7 7 4	7 7 5	7 7 6	7 8 1	7 8 2	7 8 3	7 8 4	7 0 5	7 0 6	7 0 7	7 0 8	7 3 3	7 3 4	7 3 5	7 8 9	7 9 0	7 9 3	7 9 4	7 9 5	7 9 6	7 9 7	7 9 9	8 0 0	7 2 6	7 2 8
Alimentary System																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
Lymph node																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																											
Carcinoma																											
Carcinoma, multiple	X	X		X	X	X	X	X	X		X	X	X	X	X	X	X		X	X	X	X	X		X		
Fibroadenoma												X															
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland											X																
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																											

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA Control/1 G 50 Hz

Number of Days on Study	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3
Carcass ID Number	7 4 1	7 4 2	7 4 3	7 4 5	7 4 6	7 4 7	7 4 8	7 5 7	7 5 8	7 5 9	7 6 0	7 6 1	7 6 2	7 6 3	7 0 1	7 0 2	7 0 4	7 2 1	7 2 2	7 2 3	7 2 4	7 4 9	7 5 0	7 5 1	7 5 2
Alimentary System																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
None																									
Endocrine System																									
None																									
General Body System																									
None																									
Genital System																									
None																									
Hematopoietic System																									
Lymph node																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma					X							X							X						
Carcinoma, multiple	X	X	X	X		X	X	X	X	X	X		X	X	X	X	X	X		X	X	X	X	X	X
Fibroadenoma																									
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																									
Special Senses System																									
None																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X						X	X							X							X			

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA Control/1 G 50 Hz

Number of Days on Study	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	
Carcass ID Number	7 5 3	7 5 4	7 5 5	7 5 6	7 7 0	7 8 5	7 8 6	7 8 7	7 8 8	7 1 3	7 1 4	7 1 5	7 3 7	7 3 8	7 3 9	7 6 5	7 6 6	7 6 7	7 6 8	7 7 1	7 7 2	7 7 7	7 7 8	7 7 9	7 8 0	Total Tissues/ Tumors
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
Lymph node																										2
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Adenoma																X										1
Carcinoma												X													X	8
Carcinoma, multiple	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X		X	X	X		X		78
Fibroadenoma												X														2
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma, metastatic, mammary gland																										1
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Leukemia mononuclear										X																16

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA/5 G 50 Hz

Number of Days on Study	0 5 9	0 6 5	0 7 0	0 7 7	0 7 7	0 7 9	0 7 9	0 8 4	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0	0 9 0
Carcass ID Number	9 0 2	9 0 1	9 8 5	9 4 8	9 6 0	9 8 7	9 8 8	9 4 0	9 2 5	9 2 6	9 2 7	9 2 8	9 3 3	9 3 4	9 3 5	9 3 6	9 5 7	9 5 8	9 5 9	9 6 1	9 6 2	9 6 3	9 6 4	9 8 9	9 9 0		
Alimentary System																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Carcinoma		X													X												
Carcinoma, multiple			X	X	X	X	X	X	X		X	X	X	X		X	X	X	X	X	X	X	X	X	X		
Fibroadenoma																									X		
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Carcinoma, metastatic, mammary gland				X																							
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Leukemia mononuclear		X	X	X		X	X																	X			

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA/5 G 50 Hz

Number of Days on Study	0 9 0	0 9 0	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2
Carcass ID Number	9 9 1	9 9 2	9 0 3	9 0 4	9 1 7	9 1 8	9 1 9	9 2 0	9 5 3	9 5 4	9 5 5	9 5 6	9 8 1	9 8 2	9 8 3	9 8 4	9 8 6	9 2 1	9 2 2	9 2 3	9 2 4	9 4 9	9 5 0	9 5 1	9 5 2		
Alimentary System																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Carcinoma						X			X				X			X											
Carcinoma, multiple	X	X	X	X	X		X	X		X	X	X		X	X		X	X	X	X	X	X	X	X	X		
Fibroadenoma																											
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Carcinoma, metastatic, mammary gland																											
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Leukemia mononuclear													X											X	X		

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA/5 G 50 Hz

Number of Days on Study	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3
Carcass ID Number	9 6 9	9 7 0	9 7 1	9 7 2	9 7 7	9 7 8	9 7 9	9 8 0	9 9 7	9 9 8	9 9 9	0 0 0	9 0 5	9 0 6	9 0 7	9 0 8	9 0 9	9 1 0	9 1 1	9 1 2	9 4 1	9 4 2	9 4 3	9 4 4	9 4 3	9 7 3
Alimentary System																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma										X								X									
Carcinoma, multiple	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X			X	X	X	X	X	X	X	X	
Fibroadenoma																											
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, metastatic, mammary gland																											
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leukemia mononuclear																											

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA/5 G 50 Hz

Number of Days on Study	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	
Carcass ID Number	9 7 4	9 7 5	9 7 6	9 9 3	9 9 4	9 9 5	9 9 6	9 1 3	9 1 4	9 1 5	9 1 6	9 2 9	9 3 0	9 3 1	9 3 2	9 3 7	9 3 8	9 3 9	9 4 5	9 4 6	9 4 7	9 6 5	9 6 6	9 6 7	9 6 8	Total Tissues/ Tumors
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
None																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma																								X		9
Carcinoma, multiple	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X		X	X	X	X	X		X	87
Fibroadenoma																										1
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma, metastatic, mammary gland																										1
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Leukemia mononuclear														X												10

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA/1 G 60 Hz

	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Number of Days on Study	6	7	8	8	8	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9	9
	4	0	0	4	9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Carcass ID Number	0	3	1	7	6	1	1	1	2	4	4	4	4	6	6	6	6	7	7	7	8	8	8	8	8
	5	3	6	3	9	7	8	9	0	5	6	7	8	5	6	7	8	7	8	9	0	5	6	7	8
Alimentary System																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																									
Cardiovascular System																									
None																									
Endocrine System																									
None																									
General Body System																									
None																									
Genital System																									
None																									
Hematopoietic System																									
None																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																	X								
Carcinoma										X															
Carcinoma, multiple	X	X	X	X	X	X	X	X	X			X	X	X	X	X	X		X	X	X	X	X	X	X
Carcinoma, metastatic, Zymbal's gland					X																				
Fibroadenoma																			X						
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
None																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X		X								X										X

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA/1 G 60 Hz

Number of Days on Study	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 1	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2
Carcass ID Number	8 1 3	8 1 4	8 1 5	8 3 4	8 3 5	8 3 6	8 6 1	8 6 2	8 6 3	8 6 4	8 7 0	8 7 1	8 7 2	8 9 3	8 9 4	8 9 5	8 9 6	8 9 9	8 0 1 0	8 1 1	8 1 2	8 2 1	8 2 2	8 2 3	8 2 4	
Alimentary System																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, metastatic, mammary gland																				X							
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma																											
Carcinoma							X																				
Carcinoma, multiple	X	X	X	X	X	X		X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Carcinoma, metastatic, Zymbal's gland																											
Fibroadenoma																											
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leukemia mononuclear										X	X		X										X				

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA/1 G 60 Hz

Number of Days on Study	0929	0922	0931	0932	0941	0942	0943	0944	0957	0958	0959	0960	0906	0907	0908	0925	0926	0927	0928	0937	0938	0939	0940	0981	0982
Carcass ID Number	82	83	83	83	84	84	84	84	85	85	85	86	00	00	00	02	02	02	02	03	03	03	04	08	08
	9	0	1	2	1	2	3	4	7	8	9	0	6	7	8	5	6	7	8	7	8	9	0	1	2
Alimentary System																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																									
Cardiovascular System																									
None																									
Endocrine System																									
None																									
General Body System																									
None																									
Genital System																									
None																									
Hematopoietic System																									
None																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																			X		X				
Carcinoma, multiple	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X		X	X	X	X	X
Carcinoma, metastatic, Zymbal's gland																									
Fibroadenoma																									
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Special Senses System																									
None																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear								X													X		X	X	

TABLE A2
Individual Animal Tumor Pathology of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 20 mg DMBA/1 G 60 Hz

Number of Days on Study	093	093	093	093	093	093	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	
Carcass ID Number	883	884	889	890	891	892	801	802	803	804	849	850	851	852	853	854	855	856	874	875	876	897	898	899	900	Total Tissues/ Tumors
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma, metastatic, mammary gland																										1
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
None																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Adenoma																										1
Carcinoma							X																			5
Carcinoma, multiple	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	91
Carcinoma, metastatic, Zymbal's gland																										1
Fibroadenoma																										1
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Leukemia mononuclear																										12

TABLE A3
Statistical Analysis of Primary Neoplasms in Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
Mammary Gland: Fibroadenoma or Adenoma				
Overall rate[b]	5/100 (5%)	3/100 (3%)	1/100 (1%)	2/100 (2%)
Adjusted rate[c]	5.1%	3.2%	1.0%	2.0%
Terminal rate[d]	5/94 (5%)	3/87 (3%)	1/92 (1%)	2/95 (2%)
First incidence (days)	90 (T)	90 (T)	90 (T)	90 (T)
Poly-3 test[e]	P=0.104N	P=0.373N	P=0.108N	P=0.217N
Mammary Gland: Carcinoma				
Overall rate	92/100 (92%)	86/100 (86%)	96/100 (96%)	96/100 (96%)
Adjusted rate	92.7%	88.6%	96.7%	96.0%
Terminal rate	87/94 (93%)	79/87 (91%)	89/92 (97%)	91/95 (96%)
First incidence (days)	72	73	65	64
Poly-3 test	P=0.068	P=0.222N	P=0.168	P=0.238
Mammary Gland: Adenoma or Carcinoma				
Overall rate	93/100 (93%)	86/100 (86%)	96/100 (96%)	96/100 (96%)
Adjusted rate	93.7%	88.6%	96.7%	96.0%
Terminal rate	88/94 (94%)	79/87 (91%)	89/92 (97%)	91/95 (96%)
First incidence (days)	72	73	65	64
Poly-3 test	P=0.096	P=0.148N	P=0.251	P=0.337
Mammary Gland: Fibroadenoma, Adenoma, or Carcinoma				
Overall rate	93/100 (93%)	86/100 (86%)	96/100 (96%)	96/100 (96%)
Adjusted rate	93.7%	88.6%	96.7%	96.0%
Terminal rate	88/94 (94%)	79/87 (91%)	89/92 (97%)	91/95 (96%)
First incidence (days)	72	73	65	64
Poly-3 test	P=0.096	P=0.148N	P=0.251	P=0.337
All Organs: Mononuclear Cell Leukemia				
Overall rate	15/100 (15%)	16/100 (16%)	10/100 (10%)	12/100 (12%)
Adjusted rate	15.1%	16.1%	10.1%	12.2%
Terminal rate	11/94 (12%)	6/87 (7%)	5/92 (5%)	11/95 (12%)
First incidence (days)	58	49	65	89
Poly-3 test	P=0.143N	P=0.497	P=0.202N	P=0.352N
All Organs: Benign Neoplasms				
Overall rate	5/100 (5%)	3/100 (3%)	1/100 (1%)	2/100 (2%)
Adjusted rate	5.1%	3.2%	1.0%	2.0%
Terminal rate	5/94 (5%)	3/87 (3%)	1/92 (1%)	2/95 (2%)
First incidence (days)	90 (T)	90 (T)	90 (T)	90 (T)
Poly-3 test	P=0.104N	P=0.373N	P=0.108N	P=0.217N
All Organs: Malignant Neoplasms				
Overall rate	93/100 (93%)	92/100 (92%)	96/100 (96%)	96/100 (96%)
Adjusted rate	93.0%	92.0%	96.7%	96.0%
Terminal rate	87/94 (93%)	79/87 (91%)	89/92 (97%)	91/95 (96%)
First incidence (days)	58	49	65	64
Poly-3 test	P=0.131	P=0.500N	P=0.193	P=0.268

TABLE A3
Statistical Analysis of Primary Neoplasms in Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study

	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
All Organs: Benign or Malignant Neoplasms				
Overall rate	94/100 (94%)	92/100 (92%)	96/100 (96%)	96/100 (96%)
Adjusted rate	94.0%	92.0%	96.7%	96.0%
Terminal rate	88/94 (94%)	79/87 (91%)	89/92 (97%)	91/95 (96%)
First incidence (days)	58	49	65	64
Poly-3 test	P=0.178	P=0.391N	P=0.284	P=0.373

(T)Terminal sacrifice
[a] Animals were administered 5 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] Number of neoplasm-bearing animals/number of animals necropsied
[c] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[d] Observed incidence at terminal kill
[e] Beneath the 20 mg DMBA control incidence are the P values associated with the trend test; the trend does not include the 20 mg DMBA/1 G 60-Hz group. Beneath the DMBA/magnetic field group incidence are the P values corresponding to pairwise comparisons between the 20 mg DMBA control group and that DMBA/magnetic field group. The Poly-3 test accounts for differential mortality in animals that do not reach terminal sacrifice. A negative trend or a lower incidence in a dose group is indicated by **N**.

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
Disposition Summary				
Animals initially in study	100	100	100	100
Early deaths				
Moribund	3	7	4	3
Natural deaths	3	6	4	2
Survivors				
Died last week of study	1	1		1
Terminal sacrifice	93	86	92	94
Animals examined microscopically	100	100	100	100
Alimentary System				
Liver	(100)	(100)	(100)	(100)
Angiectasis			1 (1%)	
Clear cell focus	1 (1%)		3 (3%)	3 (3%)
Fatty change		2 (2%)	1 (1%)	2 (2%)
Hematopoietic cell proliferation	19 (19%)	12 (12%)	12 (12%)	22 (22%)
Hepatodiaphragmatic nodule	1 (1%)			
Necrosis		1 (1%)	1 (1%)	2 (2%)
Centrilobular, necrosis	1 (1%)	3 (3%)	1 (1%)	1 (1%)
Cardiovascular System				
None				
Endocrine System				
None				
General Body System				
None				
Genital System				
None				
Hematopoietic System				
None				
Integumentary System				
Mammary gland	(100)	(100)	(100)	(100)
Dilatation			1 (1%)	
Hyperplasia	4 (4%)		3 (3%)	7 (7%)
Inflammation, chronic			1 (1%)	2 (2%)
Musculoskeletal System				
None				

[a] Number of animals examined microscopically at the site and the number of animals with lesion; animals were administered 5 mg DMBA at the beginning of weeks 1, 2, 3, and 4.

TABLE A4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study

	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
Nervous System				
None				
Respiratory System				
Lung	(100)	(100)	(100)	(100)
Foreign body			1 (1%)	
Inflammation, chronic	1 (1%)		1 (1%)	
Thrombosis				1 (1%)
Alveolar epithelium, hyperplasia	6 (6%)		5 (5%)	4 (4%)
Alveolus, infiltration cellular, histiocyte	11 (11%)	2 (2%)	15 (15%)	6 (6%)
Trachea	(1)			
Metaplasia, squamous	1 (100%)			
Mineralization	1 (100%)			
Special Senses System				
None				
Urinary System				
Kidney	(100)	(100)	(100)	(100)
Hydronephrosis		1 (1%)		1 (1%)
Infarct		1 (1%)		
Inflammation, chronic active			1 (1%)	
Mineralization	2 (2%)		1 (1%)	2 (2%)
Nephropathy	15 (15%)	16 (16%)	10 (10%)	16 (16%)
Pelvis, inflammation, suppurative			1 (1%)	

APPENDIX B
SUMMARY OF LESIONS IN FEMALE RATS IN THE SECOND 13-WEEK 7,12-DIMETHYLBENZ(A)ANTHRACENE INITIATION/ MAGNETIC FIELD PROMOTION STUDY

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	8 mg DMBA Control	8 mg DMBA/ 1 G 50 Hz	8 mg DMBA/ 5 G 50 Hz
Disposition Summary			
Animals initially in study	100	100	100
Early death			
Moribund			1
Survivors			
Terminal sacrifice	100	100	99
Animals examined microscopically	100	100	100
Alimentary System			
None			
Cardiovascular System			
None			
Endocrine System			
None			
General Body System			
None			
Genital System			
Clitoral gland		(1)	
Carcinoma		1 (100%)	
Hematopoietic System			
None			
Integumentary System			
Mammary gland	(100)	(100)	(100)
Adenoma			1 (1%)
Carcinoma	20 (20%)	24 (24%)	15 (15%)
Carcinoma, multiple	23 (23%)	24 (24%)	23 (23%)
Musculoskeletal System			
None			
Nervous System			
None			
Respiratory System			
None			

TABLE B1
Summary of the Incidence of Neoplasms in Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study

	8 mg DMBA Control	8 mg DMBA/ 1 G 50 Hz	8 mg DMBA/ 5 G 50 Hz
Special Senses System			
None			
Urinary System			
None			
Systemic Lesions			
Multiple organs[b]	(100)	(100)	(100)
Leukemia mononuclear			1 (1%)
Neoplasm Summary			
Total animals with primary neoplasms[c]	43	48	38
Total primary neoplasms	43	49	40
Total animals with benign neoplasms			1
Total benign neoplasms			1
Total animals with malignant neoplasms	43	48	38
Total malignant neoplasms	43	49	39

[a] Number of animals examined microscopically at the site and the number of animals with neoplasm; animals were administered 2 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]: 8 mg DMBA Control

Number of Days on Study	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2
Carcass ID Number	0 1 1	0 1 2	0 1 3	0 1 4	0 1 5	0 1 6	0 1 7	0 1 8	0 1 9	0 2 0	0 3 1	0 3 2	0 3 3	0 3 4	0 3 5	0 3 6	0 3 7	0 3 8	0 3 9	0 4 0	0 4 1	0 4 2	0 4 3	0 4 4	0 4 5
Alimentary System																									
None																									
Cardiovascular System																									
None																									
Endocrine System																									
None																									
General Body System																									
None																									
Genital System																									
None																									
Hematopoietic System																									
None																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma			X												X										
Carcinoma, multiple		X		X							X									X					
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
None																									
Special Senses System																									
None																									
Urinary System																									
None																									
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

[a] Animals were administered 2 mg DMBA at the beginning of weeks 1, 2, 3, and 4.

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA Control

Number of Days on Study	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3
Carcass ID Number	0 5 6	0 5 7	0 5 8	0 5 9	0 6 0	0 6 6	0 7 7	0 7 7	0 7 8	0 7 9	0 8 0	0 0 1	0 0 2	0 0 3	0 0 4	0 0 5	0 0 6	0 0 7	0 0 8	0 0 9	0 1 0	0 1 2	0 2 2	0 2 3	0 2 4	0 2 5
Alimentary System																											
None																											
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma			X						X		X		X					X							X		
Carcinoma, multiple	X							X															X				
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
None																											
Special Senses System																											
None																											
Urinary System																											
None																											
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA Control

Number of Days on Study	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4
Carcass ID Number	0 2 6	0 2 7	0 2 8	0 2 9	0 3 0	0 4 6	0 4 7	0 4 8	0 4 9	0 5 0	0 5 1	0 5 2	0 5 3	0 5 4	0 5 5	0 9 1	0 9 2	0 9 3	0 9 4	0 9 5	0 6 1	0 6 2	0 6 3	0 6 4	0 6 5
Alimentary System																											
None																											
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma			X	X				X				X		X	X	X	X										
Carcinoma, multiple		X					X		X		X		X							X		X	X				
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
None																											
Special Senses System																											
None																											
Urinary System																											
None																											
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA Control

Carcass ID Number	066	067	068	069	070	071	072	073	074	075	081	082	083	084	085	086	087	088	089	090	096	097	098	099	100	Total Tissues/ Tumors
Number of Days on Study	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	094	
Alimentary System																										
None																										
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
None																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma						X	X		X									X								20
Carcinoma, multiple	X		X									X	X				X			X		X		X		23
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
None																										
Special Senses System																										
None																										
Urinary System																										
None																										
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA/1 G 50 Hz

Number of Days on Study	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2
Carcass ID Number	0 1 6	0 1 7	0 1 8	0 1 9	0 2 0	0 3 1	0 3 2	0 3 3	0 3 4	0 3 5	0 3 6	0 3 7	0 3 8	0 3 9	0 4 0	0 4 1	0 4 2	0 4 3	0 4 4	0 4 5	0 6 1	0 6 2	0 6 3	0 6 4	0 6 5
Alimentary System																											
None																											
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
Clitoral gland																											
Carcinoma																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																				X							
Carcinoma, multiple		X			X						X					X		X			X				X	
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
None																											
Special Senses System																											
None																											
Urinary System																											
None																											
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA/1 G 50 Hz

Number of Days on Study	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3
Carcass ID Number	0 6 6	0 6 7	0 6 8	0 6 9	0 7 0	0 9 6	0 9 7	0 9 8	0 9 9	1 0 0	0 0 6	0 0 7	0 0 8	0 0 9	0 1 0	0 1 1	0 1 2	0 1 3	0 1 4	0 1 5	0 2 6	0 2 7	0 2 8	0 2 9	0 3 0
Alimentary System																									
None																									
Cardiovascular System																									
None																									
Endocrine System																									
None																									
General Body System																									
None																									
Genital System																									
Clitoral gland																									
Carcinoma																									
Hematopoietic System																									
None																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma		X		X			X	X	X		X		X	X							X				
Carcinoma, multiple					X	X										X						X			
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
None																									
Special Senses System																									
None																									
Urinary System																									
None																									
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA/1 G 50 Hz

Number of Days on Study	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4
Carcass ID Number	0 5 6	0 5 7	0 5 8	0 5 9	0 6 0	0 7 1	0 7 2	0 7 3	0 7 4	0 7 5	0 9 1	0 9 2	0 9 3	0 9 4	0 9 5	0 0 1	0 0 2	0 0 3	0 0 4	0 0 5	0 2 1	0 2 2	0 2 3	0 2 4	0 2 5
Alimentary System																											
None																											
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
Clitoral gland																											
Carcinoma																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma		X		X	X			X	X				X					X		X				X	X	
Carcinoma, multiple			X												X		X						X	X		X	
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
None																											
Special Senses System																											
None																											
Urinary System																											
None																											
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA/1 G 50 Hz

Number of Days on Study	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	
Carcass ID Number	0 4 6	0 4 7	0 4 8	0 4 9	0 5 0	0 5 1	0 5 2	0 5 3	0 5 4	0 5 5	0 7 6	0 7 7	0 7 8	0 7 9	0 8 0	0 8 1	0 8 2	0 8 3	0 8 4	0 8 5	0 8 6	0 8 7	0 8 8	0 8 9	0 9 0	Total Tissues/ Tumors	
Alimentary System																											
None																											
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
Clitoral gland																					+					1	
Carcinoma																					X					1	
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	
Carcinoma						X			X		X									X	X			X		24	
Carcinoma, multiple				X	X							X				X			X			X	X			24	
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
None																											
Special Senses System																											
None																											
Urinary System																											
None																											
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100	

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA/5 G 50 Hz

Number of Days on Study	0 8 1	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2
Carcass ID Number	0 3 3	0 2 1	0 2 2	0 2 3	0 2 4	0 2 5	0 4 1	0 4 2	0 4 3	0 4 4	0 4 5	0 5 1	0 5 2	0 5 3	0 5 4	0 5 5	0 5 6	0 5 7	0 5 8	0 5 9	0 6 0	0 7 6	0 7 7	0 7 8	0 7 9
Alimentary System																											
None																											
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																											
Carcinoma													X												X	X	
Carcinoma, multiple	X	X				X	X									X	X		X				X				
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
None																											
Special Senses System																											
None																											
Urinary System																											
None																											
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA/5 G 50 Hz

Number of Days on Study	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 2	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3
Carcass ID Number	0 8 0	0 8 6	0 8 7	0 8 8	0 8 9	0 9 0	0 2 6	0 2 7	0 2 8	0 2 9	0 3 0	0 3 6	0 3 7	0 3 8	0 3 9	0 4 0	0 4 6	0 4 7	0 4 8	0 4 9	0 5 0	0 6 1	0 6 2	0 6 3	0 6 4
Alimentary System																									
None																									
Cardiovascular System																									
None																									
Endocrine System																									
None																									
General Body System																									
None																									
Genital System																									
None																									
Hematopoietic System																									
None																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma			X						X									X				X		X	
Carcinoma, multiple				X			X							X									X		
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
None																									
Special Senses System																									
None																									
Urinary System																									
None																									
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																									

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA/5 G 50 Hz

Number of Days on Study	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 3	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4
Carcass ID Number	0 0 6 5	0 0 6 6	0 0 6 7	0 0 6 8	0 0 6 9	0 0 7 0	0 0 9 1	0 0 9 2	0 0 9 3	0 0 9 4	0 0 9 5	0 0 9 6	0 0 9 7	0 0 9 8	0 0 9 9	0 1 0 0	0 0 0 1	0 0 0 2	0 0 0 3	0 0 0 4	0 0 0 5	0 0 0 6	0 0 0 7	0 0 0 8	0 0 0 9	
Alimentary System																										
None																										
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
None																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma																										
Carcinoma		X	X	X		X										X			X							
Carcinoma, multiple	X							X		X							X									
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
None																										
Special Senses System																										
None																										
Urinary System																										
None																										
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leukemia mononuclear																										

TABLE B2
Individual Animal Tumor Pathology of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study: 8 mg DMBA/5 G 50 Hz

Number of Days on Study	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	0 9 4	
Carcass ID Number	0 1 0	0 1 1	0 1 2	0 1 3	0 1 4	0 1 5	0 1 6	0 1 7	0 1 8	0 1 9	0 2 0	0 3 1	0 3 2	0 3 4	0 3 5	0 7 1	0 7 2	0 7 3	0 7 4	0 7 5	0 8 1	0 8 2	0 8 3	0 8 4	0 8 5	Total Tissues/ Tumors
Alimentary System																										
None																										
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
None																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Adenoma																				X						1
Carcinoma											X															15
Carcinoma, multiple		X				X	X			X						X				X				X		23
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
None																										
Special Senses System																										
None																										
Urinary System																										
None																										
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Leukemia mononuclear																										1

TABLE B3
Statistical Analysis of Primary Neoplasms in Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	8 mg DMBA Control	8 mg DMBA/ 1 G 50 Hz	8 mg DMBA/ 5 G 50 Hz
Mammary Gland: Carcinoma			
Overall rate[b]	43/100 (43%)	48/100 (48%)	38/100 (38%)
Adjusted rate[c]	43.0%	48.0%	38.0%
Terminal rate[d]	43/100 (43%)	48/100 (48%)	37/99 (37%)
First incidence (days)	92 (T)	92 (T)	81
Poly-3 test[e]	P=0.166N	P=0.286	P=0.283N
Mammary Gland: Adenoma or Carcinoma			
Overall rate	43/100 (43%)	48/100 (48%)	38/100 (38%)
Adjusted rate	43.0%	48.0%	38.0%
Terminal rate	43/100 (43%)	48/100 (48%)	37/99 (37%)
First incidence (days)	92 (T)	92 (T)	81
Poly-3 test	P=0.166N	P=0.286	P=0.283N
All Organs: Malignant Neoplasms			
Overall rate	43/100 (43%)	48/100 (48%)	38/100 (38%)
Adjusted rate	43.0%	48.0%	38.0%
Terminal rate	43/100 (43%)	48/100 (48%)	37/99 (37%)
First incidence (days)	92 (T)	92 (T)	81
Poly-3 test	P=0.166N	P=0.286	P=0.283N
All Organs: Benign or Malignant Neoplasms			
Overall rate	43/100 (43%)	48/100 (48%)	38/100 (38%)
Adjusted rate	43.0%	48.0%	38.0%
Terminal rate	43/100 (43%)	48/100 (48%)	37/99 (37%)
First incidence (days)	92 (T)	92 (T)	81
Poly-3 test	P=0.166N	P=0.286	P=0.283N

(T)Terminal sacrifice
[a] Animals were administered 2 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] Number of neoplasm-bearing animals/number of animals necropsied
[c] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[d] Observed incidence at terminal kill
[e] Beneath the 8 mg DMBA control incidence are the P values associated with the trend test. Beneath the DMBA/magnetic field group incidence are the P values corresponding to pairwise comparisons between the 8 mg DMBA control group and that DMBA/magnetic field group. The Poly-3 test accounts for differential mortality in animals that do not reach terminal sacrifice. A negative trend or a lower incidence in a dose group is indicated by **N**.

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	8 mg DMBA Control	8 mg DMBA/ 1 G 50 Hz	8 mg DMBA/ 5 G 50 Hz
Disposition Summary			
Animals initially in study	100	100	100
Early death			
Moribund			1
Survivors			
Terminal sacrifice	100	100	99
Animals examined microscopically	100	100	100
Alimentary System			
None			
Cardiovascular System			
None			
Endocrine System			
None			
General Body System			
None			
Genital System			
None			
Hematopoietic System			
None			
Integumentary System			
Mammary gland	(100)	(100)	(100)
Galactocele			1 (1%)
Hyperplasia			1 (1%)
Musculoskeletal System			
None			
Nervous System			
None			
Respiratory System			
None			

[a] Number of animals examined microscopically at the site and the number of animals with lesion; animals were administered 2 mg DMBA at the beginning of weeks 1, 2, 3, and 4.

TABLE B4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study

	8 mg DMBA Control	8 mg DMBA/ 1 G 50 Hz	8 mg DMBA/ 5 G 50 Hz
Special Senses System			
None			
Urinary System			
None			

APPENDIX C
SUMMARY OF LESIONS IN FEMALE RATS IN THE 26-WEEK 7,12-DIMETHYLBENZ(A)ANTHRACENE INITIATION/ MAGNETIC FIELD PROMOTION STUDY

TABLE C1
Summary of the Incidence of Neoplasms in Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
Disposition Summary				
Animals initially in study	100	100	100	100
Early deaths				
Moribund	6	4	5	3
Natural deaths	6	11	4	3
Survivors				
Terminal sacrifice	88	85	91	94
Animals examined microscopically	100	100	100	100
Alimentary System				
Liver	(98)	(99)	(100)	(100)
Hepatocellular adenoma	1 (1%)			
Histiocytic sarcoma		1 (1%)		
Cardiovascular System				
None				
Endocrine System				
None				
General Body System				
None				
Genital System				
None				
Hematopoietic System				
Lymph node	(3)	(3)		(1)
Lymph node, mandibular				(1)
Integumentary System				
Mammary gland	(100)	(100)	(100)	(100)
Adenoma	2 (2%)			
Carcinoma	7 (7%)	16 (16%)	16 (16%)	15 (15%)
Carcinoma, multiple	89 (89%)	74 (74%)	79 (79%)	70 (70%)
Fibroadenoma	21 (21%)	24 (24%)	15 (15%)	24 (24%)
Fibroadenoma, multiple	50 (50%)	52 (52%)	58 (58%)	44 (44%)
Skin	(19)	(8)	(13)	(10)
Basal cell carcinoma		1 (13%)		
Squamous cell carcinoma	1 (5%)			
Trichoepithelioma	6 (32%)	6 (75%)	10 (77%)	8 (80%)
Subcutaneous tissue, fibroma	1 (5%)			
Subcutaneous tissue, hemangioma				1 (10%)
Musculoskeletal System				
None				

TABLE C1
Summary of the Incidence of Neoplasms in Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study

	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
Nervous System				
None				
Respiratory System				
Lung	(98)	(100)	(100)	(100)
Carcinoma, metastatic, mammary gland	4 (4%)	4 (4%)	1 (1%)	4 (4%)
Histiocytic sarcoma		1 (1%)		
Special Senses System				
Zymbal's gland	(1)			
Carcinoma	1 (100%)			
Urinary System				
Kidney	(100)	(98)	(100)	(100)
Histiocytic sarcoma		1 (1%)		
Sarcoma	1 (1%)			
Renal tubule, adenoma			1 (1%)	
Systemic Lesions				
Multiple organs[b]	(100)	(100)	(100)	(100)
Histiocytic sarcoma		1 (1%)		
Leukemia mononuclear	4 (4%)	10 (10%)	2 (2%)	6 (6%)
Neoplasm Summary				
Total animals with primary neoplasms[c]	97	99	98	94
Total primary neoplasms	197	195	185	175
Total animals with benign neoplasms	74	77	74	70
Total benign neoplasms	86	86	86	80
Total animals with malignant neoplasms	96	91	95	86
Total malignant neoplasms	111	109	99	95
Total animals with metastatic neoplasms	4	4	1	4
Total metastatic neoplasms	4	4	1	4

[a] Number of animals examined microscopically at the site and the number of animals with neoplasm; animals were administered 10 mg DMBA on day 1 of the study.
[b] Number of animals with any tissue examined microscopically
[c] Primary neoplasms: all neoplasms except metastatic neoplasms

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study[a]: 10 mg DMBA Control

Number of Days on Study	0 8 9	1 1 0	1 1 3	1 1 3	1 3 5	1 4 5	1 5 1	1 6 2	1 7 3	1 7 6	1 7 6	1 8 2	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3
Carcass ID Number	0 2 4	0 9 1	0 1 1	0 7 2	0 9 2	0 4 1	0 2 1	0 6 2	0 7 3	0 0 8	0 7 9	0 6 5	0 1 6	0 1 7	0 1 8	0 1 9	0 2 0	0 6 1	0 6 3	0 6 4	0 8 1	0 8 2	0 8 3	0 8 4	0 8 5	
Alimentary System																										
Liver	+	+	+	+	+	+	M	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Hepatocellular adenoma																										
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
Lymph node			+						+								+									
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Adenoma						X																				
Carcinoma																								X		
Carcinoma, multiple	X		X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X		X	
Fibroadenoma														X			X					X	X		X	
Fibroadenoma, multiple										X		X	X		X	X			X	X	X			X		
Skin															+	+	+				+			+		
Squamous cell carcinoma																										
Trichoepithelioma															X											
Subcutaneous tissue, fibroma																	X									
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	M	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, metastatic, mammary gland																										
Special Senses System																										
Zymbal's gland																										
Carcinoma																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Sarcoma																										
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Leukemia mononuclear			X						X		X															

[a] Animals were administered 10 mg DMBA on day 1 of the study.

+: Tissue examined microscopically
A: Autolysis precludes examination
M: Missing tissue
I: Insufficient tissue
X: Lesion present
Blank: Not examined

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA Control

Number of Days on Study	183	183	183	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	185	185	185
Carcass ID Number	0093	0094	0095	0101	0002	0003	0004	0005	0026	0027	0028	0029	0030	0042	0043	0044	0045	0076	0077	0078	0080	0012	0013	0014	0015
Alimentary System																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma									X																
Cardiovascular System																									
None																									
Endocrine System																									
None																									
General Body System																									
None																									
Genital System																									
None																									
Hematopoietic System																									
Lymph node																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma																									
Carcinoma																									X
Carcinoma, multiple	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	
Fibroadenoma		X	X							X	X			X	X							X			
Fibroadenoma, multiple	X				X	X	X						X			X		X		X	X			X	X
Skin					+		+			+						+	+						+		
Squamous cell carcinoma																									
Trichoepithelioma					X		X																X		
Subcutaneous tissue, fibroma																									
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland	X											X				X									
Special Senses System																									
Zymbal's gland																								+	
Carcinoma																								X	
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma																				X					
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear			X																						

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA Control

Number of Days on Study	185	185	185	185	185	185	185	185	185	185	185	185	186	186	186	186	186	186	186	186	186	186	186	186	186	186
Carcass ID Number	02202	02203	02205	06606	06607	06608	06609	07700	07701	07704	07705	00106	00107	00109	01310	03312	03323	03334	03335	03336	03337	03338	03339	04340
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatocellular adenoma																										
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
Lymph node																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Adenoma														X												
Carcinoma								X							X						X					
Carcinoma, multiple	X	X	X	X	X	X	X		X	X	X	X	X	X		X	X	X	X	X	X		X	X	X	X	X
Fibroadenoma							X		X						X				X							
Fibroadenoma, multiple	X	X		X	X	X		X			X	X	X		X					X		X		X	X	X
Skin					+										+					+						
Squamous cell carcinoma															X											
Trichoepithelioma					X																					
Subcutaneous tissue, fibroma																										
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																										
Special Senses System																										
Zymbal's gland																										
Carcinoma																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Sarcoma																										
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																										

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA Control

Number of Days on Study	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	1 8 7	
Carcass ID Number	0 5 1	0 5 2	0 5 3	0 5 4	0 5 5	0 4 6	0 4 7	0 4 8	0 4 9	0 5 0	0 5 6	0 5 7	0 5 8	0 5 9	0 6 0	0 8 6	0 8 7	0 8 8	0 8 9	0 9 0	0 9 6	0 9 7	0 9 8	0 9 9	1 0 0	Total Tissues/ Tumors
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	98
Hepatocellular adenoma																										1
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
Lymph node																										3
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Adenoma																										2
Carcinoma														X								X				7
Carcinoma, multiple	X	X	X	X		X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X		X	X	89
Fibroadenoma	X						X			X	X	X														21
Fibroadenoma, multiple		X	X	X		X			X				X	X		X	X	X	X	X	X			X	X	50
Skin	+															+		+				+	+			19
Squamous cell carcinoma																										1
Trichoepithelioma																X										6
Subcutaneous tissue, fibroma																										1
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	98
Carcinoma, metastatic, mammary gland														X												4
Special Senses System																										
Zymbal's gland																										1
Carcinoma																										1
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Sarcoma																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Leukemia mononuclear																										4

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/1 G 50 Hz

Number of Days on Study	0 9 1	1 1 4	1 1 5	1 1 5	1 2 7	1 3 1	1 3 2	1 3 4	1 5 7	1 6 0	1 6 2	1 6 4	1 6 6	1 7 2	1 8 2	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3
Carcass ID Number	2 7 3	2 4 0	2 4 7	2 6 2	2 8 2	2 7 1	2 5 4	2 5 8	2 3 7	2 0 8	2 0 1	2 8 3	2 5 5	2 6 9	2 9 1	2 5 1	2 5 2	2 5 3	2 5 6	2 5 7	2 5 9	2 6 0	2 8 1	2 8 4	2 8 5		
Alimentary System																											
Liver	+	+	+	+	+	+	M	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Histiocytic sarcoma																											
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
Lymph node												+	+														
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Carcinoma			X			X	X		X						X												
Carcinoma, multiple		X		X	X			X		X	X	X	X	X		X	X	X	X	X	X	X	X	X	X		
Fibroadenoma								X		X				X					X	X		X					
Fibroadenoma, multiple									X			X	X				X	X			X						
Skin																											
Basal cell carcinoma																											
Trichoepithelioma																											
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Carcinoma, metastatic, mammary gland						X																					
Histiocytic sarcoma																											
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	M	+	+	+	+	+	+	+	A	+	+	+	+	+	+	+	+	+	+		
Histiocytic sarcoma																											
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Histiocytic sarcoma																											
Leukemia mononuclear	X	X			X				X		X	X	X														

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA 1 G 50 Hz

Number of Days on Study	183	183	183	183	183	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	184	185
Carcass ID Number	296	299	298	299	300	300	300	300	301	301	301	301	301	301	301	301	301	301	302	302	302	302	302	302	302	302
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
Lymph node								+																		
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma					X																		X			
Carcinoma, multiple	X	X	X	X		X	X	X	X	X	X	X	X	X		X	X	X		X	X	X		X	X	
Fibroadenoma		X		X	X						X															X
Fibroadenoma, multiple	X		X			X	X	X	X	X		X	X	X		X	X	X	X	X	X	X	X	X	X	
Skin	+	+										+	+						+							
Basal cell carcinoma		X																								
Trichoepithelioma												X	X						X							
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																										
Histiocytic sarcoma																										
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Histiocytic sarcoma																										
Leukemia mononuclear								X																		

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/1 G 50 Hz

Number of Days on Study	185	185	185	185	185	185	185	185	185	185	185	185	185	185	185	185	185	185	186	186	186	186	186	186	186	186
Carcass ID Number	203	204	205	241	242	243	244	245	276	277	278	279	280	292	293	294	295	296	227	228	229	230	231	232	233	
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Histiocytic sarcoma																									X	
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
Lymph node																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma																	X		X					X		
Carcinoma, multiple	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X		X		X	X		X		X	X
Fibroadenoma						X		X				X													X	
Fibroadenoma, multiple			X	X			X		X	X	X		X	X	X		X					X	X	X		X
Skin	+								+																	
Basal cell carcinoma																										
Trichoepithelioma	X								X																	
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Carcinoma, metastatic, mammary gland																										
Histiocytic sarcoma																									X	
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Histiocytic sarcoma																									X	
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
Histiocytic sarcoma																									X	
Leukemia mononuclear																				X						

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/1 G 50 Hz

Number of Days on Study	186	186	186	186	186	186	186	186	186	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	
Carcass ID Number	2344	2355	2661	2663	2664	2665	2672	2674	2675	2736	2738	2739	2746	2748	2749	2750	2766	2767	2768	2770	2786	2787	2788	2789	2790	Total Tissues/ Tumors
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	99
Histiocytic sarcoma																										1
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
Lymph node																										3
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma											X	X			X	X		X			X					16
Carcinoma, multiple	X	X	X	X	X	X	X	X	X	X			X	X			X					X	X			74
Fibroadenoma			X			X		X	X			X			X	X						X			X	24
Fibroadenoma, multiple		X		X						X	X		X	X			X	X	X	X	X		X	X		52
Skin				+																						8
Basal cell carcinoma																										1
Trichoepithelioma				X																						6
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma, metastatic, mammary gland				X				X		X																4
Histiocytic sarcoma																										1
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	98
Histiocytic sarcoma																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Histiocytic sarcoma																										1
Leukemia mononuclear									X																	10

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/5 G 50 Hz

Number of Days on Study	0 7 7	0 8 9	1 0 6	1 3 5	1 3 8	1 6 2	1 6 5	1 7 3	1 7 6	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3	1 8 3
Carcass ID Number	4 7 7	4 6 3	4 2 3	4 4 6	4 5 2	5 0 0	4 0 8	4 0 7	4 4 8	4 0 6	4 0 9	4 1 0	4 1 1	4 3 2	4 3 3	4 3 4	4 3 5	4 4 7	4 4 9	4 5 0	4 8 1	4 8 2	4 8 3	4 8 4	4 8 5
Alimentary System																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma			X												X				X	X						X	X
Carcinoma, multiple		X		X	X	X	X	X	X	X	X	X	X	X		X		X			X	X	X	X			
Fibroadenoma												X												X			
Fibroadenoma, multiple					X			X		X		X	X	X	X	X	X	X			X	X		X	X		
Skin																		+									
Trichoepithelioma																											
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland						X																					
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																											
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear					X																						

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/5 G 50 Hz

Number of Days on Study	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5
Carcass ID Number	4 1 1	4 1 2	4 1 3	4 1 4	4 1 5	4 2 1	4 2 2	4 2 4	4 2 5	4 2 6	4 2 7	4 2 8	4 2 9	4 3 0	4 9 1	4 9 2	4 9 3	4 9 4	4 9 5	4 1 6	4 1 7	4 1 8	4 1 9	4 2 0	4 4 1
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
None																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma													X			X		X								
Carcinoma, multiple	X	X		X	X	X	X	X	X	X	X	X		X			X		X	X	X	X	X	X		
Fibroadenoma								X						X				X							X	
Fibroadenoma, multiple		X	X	X	X	X	X		X		X	X					X		X	X	X	X				
Skin								+			+			+												+
Trichoepithelioma								X			X			X												X
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																										
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma																										
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																										

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/5 G 50 Hz

Number of Days on Study	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6
Carcass ID Number	4 4 2	4 4 3	4 4 4	4 4 5	4 5 1	4 5 3	4 5 4	4 5 5	4 5 6	4 6 6	4 6 7	4 6 8	4 6 9	4 7 0	4 0 1	4 0 2	4 0 3	4 0 4	4 0 5	4 3 6	4 3 7	4 3 8	4 3 9	4 4 0	4 5 6	4 5 7
Alimentary System																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
None																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma																						X	X				
Carcinoma, multiple	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X			X	X	X	
Fibroadenoma				X	X	X			X								X		X			X		X		
Fibroadenoma, multiple	X	X	X				X	X		X	X	X	X	X						X						X	X
Skin								+	+	+																	
Trichoepithelioma								X	X	X																	
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																											
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Renal tubule, adenoma					X																						
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear						X																					

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/5 G 50 Hz

Number of Days on Study	186	186	186	186	186	186	186	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	
Carcass ID Number	45 8	45 9	46 0	49 6	49 7	49 8	49 9	46 1	46 2	46 4	46 5	47 1	47 2	47 3	47 4	47 5	47 6	47 8	47 9	48 0	48 6	48 7	48 8	48 9	49 0	Total Tissues/ Tumors
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
None																										
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma				X	X			X								X								X		16
Carcinoma, multiple	X	X	X			X	X		X	X	X	X	X	X			X	X	X	X	X	X	X	X		X	79
Fibroadenoma					X																						15
Fibroadenoma, multiple	X			X		X			X	X	X	X	X	X	X	X		X	X	X		X	X	X	X		58
Skin								+				+					+	+				+					13
Trichoepithelioma												X						X				X					10
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma, metastatic, mammary gland																										1
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Renal tubule, adenoma																										1
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Leukemia mononuclear																										2

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/1 G 60 Hz

Number of Days on Study	071	085	151	162	162	174	183	183	183	183	183	183	183	183	183	183	183	183	183	183	183	183	183	183	183
Carcass ID Number	325	371	368	350	380	336	301	302	303	304	305	321	322	323	324	386	387	388	389	390	391	392	393	394	395
Alimentary System																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
None																									
Endocrine System																									
None																									
General Body System																									
None																									
Genital System																									
None																									
Hematopoietic System																									
Lymph node			+																						
Lymph node, mandibular			+																						
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma												X									X				X
Carcinoma, multiple			X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X		X	X	X	
Fibroadenoma					X							X		X											
Fibroadenoma, multiple				X			X	X			X					X			X		X		X	X	X
Skin																								+	
Trichoepithelioma																									
Subcutaneous tissue, hemangioma																									
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland									X																
Special Senses System																									
None																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear	X		X			X				X						X									

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/1 G 60 Hz

Number of Days on Study	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 4	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5
Carcass ID Number	3 1 1	3 1 2	3 1 3	3 1 4	3 1 5	3 4 1	3 4 2	3 4 3	3 4 4	3 4 5	3 6 6	3 6 7	3 6 9	3 7 0	3 7 2	3 7 3	3 7 4	3 7 5	3 3 1	3 3 2	3 3 3	3 3 4	3 3 5	3 3 7	3 3 8
Alimentary System																									
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																									
None																									
Endocrine System																									
None																									
General Body System																									
None																									
Genital System																									
None																									
Hematopoietic System																									
Lymph node																									
Lymph node, mandibular																									
Integumentary System																									
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma												X		X											
Carcinoma, multiple	X		X	X	X	X	X	X	X	X	X					X	X	X	X	X	X	X	X	X	X
Fibroadenoma		X				X		X								X			X						
Fibroadenoma, multiple	X		X	X	X				X		X	X	X	X			X			X		X	X		X
Skin												+		+											
Trichoepithelioma												X													
Subcutaneous tissue, hemangioma																									
Musculoskeletal System																									
None																									
Nervous System																									
None																									
Respiratory System																									
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland																X									
Special Senses System																									
None																									
Urinary System																									
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																									
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																									

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/1 G 60 Hz

Number of Days on Study	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 5	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6	1 8 6
Carcass ID Number	3 3 9	3 4 0	3 4 6	3 4 7	3 4 8	3 4 9	3 5 6	3 5 7	3 5 8	3 5 9	3 6 0	3 5 1	3 5 2	3 5 3	3 5 4	3 5 5	3 6 1	3 6 2	3 6 3	3 6 4	3 6 5	3 7 6	3 7 7	3 7 8	3 7 9
Alimentary System																											
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Cardiovascular System																											
None																											
Endocrine System																											
None																											
General Body System																											
None																											
Genital System																											
None																											
Hematopoietic System																											
Lymph node																											
Lymph node, mandibular																											
Integumentary System																											
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma							X							X			X								X		
Carcinoma, multiple	X	X	X	X	X			X	X	X	X			X	X			X	X	X		X	X				
Fibroadenoma	X	X	X				X		X	X				X						X			X	X			
Fibroadenoma, multiple				X							X	X	X			X	X					X					
Skin							+														+				+	+	
Trichoepithelioma							X														X				X	X	
Subcutaneous tissue, hemangioma							X																				
Musculoskeletal System																											
None																											
Nervous System																											
None																											
Respiratory System																											
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Carcinoma, metastatic, mammary gland													X														
Special Senses System																											
None																											
Urinary System																											
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Systemic Lesions																											
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Leukemia mononuclear																											

TABLE C2
Individual Animal Tumor Pathology of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study: 10 mg DMBA/1 G 60 Hz

Number of Days on Study	186	186	186	186	186	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	187	
Carcass ID Number	38 1	38 2	38 3	38 4	38 5	30 6	00 7	00 8	00 9	31 0	11 6	11 7	11 8	11 9	12 0	22 6	22 7	22 8	22 9	23 0	39 6	39 7	39 8	39 9	40 0	Total Tissues/ Tumors
Alimentary System																										
Liver	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Cardiovascular System																										
None																										
Endocrine System																										
None																										
General Body System																										
None																										
Genital System																										
None																										
Hematopoietic System																										
Lymph node																										1
Lymph node, mandibular																										1
Integumentary System																										
Mammary gland	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma				X	X	X			X					X									X			15
Carcinoma, multiple	X	X	X				X	X		X	X	X	X		X					X	X	X		X		70
Fibroadenoma		X					X		X	X			X											X		24
Fibroadenoma, multiple			X			X		X			X			X	X	X	X			X	X	X	X		X	44
Skin									+												+	+				10
Trichoepithelioma									X												X	X				8
Subcutaneous tissue, hemangioma																										1
Musculoskeletal System																										
None																										
Nervous System																										
None																										
Respiratory System																										
Lung	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Carcinoma, metastatic, mammary gland													X													4
Special Senses System																										
None																										
Urinary System																										
Kidney	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Systemic Lesions																										
Multiple organs	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	100
Leukemia mononuclear							X																			6

TABLE C3
Statistical Analysis of Primary Neoplasms in Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/ Magnetic Field Promotion Study[a]

	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
Mammary Gland: Fibroadenoma				
Overall rate[b]	71/100 (71%)	76/100 (76%)	73/100 (73%)	68/100 (68%)
Adjusted rate[c]	75.0%	80.3%	76.0%	69.7%
Terminal rate[d]	69/88 (78%)	70/85 (82%)	71/91 (78%)	66/94 (70%)
First incidence (days)	176	134	138	162
Poly-3 test[e]	P=0.491N	P=0.233	P=0.504	P=0.252N
Mammary Gland: Fibroadenoma or Adenoma				
Overall rate	72/100 (72%)	76/100 (76%)	73/100 (73%)	68/100 (68%)
Adjusted rate	75.6%	80.3%	76.0%	69.7%
Terminal rate	69/88 (78%)	70/85 (82%)	71/91 (78%)	66/94 (70%)
First incidence (days)	145	134	138	162
Poly-3 test	P=0.459N	P=0.267	P=0.547	P=0.220N
Mammary Gland: Carcinoma				
Overall rate	96/100 (96%)	90/100 (90%)	95/100 (95%)	85/100 (85%)
Adjusted rate	96.8%	90.8%	95.9%	86.6%
Terminal rate	85/88 (97%)	76/85 (89%)	87/91 (96%)	81/94 (86%)
First incidence (days)	89	114	89	151
Poly-3 test	P=0.438	P=0.072N	P=0.521N	P=0.009N
Mammary Gland: Adenoma or Carcinoma				
Overall rate	96/100 (96%)	90/100 (90%)	95/100 (95%)	85/100 (85%)
Adjusted rate	96.8%	90.8%	95.9%	86.6%
Terminal rate	85/88 (97%)	76/85 (89%)	87/91 (96%)	81/94 (86%)
First incidence (days)	89	114	89	151
Poly-3 test	P=0.438	P=0.072N	P=0.521N	P=0.009N
Mammary Gland: Fibroadenoma, Adenoma, or Carcinoma				
Overall rate	97/100 (97%)	98/100 (98%)	97/100 (97%)	91/100 (91%)
Adjusted rate	97.8%	98.9%	97.9%	92.7%
Terminal rate	86/88 (98%)	84/85 (99%)	89/91 (98%)	87/94 (93%)
First incidence (days)	89	114	89	151
Poly-3 test	P=0.608N	P=0.479	P=0.666	P=0.087N
Skin: Trichoepithelioma				
Overall rate	6/100 (6%)	6/100 (6%)	10/100 (10%)	8/100 (8%)
Adjusted rate	6.3%	6.5%	10.5%	8.3%
Terminal rate	6/88 (7%)	6/85 (7%)	10/91 (11%)	8/94 (9%)
First incidence (days)	183 (T)	183 (T)	183 (T)	183 (T)
Poly-3 test	P=0.161	P=0.602	P=0.222	P=0.410
Skin: Trichoepithelioma or Basal Cell Carcinoma				
Overall rate	6/100 (6%)	7/100 (7%)	10/100 (10%)	8/100 (8%)
Adjusted rate	6.3%	7.6%	10.5%	8.3%
Terminal rate	6/88 (7%)	7/85 (8%)	10/91 (11%)	8/94 (9%)
First incidence (days)	183 (T)	183 (T)	183 (T)	183 (T)
Poly-3 test	P=0.192	P=0.484	P=0.222	P=0.410

TABLE C3
Statistical Analysis of Primary Neoplasms in Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study

	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
Skin: Trichoepithelioma, Basal Cell Carcinoma, or Squamous Cell Carcinoma				
Overall rate	7/100 (7%)	7/100 (7%)	10/100 (10%)	8/100 (8%)
Adjusted rate	7.4%	7.6%	10.5%	8.3%
Terminal rate	7/88 (8%)	7/85 (8%)	10/91 (11%)	8/94 (9%)
First incidence (days)	183 (T)	183 (T)	183 (T)	183 (T)
Poly-3 test	P=0.257	P=0.593	P=0.313	P=0.520
All Organs: Mononuclear Cell Leukemia				
Overall rate	4/100 (4%)	10/100 (10%)	2/100 (2%)	6/100 (6%)
Adjusted rate	4.2%	10.4%	2.1%	6.1%
Terminal rate	1/88 (1%)	3/85 (4%)	1/91 (1%)	3/94 (3%)
First incidence (days)	113	91	138	71
Poly-3 test	P=0.114N	P=0.084	P=0.338N	P=0.392
All Organs: Benign Neoplasms				
Overall rate	74/100 (74%)	77/100 (77%)	74/100 (74%)	70/100 (70%)
Adjusted rate	77.7%	81.4%	77.0%	71.7%
Terminal rate	71/88 (81%)	71/85 (84%)	72/91 (79%)	68/94 (72%)
First incidence (days)	145	134	138	162
Poly-3 test	P=0.403N	P=0.324	P=0.521N	P=0.211N
All Organs: Malignant Neoplasms				
Overall rate	96/100 (96%)	91/100 (91%)	95/100 (95%)	86/100 (86%)
Adjusted rate	96.8%	91.0%	95.9%	86.8%
Terminal rate	85/88 (97%)	76/85 (89%)	87/91 (96%)	81/94 (86%)
First incidence (days)	89	91	89	71
Poly-3 test	P=0.445	P=0.079N	P=0.521N	P=0.010N
All Organs: Benign or Malignant Neoplasms				
Overall rate	97/100 (97%)	99/100 (99%)	98/100 (98%)	94/100 (94%)
Adjusted rate	97.8%	99.0%	98.9%	94.9%
Terminal rate	86/88 (98%)	84/85 (99%)	90/91 (99%)	89/94 (95%)
First incidence (days)	89	91	89	71
Poly-3 test	P=0.483	P=0.447	P=0.468	P=0.235N

(T)Terminal sacrifice
[a] Animals were administered 10 mg DMBA on day 1 of the study.
[b] Number of neoplasm-bearing animals/number of animals necropsied
[c] Poly-3 estimated neoplasm incidence after adjustment for intercurrent mortality
[d] Observed incidence at terminal kill
[e] Beneath the 10 mg DMBA control incidence are the P values associated with the trend test; the trend test does not include the 10 mg DMBA/1 G 60-Hz group. Beneath the DMBA/magnetic field group incidence are the P values corresponding to pairwise comparisons between the 10 mg DMBA control group and that DMBA/magnetic field group. The Poly-3 test accounts for differential mortality in animals that do not reach terminal sacrifice. A negative trend or a lower incidence in a dose group is indicated by **N**.

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
Disposition Summary				
Animals initially in study	100	100	100	100
Early deaths				
Moribund	6	4	5	3
Natural deaths	6	11	4	3
Survivors				
Terminal sacrifice	88	85	91	94
Animals examined microscopically	100	100	100	100
Alimentary System				
Liver	(98)	(99)	(100)	(100)
Angiectasis	6 (6%)	3 (3%)	4 (4%)	3 (3%)
Basophilic focus	4 (4%)	3 (3%)	13 (13%)	7 (7%)
Clear cell focus	8 (8%)	11 (11%)	14 (14%)	5 (5%)
Cyst		1 (1%)		
Eosinophilic focus	1 (1%)	2 (2%)		
Fatty change			2 (2%)	
Hematopoietic cell proliferation	7 (7%)	5 (5%)	5 (5%)	4 (4%)
Infiltration cellular, mixed cell		1 (1%)		
Mixed cell focus			1 (1%)	
Necrosis			2 (2%)	
Vacuolization cytoplasmic	1 (1%)			
Centrilobular, necrosis	4 (4%)	6 (6%)	4 (4%)	1 (1%)
Cardiovascular System				
None				
Endocrine System				
None				
General Body System				
None				
Genital System				
None				
Hematopoietic System				
Lymph node	(3)	(3)		(1)
Necrosis	1 (33%)			

[a] Number of animals examined microscopically at the site and the number of animals with lesion; animals were administered 10 mg DMBA on day 1 of the study.

TABLE C4
Summary of the Incidence of Nonneoplastic Lesions in Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study

	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
Integumentary System				
Mammary gland	(100)	(100)	(100)	(100)
Dilatation		1 (1%)		
Galactocele		2 (2%)	1 (1%)	3 (3%)
Hyperplasia	1 (1%)	1 (1%)		1 (1%)
Inflammation, chronic active				1 (1%)
Skin	(19)	(8)	(13)	(10)
Cyst epithelial inclusion	6 (32%)		3 (23%)	1 (10%)
Hyperplasia, basal cell	6 (32%)	1 (13%)	1 (8%)	
Inflammation, chronic active	1 (5%)			
Inflammation, granulomatous				1 (10%)
Musculoskeletal System				
None				
Nervous System				
None				
Respiratory System				
Lung	(98)	(100)	(100)	(100)
Inflammation, chronic		1 (1%)		
Inflammation, granulomatous	1 (1%)		1 (1%)	1 (1%)
Thrombosis	1 (1%)	3 (3%)	1 (1%)	2 (2%)
Alveolar epithelium, hyperplasia	21 (21%)	10 (10%)	14 (14%)	10 (10%)
Alveolus, infiltration cellular, histiocyte	21 (21%)	18 (18%)	14 (14%)	15 (15%)
Special Senses System				
None				
Urinary System				
Kidney	(100)	(98)	(100)	(100)
Accumulation, hyaline droplet		1 (1%)		
Hydronephrosis			1 (1%)	
Infarct			1 (1%)	
Infiltration cellular, mixed cell		1 (1%)		
Inflammation, suppurative			1 (1%)	
Mineralization	1 (1%)	1 (1%)	5 (5%)	3 (3%)
Nephropathy	24 (24%)	15 (15%)	27 (27%)	25 (25%)
Thrombosis		1 (1%)		
Pelvis, inflammation, suppurative				1 (1%)

APPENDIX D
MELATONIN ANALYSES

TABLE D1
Pineal Gland Melatonin Concentrations of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	Vehicle Control	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
n	10	10	10	10	10
Week 4	1,310 ± 1,063	1,138 ± 869	947 ± 444	1,036 ± 1,042[b]	937 ± 643
Week 8	2,150 ± 1,095	1,031 ± 470	1,642 ± 1,018	1,957 ± 1,961	1,070 ± 973
Week 12	1,927 ± 1,408	1,698 ± 1,005	2,023 ± 1,383	1,657 ± 1,251	1,675 ± 1,258

[a] Mean pg/pineal gland ± standard deviation; animals were administered 5 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] n=8

TABLE D2
Serum Melatonin Concentrations of Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	Vehicle Control	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
n	10	10	10	10	10
Week 4	30.1 ± 19.8	27.7 ± 17.8	25.2 ± 11.3	26.5 ± 14.8[b]	24.5 ± 19.9[b]
Week 8	105.0 ± 88.5	62.1 ± 14.1	86.3 ± 37.2	76.6 ± 17.9	78.2 ± 47.6
Week 12	43.2 ± 31.3	30.2 ± 16.3	31.3 ± 10.2	29.8 ± 13.2[b]	48.7 ± 36.8[b]

[a] Mean pg/mL ± standard deviation; animals were administered 5 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] n=9

TABLE D3
Pineal Gland Melatonin Concentrations of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	8 mg DMBA Control	8 mg DMBA/ 1 G 50 Hz	8 mg DMBA/ 5 G 50 Hz
n	10	10	10
Week 4	1,820 ± 1,147[b]	1,204 ± 1,029	1,452 ± 1,077
Week 8	928 ± 916	785 ± 560	652 ± 498
Week 12	499 ± 453	720 ± 545	999 ± 694

[a] Mean pg/pineal gland ± standard deviation; animals were administered 2 mg DMBA at the beginning of weeks 1, 2, 3, and 4.
[b] n=9

TABLE D4
Serum Melatonin Concentrations of Female Rats in the Second 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	8 mg DMBA Control	8 mg DMBA/ 1 G 50 Hz	8 mg DMBA/ 5 G 50 Hz
n	10	10	10
Week 4	64.4 ± 25.5	55.7 ± 27.6	58.8 ± 22.3
Week 8	38.7 ± 25.3	41.0 ± 14.5	39.7 ± 21.7
Week 12	39.3 ± 17.9	40.5 ± 13.3	56.0 ± 21.6

[a] Mean pg/mL ± standard deviation; animals were administered 2 mg DMBA at the beginning of weeks 1, 2, 3, and 4.

TABLE D5
Pineal Gland Melatonin Concentrations of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	Vehicle Control	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
n	10	10	10	10	10
Week 4	2,139 ± 2,467	1,236 ± 757	1,007 ± 957	1,309 ± 1,127	1,697 ± 2,098
Week 8[b]	3,521 ± 3,218	3,301 ± 2,677[c]	3,417 ± 2,566	2,319 ± 1,784[d]	1,921 ± 2,128[d]
Week 12	1,472 ± 889	1,432 ± 786	1,711 ± 735	2,556 ± 1,114*	2,322 ± 752*

* Significantly different ($P \leq 0.05$) from 10 mg DMBA control group by Dunnett's test
[a] Mean pg/pineal gland ± standard deviation; animals were administered 10 mg DMBA on day 1 of the study.
[b] Samples were inadvertently thawed approximately 2 days prior to analysis.
[c] n=9
[d] n=8

TABLE D6
Serum Melatonin Concentrations of Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	Vehicle Control	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
n	10	10	10	10	10
Week 4	46.0 ± 21.7	40.2 ± 21.1	39.9 ± 17.2	38.2 ± 18.3	43.8 ± 20.0
Week 8[b]	73.7 ± 59.7	88.7 ± 175.4	53.7 ± 24.4	96.4 ± 120.3	47.4 ± 13.5
Week 12	54.7 ± 16.9	67.4 ± 41.7	75.5 ± 35.9	66.8 ± 11.2	85.6 ± 46.3

[a] Mean pg/mL ± standard deviation; animals were administered 10 mg DMBA on day 1 of the study.
[b] Samples were inadvertently thawed approximately 2 days prior to analysis.

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

TABLE E1
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Female Rats in the First 13-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	20 mg DMBA Control	20 mg DMBA/ 1 G 50 Hz	20 mg DMBA/ 5 G 50 Hz	20 mg DMBA/ 1 G 60 Hz
n	92	86	92	92
Necropsy body wt	328 ± 4	340 ± 5	331 ± 4	344 ± 7*
R. Kidney				
Absolute	1.288 ± 0.013	1.344 ± 0.016*	1.322 ± 0.015	1.299 ± 0.015
Relative	3.94 ± 0.04	3.98 ± 0.05	4.01 ± 0.05	3.84 ± 0.05
Liver				
Absolute	13.745 ± 0.312	13.669 ± 0.234	13.746 ± 0.371	14.050 ± 0.480
Relative	42.18 ± 1.08	40.44 ± 0.63	41.91 ± 1.32	41.69 ± 1.51

* Significantly different (P≤0.05) from the 20 mg DMBA control group by Williams' or Dunnett's test
[a] Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error); animals were administered 5 mg DMBA at the beginning of weeks 1, 2, 3, and 4.

TABLE E2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Female Rats in the 26-Week 7,12-Dimethylbenz(a)anthracene (DMBA) Initiation/Magnetic Field Promotion Study[a]

	10 mg DMBA Control	10 mg DMBA/ 1 G 50 Hz	10 mg DMBA/ 5 G 50 Hz	10 mg DMBA/ 1 G 60 Hz
n	88	85	91	94
Necropsy body wt	379 ± 5	395 ± 6	405 ± 6**	388 ± 5
R. Kidney				
Absolute	1.495 ± 0.021	1.474 ± 0.018	1.540 ± 0.017[b]	1.425 ± 0.025*
Relative	3.97 ± 0.05	3.77 ± 0.05*	3.86 ± 0.06[b]	3.70 ± 0.06**
Liver				
Absolute	15.369 ± 0.340	16.173 ± 0.623	15.812 ± 0.358	15.231 ± 0.362
Relative	40.49 ± 0.67	41.53 ± 1.90	39.24 ± 0.77	39.63 ± 1.13

* Significantly different (P≤0.05) from the 10 mg DMBA control group by Williams' or Dunnett's test
** P≤0.01
[a] Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error); animals were administered 10 mg DMBA on day 1 of the study.
[b] n=90

APPENDIX F
CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

CHEMICAL CHARACTERIZATION AND DOSE FORMULATION STUDIES

PROCUREMENT AND CHARACTERIZATION

7,12-Dimethylbenz(a)anthracene

7,12-Dimethylbenz(a)anthracene (DMBA) was purchased by the analytical chemistry laboratory, Midwest Research Institute (Kansas City, MO), from TCI America (Portland, OR) in one lot (FID01), which was used during the 13-week studies and the 26-week study. Identity, purity, and stability analyses were conducted by the analytical chemistry laboratory. Reports on analyses performed in support of the DMBA initiation/magnetic field promotion studies are on file at the National Institute of Environmental Health Sciences.

The chemical, a light-yellow, crystalline powder with a melting point of 121° to 122° C, was identified as DMBA by infrared and nuclear magnetic resonance spectrometry. All spectra were consistent with those expected for the structure and with the literature spectra (*Aldrich*, 1985, 1993). The infrared and nuclear magnetic resonance spectra are presented in Figures F1 and F2.

The purity of lot FID01 was determined by high-performance liquid chromatography (HPLC) with a Beckman Ultrasphere ODS column, ultraviolet detection at 220 nm, and a mobile phase of acetonitrile:water (85:15). The flow rate was 1 mL/minute. Three impurities with a combined area of approximately 1.4% relative to the major peak area were detected. The purity of lot FID01 was determined to be approximately 99%. These results were in agreement with the purity information supplied by the manufacturer, which indicated a purity of 98.6%.

Bulk chemical stability studies of lot M111384 of DMBA, not used in the current studies, were performed by gas chromatography with a 3% Dexsil 400 on 80/100 Chromosorb W AW glass column with flame ionization detection at an isothermal oven temperature of 300° C. A nitrogen carrier gas at a flow rate of 70 mL/minute was used. Octacosane was used as an internal standard. Results indicated that DMBA did not degrade compared to a frozen reference sample over a 2-week period when stored refrigerated, at room temperature, or warmed to 60° C when protected from light. The bulk chemical was stored at room temperature throughout the studies. Lot FID01 was also evaluated for purity and stability at the end of the last study.

Sesame Oil

Sesame oil was obtained by MRI from Welch, Holme, and Clark Company, Inc. (Newark, NJ), in one lot (39-252), which was used during the 13-week studies and the 26-week study. Identity and peroxide content determinations were performed by the analytical chemistry laboratory. The chemical, a slightly yellow oil, was identified as sesame oil by infrared spectrometry; the spectrum was consistent with that expected for sesame oil. The peroxide content was determined by titration. Samples were dissolved in isooctane:glacial acetic acid (2:3), and saturated potassium iodide was added. After 1 minute, reagent-grade water was added while the solution was stirred magnetically. The solution was titrated with 0.005 N sodium thiosulfate until it became pale yellow; 1% starch indicator was added, and the solution was titrated with additional sodium thiosulfate to the starch endpoint. The peroxide content of the first shipment of sesame oil (used during the first 13-week study and the 26-week study) received by the study laboratory was 0.87 ± 0.10 mEq peroxide/kg. Approximately 10 months later, a peroxide determination was performed on samples from a second shipment of sesame oil (used during the second 13-week study); the peroxide content was determined to be 6.89 ± 0.07 mEq/kg. Bulk sesame oil was stored refrigerated at the study laboratory.

PREPARATION AND ANALYSIS OF DOSE FORMULATIONS

The dose formulations were prepared on the day of dosing by mixing DMBA with sesame oil to give the desired concentration (Table F1). Samples of the 5 and 10 mg/mL formulations prepared on 7 June 1996 were shipped to MRI for analysis to determine dose formulation proficiency. Samples were analyzed by HPLC with a Zorbax C_{18} column with ultraviolet (254 nm) detection and a solvent system of water:acetonitrile:tetrahydrofuran (10:65:25). The flow rate was 1 mL/minute. Octanophenone was added as an internal standard. All samples examined (6/6) were within 2% of the target concentration (Table F2).

Stability studies of 2 and 15 mg/mL formulations were performed by the analytical chemistry laboratory. Samples were analyzed by HPLC as described for the dose formulation proficiency analyses. Stability of the formulations was confirmed for up to 35 days when stored at room temperature or refrigerated at approximately 5° C. Formulations were also stable when stored for 3 hours open to air and light.

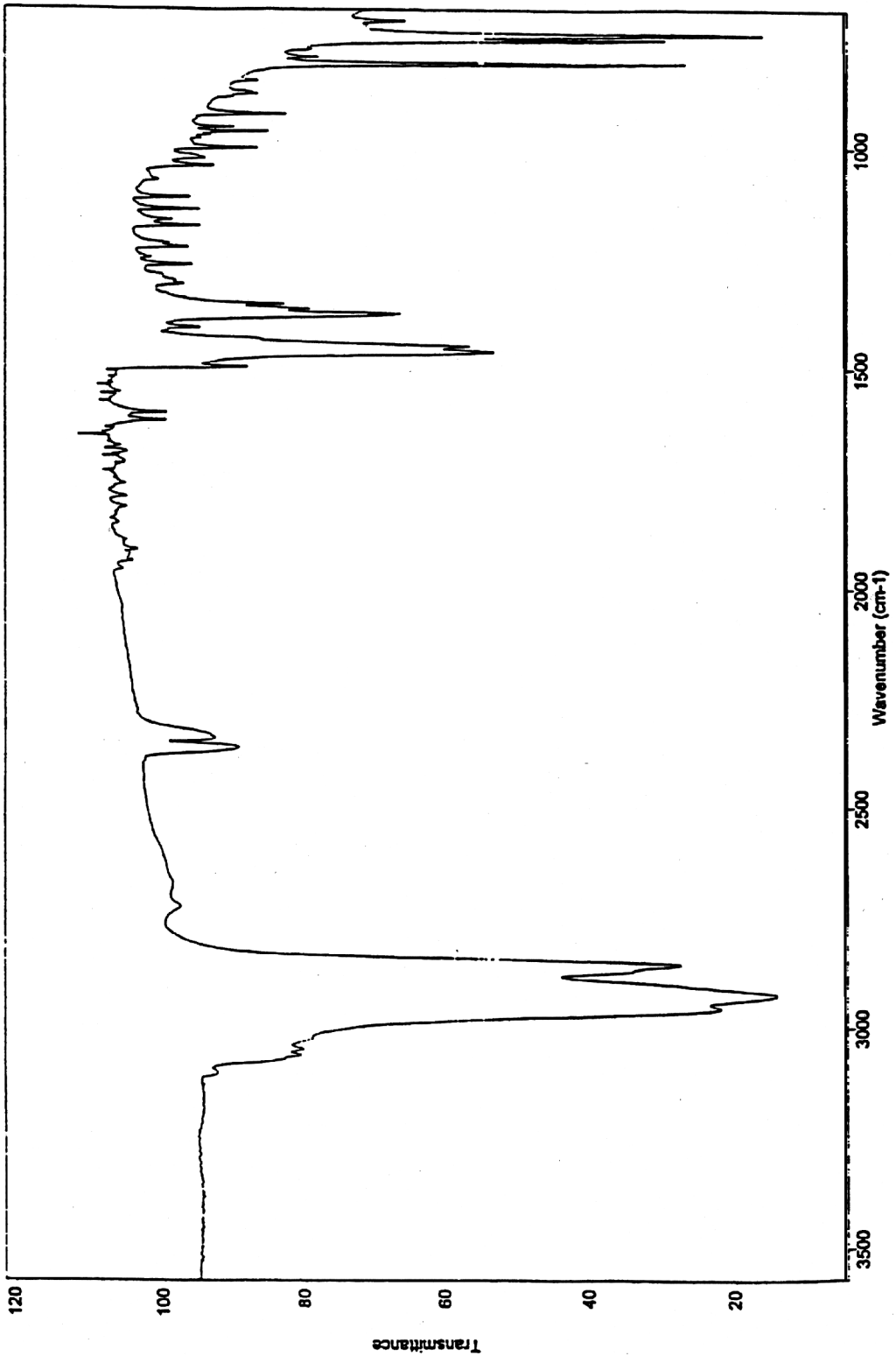
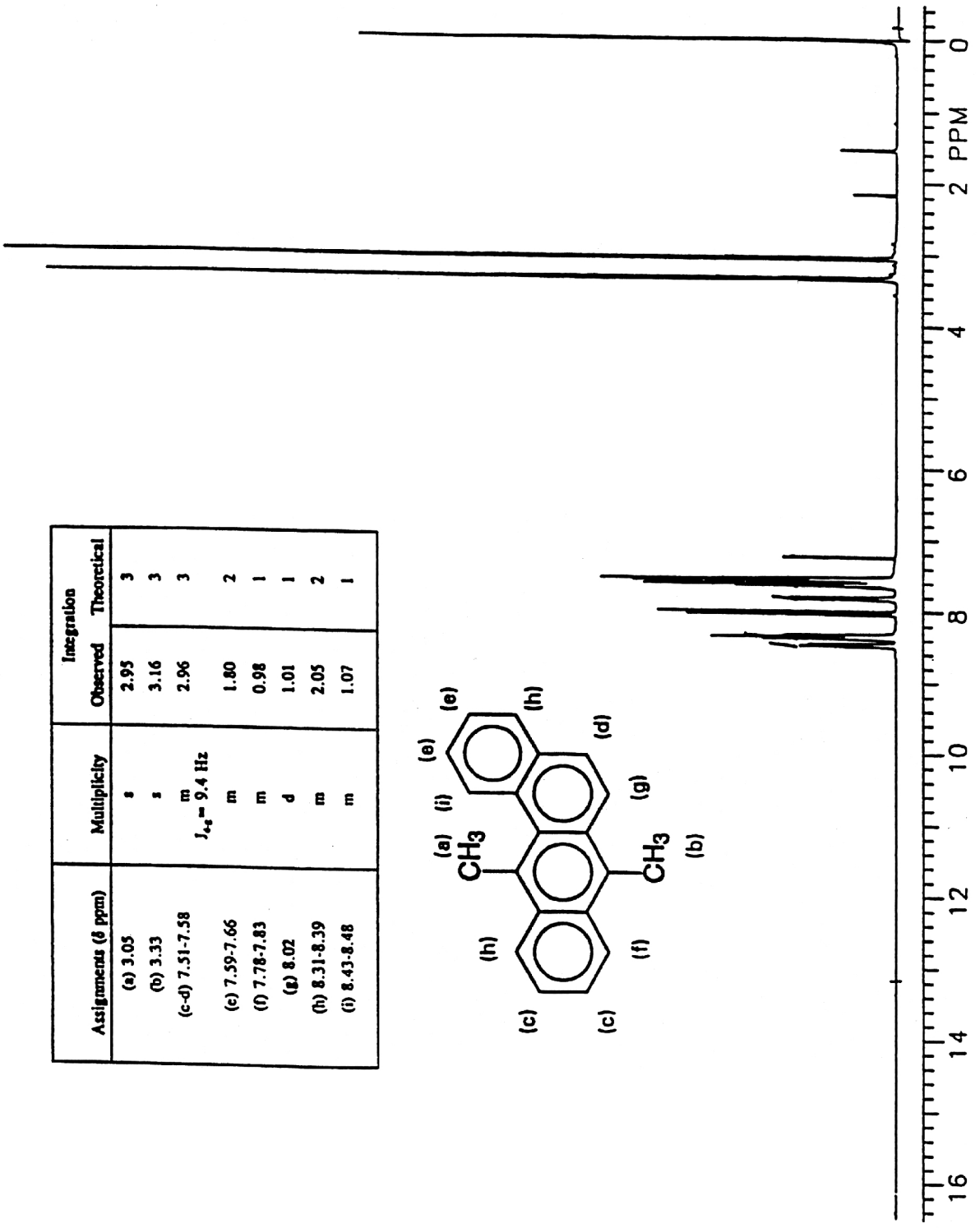


FIGURE F1
Infrared Absorption Spectrum of 7,12-Dimethylbenz(a)anthracene



Assignments (δ ppm)	Multiplicity	Integration Observed	Integration Theoretical
(a) 3.05	s	2.95	3
(b) 3.33	s	3.16	3
(c-d) 7.51-7.58	m J_{4-5} = 9.4 Hz	2.96	3
(e) 7.59-7.66	m	1.80	2
(f) 7.78-7.83	m	0.98	1
(g) 8.02	d	1.01	1
(h) 8.31-8.39	m	2.05	2
(i) 8.43-8.48	m	1.07	1

FIGURE F2
Nuclear Magnetic Resonance Spectrum of 7,12-Dimethylbenz(a)anthracene

TABLE F1
Preparation of Dose Formulations in the 13- and 26-Week 7,12-Dimethylbenz(a)anthracene Initiation/Magnetic Field Promotion Studies

First 13-Week Study	Second 13-Week Study	26-Week Study
Preparation		
Doses were prepared by weighing the appropriate amount of 7,12-dimethylbenz(a)anthracene and mixing it by stirring for 30 minutes with warm sesame oil (≤60° C); solutions were then cooled to room temperature. Doses were prepared on the day of dosing.	Same as first 13-week study	Same as first 13-week study
Chemical Lot Number		
FID01	FID01	FID01
Study Laboratory		
Battelle Pacific Northwest Laboratories (Richland, WA)	Battelle Pacific Northwest Laboratories (Richland, WA)	Battelle Pacific Northwest Laboratories (Richland, WA)

TABLE F2
Results of Analyses of Dose Formulations Prepared for Dose Formulation Proficiency Demonstration in the 13- and 26-Week 7,12-Dimethylbenz(a)anthracene Initiation/Magnetic Field Promotion Studies

Date Prepared	Date Analyzed	Target Concentration (mg/mL)	Determined Concentration[a] (mg/mL)	Difference from Target (%)
7 June 1996	19-20 June 1996	5	4.96	−1
		5	4.98	0
		5	5.02	0
		10	10.12	+1
		10	10.15	+2
		10	10.13	+1

[a] Results of duplicate analyses

APPENDIX G
MAGNETIC FIELD PRODUCTION AND MONITORING

MAGNETIC FIELD PRODUCTION AND MONITORING

METHODS

In all three studies, rats were exposed to either 0, 1, or 5 G 50-Hz magnetic fields because a German study and a Russian study had suggested a promotion effect of 50 Hz (European power-line frequency) on DMBA-induced breast cancer in rats. In the first of two 13-week studies and in a 26-week study presented here, a 1 G 60-Hz (United States power-line frequency) group was also included. The original protocol called for the highest magnetic field intensity to be 10 G, but at this intensity the overlap of magnetic fields (stray fields) from separate exposure areas was excessive. Thus, the protocol was modified, and the highest magnetic field intensity was set at 5 G 50 Hz. Exposed rats were housed in one room (Room 122/126) while the control rats were housed in a separate room (Room 135) (Figure G1).

The magnetic field exposure system consisted of three identical field-generating coil sets, each associated with three animal exposure racks in a single exposure room (Figure G1). Each coil set consisted of four pairs of vertically oriented coils (1.05 × 3.6 m) connected in series and spaced uniformly through the room. Pairs of coils were stacked one above the other. The bottom coils produced a horizontal linear magnetic field (50 or 60 Hz) in one direction while the top coils produced a similar field in the opposite direction. The opposing fields produced by coil pairs functioned to cancel one another outside the area of the exposure rack. Coil wires were embedded in plastic and coils rested on vibration-damping feet to reduce vibration and hum; copper cooling tubes were included to control coil temperature.

Electrical power to the coils was supplied by Techron Model 7570 (Crown International, Elkhart, IN) power amplifiers via condensers that served as power-factor correctors. This arrangement tuned the coils to the proper frequency (50 or 60 Hz) and provided for a highly pure sinusoidal exposure field with a total harmonic distortion of 0.2%. Each series of coils represented a resistance of approximately 8 ohms and inductance of approximately 240 mhenry. Generation of a 5 G magnetic field required 4.5 amps at 415 V (on the coils) and thus produced approximately 200 W of heating.

Regulation and monitoring of magnetic fields and data acquisition were controlled by a Gateway 2000, 486DX33 personal computer housed in a separate control room (Room 130; Figure G1). The control/monitoring computer was equipped with a Hewlett-Packard Model 9231 measurement coprocessor board and a tape drive for system backup. Hewlett-Packard Model 8904A multifunction synthesizer units attached to the control/monitoring computer supplied signals to the power amplifiers to produce 50- or 60-Hz fields. Emdex II data logging units were used to monitor field intensities. Field data were collected by the control computer every 6 minutes, at which time the computer adjusted fields by varying the voltage supplied to the power amplifier. The fields were turned on and off automatically under computer control to provide access to animals for husbandry and observation; exposure was 18.5 hours per day, 7 days per week during the studies. When fields were turned on or off, they were increased or decreased gradually over seven to nine cycles (0.11 to 0.15 seconds) to prevent transients. In addition to the collection of field data, temperature, relative humidity (Omega Engineers, Stamford, CT), and sound (CEL Instruments, Severna Park, MD) sensors provided data to the control/monitoring computer every 6 minutes (Tables G1 and G2). All data generated during the studies were in IBM-PC format and were thus compatible with standard IBM-PC data processing programs. The tape backup was run each day to prevent loss of data due to any control/monitoring computer hard disk failure or a power outage.

In the first 13-week study and in the 26-week study, the stray 60-Hz magnetic fields did not exceed 3 mG in the 1 or 5 G 50-Hz animal exposure areas; however, the stray 50-Hz magnetic fields in the 1 G 60-Hz animal exposure area varied from 5 to 30 mG (11.4 $\pm$ 6.4 mG). In the second 13-week study, only 50-Hz magnetic fields were used, and there were no stray fields of other frequencies. The mean magnetic field intensity during the 13-week and 26-week studies was within 10% of the target at all time points. The mean stray magnetic fields for the control area were less than 1 mG in all three studies, as measured by two control sensors. There was about a 0.2 mG decline in the stray fields during the 26-week study. The stray fields were due to power lines, heating and cooling systems, and other sources. All control values were well below the 1 mG protocol requirement.

FACILITY VALIDATION

Prior to and after the end of the animal studies, studies were performed to characterize 50- and 60-Hz alternating magnetic field intensities, audible sound, electric fields, coil heating, and earth static magnetic fields in the exposure rooms. Magnetic fields were assessed with Emdex field meters (Enertech Consultants) placed at the approximate center position of each cage. Magnetic field data are presented in Table G3. Electric field levels were low (<10 V/m) because cage racks were connected to an electrical ground. Coil heating was negligible at the field levels used in these studies. At 5 G, coils heated less than 1° C and any resulting cage heating was undetectable. Magnetic field characterizations were verified by a representative of the National Institute of Standards and Technology (NIST) (Table G4). Earth's static magnetic fields were also characterized by the NIST representative (Table G4); all were within acceptable ranges. The static magnetic field component parallel to the alternating fields was between 150 and 200 mG.

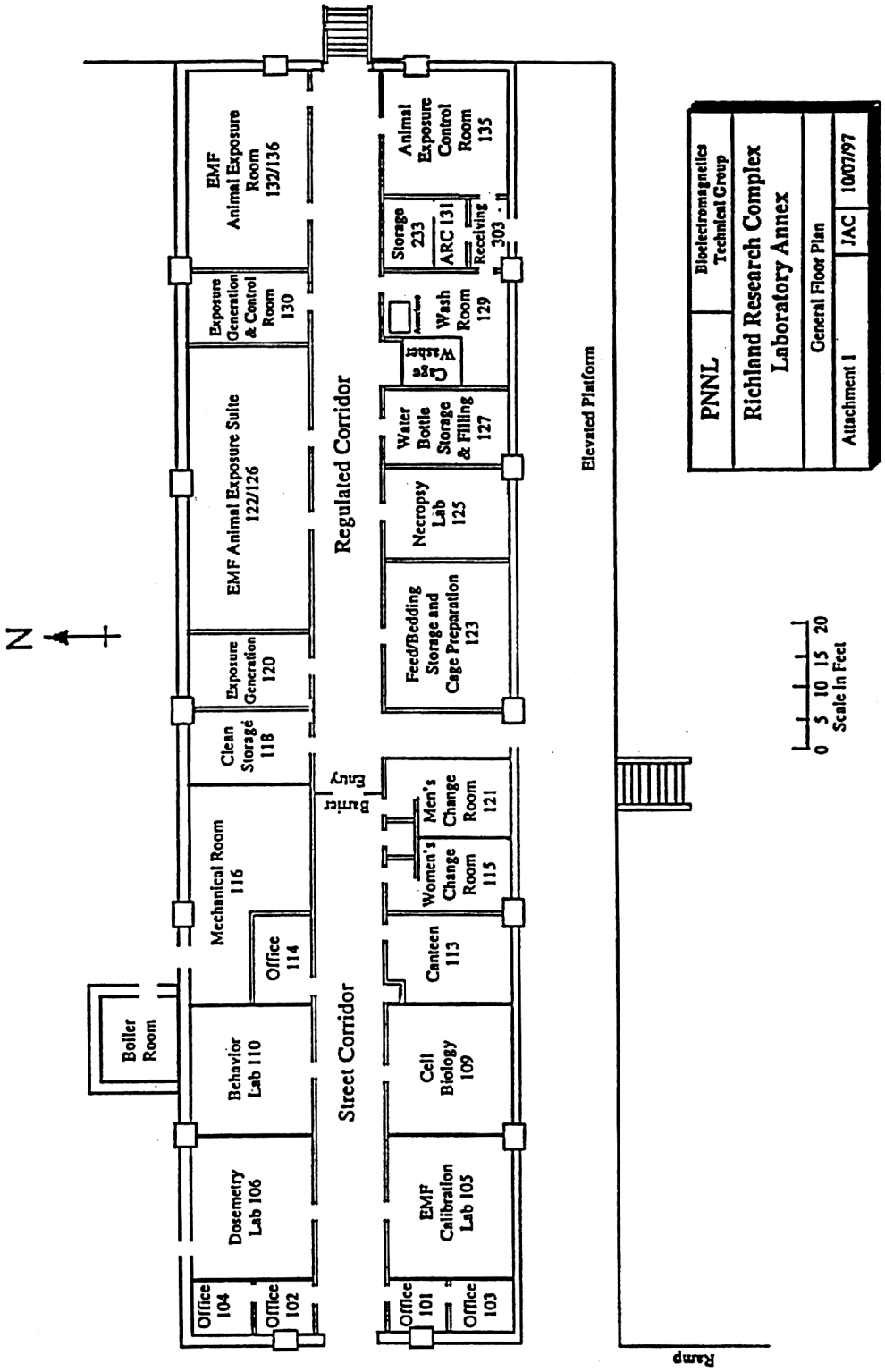


FIGURE G1
Exposure Facility Floor Plan

TABLE G1
Summary of Magnetic Field Intensities in the 13- and 26-Week 7,12-Dimethylbenz(a)anthracene Initiation/Magnetic Field Promotion Studies[a]

	0 G Control	1 G 50 Hz	5 G 50 Hz	1 G 60 Hz
First 13-Week and 26-Week Study[b]				
July 1996	—[c]	1.00 ± 0.004	5.00 ± 0.001	1.00 ± 0.002
August 1996	—	1.00 ± 0.002	5.00 ± 0.002	1.00 ± 0.004
September 1996	—	1.00 ± 0.004	5.00 ± 0.006	1.00 ± 0.006
October 1996	—	1.00 ± 0.006	5.00 ± 0.007	1.00 ± 0.004
November 1996	—	1.00 ± 0.001	5.00 ± 0.008	1.00 ± 0.002
December 1996	—	1.00 ± 0.001	5.00 ± 0.005	1.00 ± 0.001
January 1997	—	1.00 ± 0.002	5.00 ± 0.004	1.00 ± 0.002
Second 13-Week Study				
March 1997	—[d]	1.00 ± 0.001	5.00 ± 0.006	—[e]
April 1997	—	1.00 ± 0.001	5.00 ± 0.006	—
May 1997	—	1.00 ± 0.001	5.00 ± 0.006	—
June 1997	—	1.00 ± 0.000	5.00 ± 0.007	—

[a] Data are presented as the mean magnetic field intensity (G) ± standard deviation.
[b] The first 13-week study took place during the 26-week study (August through November) in the same exposure rooms.
[c] Not monitored during the studies; values measured at the beginning and the end of the studies averaged 0.19 to 0.64 mG.
[d] Not monitored during the study; values measured at the beginning and the end of the study averaged 0.19 to 0.42 mG.
[e] Not applicable; there was no 1 G 60-Hz group in the second 13-week study.

TABLE G2
Summary of Sound Levels in the 13- and 26-Week 7,12-Dimethylbenz(a)anthracene Initiation/Magnetic Field Promotion Studies[a]

	Control Room	Exposure Room
First 13-Week and 26-Week Study[b]		
July 1996	57.24 ± 2.53	62.68 ± 0.26
August 1996	57.35 ± 2.72	63.07 ± 2.02
September 1996	56.00 ± 2.56	65.81 ± 1.63
October 1996	54.60 ± 3.29	65.81 ± 1.64
November 1996	53.05 ± 3.67	63.81 ± 1.50
December 1996	52.31 ± 3.14	63.68 ± 1.40
January 1996	55.54 ± 2.90	61.55 ± 1.86
Second 13-Week Study		
March 1997	56.73 ± 1.91	59.84 ± 1.48
April 1997	57.18 ± 1.67	58.69 ± 1.43
May 1997	55.97 ± 1.13	58.09 ± 1.25
June 1997	55.39 ± 2.19	57.46 ± 2.13

[a] Data are presented as mean sound level (dB) ± standard deviation.
[b] The first 13-week study took place during the 26-week study (August through November) in the same exposure rooms.

TABLE G3
Summary of Magnetic Field Facility Validation at the Beginning and End of the 13- and 26-Week 7,12-Dimethylbenz(a)anthracene Initiation/Magnetic Field Promotion Studies[a]

	Control (East Sensor) (mG)	Control (West Sensor) (mG)	1 G 50 Hz (G)	5 G 50 Hz (G)	1 G 60 Hz (G)
26-Week Study					
Beginning[b]	0.46 ± 0.08	0.64 ± 0.09	0.987 ± 0.061	5.02 ± 0.24	0.994 ± 0.041
End	0.19 ± 0.07	0.42 ± 0.09	1.013 ± 0.061	5.06 ± 0.24	1.013 ± 0.042
Second 13-Week Study					
Beginning	0.19 ± 0.07	0.42 ± 0.09	0.988 ± 0.059	5.01 ± 0.24	—[c]
End	0.20 ± 0.08	0.41 ± 0.08	0.991 ± 0.053	5.01 ± 0.20	—

[a] Data are presented as mean ± standard deviation.
[b] The first 13-week study took place during the 26-week study.
[c] Not applicable; there was no 1 G 60-Hz group in the second 13-week study.

TABLE G4
Generated and Earth's Ambient Magnetic Fields Measured by the National Institute of Standards and Technology During the 13- and 26-Week 7,12-Dimethylbenz(a)anthracene Initiation/Magnetic Field Promotion Studies[a]

	Shelf A	Shelf B	Shelf C	Shelf D
Generated Magnetic Fields (G)				
19-20 June 1996				
Rack 1 – 60-Hz 10 G field[b]	9.89	10.40	10.48	9.93
Rack 3 – 60-Hz 1 G field	0.900	0.930	0.926	0.861
Rack 4 – 50-Hz 1 G field	0.920	0.961	0.945	0.892
24-25 February 1997				
Rack 1 – 60-Hz 1 G field	0.954	1.01	1.03	0.968
Rack 3 – 50-Hz 1 G field	0.932	0.958	1.00	0.962
Rack 4 – 50-Hz 5 G field	4.92	5.00	5.00	4.92
Ambient Static Magnetic Fields (G)				
19-20 June 1996				
Rack 1	0.160	0.167	0.188	0.194
Rack 3	0.158	0.176	0.208	0.221
Rack 4	0.179	0.188	0.192	0.196
24-25 February 1997				
Rack 1	0.171	0.175	0.193	0.187
Rack 3	0.175	0.183	0.210	0.222
Rack 4	0.179	0.188	0.192	0.196

[a] Data presented as the mean of 15 measurements at four shelf positions
[b] The study designs originally incorporated 10 G exposure groups; prior to study initiation, this exposure was changed to 5 G to eliminate field overlap between exposure modules.

APPENDIX H
SENTINEL ANIMAL PROGRAM

SENTINEL ANIMAL PROGRAM

METHODS

Rodents used in the Carcinogenesis Program of the National Toxicology Program are produced in optimally clean facilities to eliminate potential pathogens that may affect study results. The Sentinel Animal Program is part of the periodic monitoring of animal health that occurs during the toxicologic evaluation of chemical compounds. Under this program, the disease state of the rodents is monitored via serology on sera from extra (sentinel) animals in the study rooms. These animals and the study animals are subject to identical environmental conditions. The sentinel animals come from the same production source and weanling groups as the animals used for the studies of chemical compounds.

Serum samples were collected from randomly selected rats during the 13-week studies and the 26-week study. Blood from each animal was collected and allowed to clot, and the serum was separated. The samples were processed appropriately and sent to Microbiological Associates, Inc. (Bethesda, MD), for determination of antibody titers. The laboratory serology methods and viral agents for which testing was performed are tabulated below; the times at which blood was collected during the studies are also listed.

Method and Test	Time of Analysis
First 13-Week Study	
ELISA	
Mycoplasma arthritidis	Study termination
Mycoplasma pulmonis	Study termination
PVM (pneumonia virus of mice)	Study termination
RCV/SDA (rat coronavirus/ sialodacryoadenitis virus)	Study termination
Sendai	Study termination
Hemagglutination Inhibition	
H-1 (Toolan's H-1 virus)	Study termination
KRV (Kilham rat virus)	Study termination
Second 13-Week Study	
ELISA	
M. arthritidis	Study termination
M. pulmonis	Study termination
PVM	Study termination
RCV/SDA	Study termination
Sendai	Study termination
Immunofluorescence Assay	
RCV/SDA	Study termination
Hemagglutination Inhibition	
H-1	Study termination
KRV	Study termination

Method and Test	Time of Analysis
26-Week Study	
ELISA	
M. arthritidis	Study termination
M. pulmonis	Study termination
PVM	Study termination
RCV/SDA	Study termination
Sendai	Study termination
Hemagglutination Inhibition	
H-1	Study termination
KRV	Study termination

RESULTS

Three rats in the first 13-week study had positive titers for *M. arthritidis* and one rat in the second 13-week study had a positive titer for RCV/SDA. Further evaluation of samples positive for *M. arthritidis* by immunoblot and Western blot procedures indicated that the positive titers may have been due to cross reaction with antibodies of nonpathogenic *Mycoplasma* or other agents. Only sporadic samples were positive and there were no clinical findings or histopathologic changes of *M. arthritidis* infection in animals with positive titers. Retesting of the sample positive for RCV/SDA by the study laboratory using an immunofluorescence assay was negative. Accordingly, *M. arthritidis*- and RCV/SDA-positive titers were considered to be false positives.