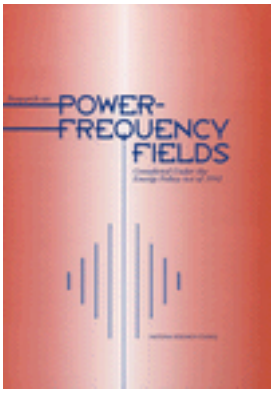

Research on Power-Frequency Fields

Completed Under the Energy Policy Act of 1992

Committee to Review the Research Activities Completed Under the Energy Policy Act of 1992
Board on Radiation Effects Research
Commission on Life Sciences
National Research Council

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PREFACE

Since the 1970s, concerns about health hazards associated with electric and magnetic fields from power lines and from workplace, school, and household use of electricity have led to many studies and continued controversy about whether adverse health effects occur. In the Energy Policy Act of 1992 (Public Law 102–486), Congress authorized a focused national research program to study the possible health effects of exposure to low-intensity, 60-hertz electric and magnetic fields. In response to this legislation and at the request of the Department of Energy (DOE), the National Research Council established a committee under the Board on Radiation Effects Research (BRER) in the Commission on Life Sciences (CLS) to aid in its review of the power-frequency magnetic field research activities completed under the Electric and Magnetic Fields Research and Public Information Dissemination (EMF-RAPID) program that was authorized by the Energy Policy Act. The Research Council's Committee to Review the Research Activities Completed Under the Energy Policy Act of 1992 (EPACT) was asked to review the EMF-RAPID program implemented by DOE and the National Institute of Environmental Health Sciences (NIEHS), and research strategies suggested by other federal and nonfederal groups.

The Research Council committee consists of persons experienced in bioelectromagnetics, biophysics, electrical engineering, epidemiology, *in vivo* animal research, toxicology, neurobehavioral and neuroendocrine science, molecular biology and genetics, mechanisms of cancer induction, and risk assessment. One member of the committee was also a member of the Research Council committee on the Possible Effects of Electromagnetic Fields on Biologic Systems, which was charged with the review of the research literature related to possible adverse health effects of power-frequency magnetic fields. The current committee also includes a former president and a former member of the board of directors of the Bioelectromagnetics Society.

The committee's study was conducted under the general guidance of BRER and CLS. The Committee has had access to documents provided by DOE and NIEHS that describe the EMF-RAPID program, 11 completed engineering reports, draft project summaries of 61 EMF-RAPID-funded projects, three reports on EMF-RAPID science review symposia, the NIEHS working-group report, and two booklets published as part of the EMF-RAPID information dissemination program.

This is the second and final report of the Research Council committee's review. The first (interim) report was produced by a committee, three of whose members are members of this committee. The committee's work was aided substantially by the cooperation of Imre Gyuk of DOE and Gary Boorman, Naomi Bernheim, Michael Galvin, Christopher Portier, and Mary Wolfe of NIEHS. Its report could not have been completed without the untiring effort of Rick Jostes, who, in addition to being responsible for keeping the committee on track and dealing with the federal agencies, contributed his own insights as a researcher in this field. He was well assisted by Peggy Johnson, Eric Truett, and Isaf Al-Nabulsi of the BRER staff.

John F. Ahearne

Chair, Committee to Review the Research Activities Completed Under the Energy Policy Act of 1992.

REVIEWER ACKNOWLEDGMENTS

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise in accordance with procedures for reviewing NRC and IOM reports approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the NRC in making the published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The content of the final report is the responsibility of the NRC and the study committee, and not the responsibility of the reviewers. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals, who are neither officials nor employees of the NRC, for their participation in the review of this report:

Robert K. Adair, Yale University
Leeka Kheifets, Electric Power Research Institute
J. Ross MacDonald, Chapel Hill, NC
John E. Moulder, Medical College of Wisconsin
Richard Saunders, National Radiological Protection Board, UK
Herman P. Schwan, The University of Pennsylvania
Charles F. Stevens, The Salk Institute for Biological Studies

While the individuals listed above have provided many constructive comments and suggestions, it must be emphasized that responsibility for the final content of this report rests entirely with the authorizing committee and the NRC.

CONTENTS

EXECUTIVE SUMMARY

Public concern has grown in recent years over the possibility that subtle or delayed adverse health effects might result from exposure to power-frequency magnetic fields surrounding transmission and distribution lines and the electrical devices that have become common in residences and workplaces. Concern over the possible health effects of exposure to low-intensity, 60-hertz (60-Hz) power-frequency magnetic fields was a driving force in setting research agendas for government and private organizations and led to a series of workshops held in 1990–1992 with participation by representatives of the Department of Energy (DOE), the National Institute for Occupational Safety and Health (NIOSH), the Environmental Protection Agency (EPA), the Electric Power Research Institute (EPRI), public utilities, state governments, and the scientific community. The workshops were designed to elicit strategies for research in the biologic effects of magnetic field (MF)[1] exposure, and various methods of disseminating research findings to the public were considered. The workshops provided the basic framework for establishment of a national program in electric and magnetic field research that was ultimately authorized by Congress in the Energy Policy Act of 1992 (Public Law 102–486). This program is commonly called EMF-RAPID (Electric and Magnetic Fields Research and Public Information Dissemination). An effort was made to ensure that the EMF-RAPID research activity was coordinated and targeted to produce answers to a number of important questions raised in the Energy Policy Act:

"(1) Determine whether or not exposures to electric and magnetic fields produced by the generation, transmission, and use of electrical energy affect human health;
(2) carry out research, development, and demonstration with respect to technologies to mitigate any adverse human health effects; and
(3) provide for dissemination of information . . . to the public".

CHARGE TO THE COMMITTEE

In response to a request from the DOE, following the directives of the Energy Policy Act of 1992, the National Research Council established a committee of scientists and engineers to review the activities conducted under the EMF-RAPID program. The Research Council committee, the Committee to Review the Research Activities Completed Under the Energy Policy Act of 1992 (known as the EPACT Committee), also was asked to review the research agenda and strategies adopted by DOE and the National Institute of Environmental Health Sciences (NIEHS), and those suggested by other federal and nonfederal groups. Specifically, the EPACT Committee was asked to:

- Review and evaluate the scientific and technical content of projects completed under the EMF-RAPID program. The results of this review, with implications of the effect and significance of the work in addressing the issues defined in the national EMF research plan, are to be reported to DOE, the EMF Interagency Committee (IAC), and the National EMF Advisory Committee (NEMFAC).

[1] Most of the projects evaluated by the committee focused on *power-frequency magnetic fields*, sometimes referred to in this report simply as *magnetic fields* (or MF). In the rare cases where electric fields are described, the term electric fields (or EF) is used. When referring to publications or project titles, or when citing material containing the electromagnetic field abbreviation *EMF*, we have retained the abbreviation EMF as the author's used it.

- Review continuing research activities for scientific content and suitability to meet the goals of the EMF-RAPID plan. Continuing projects will be given only a brief review with regard to content and direction, based on a brief statement of scope, goals, and progress submitted to the committee using a format developed specifically for that purpose to assess their potential to fulfill the goals of the national program.
- Recommend modifications to the EMF-RAPID program, as appropriate, based on information the committee acquires concerning new research findings not available when the national research agenda was developed, from briefings the committee might request, and from analysis of research strategies developed by other groups.
- Assess the scientific and technical content, and make recommendations as deemed necessary, for activities initiated under the EMF-RAPID agenda to promote the transfer of information derived from research projects.

This report, submitted at the conclusion of the EMF-RAPID program, reviews and evaluates the scientific and technical content of projects completed under the EMF-RAPID program and makes recommendations regarding the transfer of information derived from research projects. The focus of this report is on the research conducted within the EMF-RAPID program. Other work is discussed only in the context of important findings that were made in projects conducted as part of the EMF-RAPID program. An interim report, *EMF Research Activities Completed Under the Energy Policy Act of 1992*, was issued by this committee in 1995.

CONCLUSIONS

Program limitations

The EMF-RAPID program faced many organizational and administrative obstacles. For example, there was a delay of about 2 yrs in funding implementation, and total funding (about $41 million) fell substantially short of the original planned level ($65 million). Without the delay additional peer-reviewed publications might have been available as EMF-RAPID came to a close for appropriate agencies to evaluate potential health effects. If the additional monies had been available, it would have been possible to include additional important activities such as focused interlaboratory replication projects. Furthermore, the program used the National Institutes of Health (NIH) grant process for the biology studies administered by NIEHS. That process, as implemented in this program, did not lead to complete reports at project completion, because the goal was to produce papers in the peer-reviewed literature and this goal was not always met by the individual projects. Project summaries available at program's end were of uneven quality, and the majority of the summaries did not provide complete reports of the research effort. The lack of complete reports and limited availability of published journal articles at the time the program ended made it difficult to judge the quality, completeness, or significance of the biologic studies funded by the EMF-RAPID program. The NIH-style approach also provided considerable flexibility to the principal investigators in

implementation of their research plans. Those complications reduced the information available in late 1998 and made it difficult to assess the usefulness and quality of the NIEHS portion of the EMF-RAPID program.

EMF-RAPID engineering research program

The EMF-RAPID engineering research program, administered by DOE, used a contract-funding mechanism; therefore, 11 complete and final reports were available to the EPACT Committee at the program's end. Many of the engineering studies were of little use, principally because they were initiated without a hypothesis related to what effect was to be studied. Furthermore, most of the reports were completed as the EMF-RAPID program was ending and so had little effect on the program as it developed. Projects that focused on developing methods and protocols for power-frequency magnetic field measurements were conducted simultaneously with projects designed to characterize human exposure, so the recommendations of protocol-development studies were of little value to the projects designed to characterize human exposure. Of the five projects concerned with characterizing human exposures in the home, workplace, and public areas, only the Enertech study of 1,000 persons (Enertech Consultants 1998b) provided a robust set of data that one could use to analyze the typical range of human exposure to MFs in the United States. The EMF database project is of no practical use at the time of this review, because no major data sets have been entered from potential users. Of the 11 projects completed at the time of the review and available to the committee, only two are regarded as noteworthy: the Enertech study (Enertech Consultants 1998b) and the Evaluation of Field-Reduction Technologies project (IIT 1997), concerned with mitigation of MF exposures, which yielded useful results on field-reduction technologies for a variety of common sources of power-frequency MF exposures. The other engineering studies are of value primarily as a compilation of state-of-the-art MF measurement practices.

The engineering studies contributed nothing directly to the question of health effects but did show that temporally-averaged MF exposures of subjects in a broad range of occupations and residential environments were remarkably similar. A major conclusion highlighted by the engineering effort is that the range of time-averaged exposures is very small, that most people are exposed to 0.1–0.2 microtesla (0.1–0.2 μT), 60 Hz MF, and very few to more than 0.4 μT. That finding demonstrates that it is extremely difficult to obtain large numbers of subjects for epidemiologic studies with substantially different, temporally-averaged MF exposures. The inability to identify heavily-exposed and minimally-exposed populations is a severe limitation in epidemiologic efforts to assess possible risks associated with MF exposure. In addition, the results of the engineering studies demonstrated that any MF-induced biologic effects would have to exhibit remarkably low response thresholds (about 0.1–0.2 μT) in order to have important implications for adverse human health effects, or alternatively, that such health effects would have to be shown to be caused by high but infrequent exposures.

EMF-RAPID scientific research program (biology)

Quality control at program initiation

The decision to provide biologists with engineering help for generation and characterization of MFs at the beginning of the program was important, as was the effort to encourage investigators to make greater use of conventional quality-control procedures, such as blinding, replication, and positive controls. This programmatic objective was a direct result of the practices developed by DOE as it conducted its bioelectromagnetics program in 1975–1995.

Categories of results at program completion

Biologic studies in the EMF-RAPID program can be grouped in five categories:

1. No MF results reported in project summary. These are projects that at the time of reporting had not produced either positive or negative findings.
2. No EF or MF effects reported. These are studies in which the investigators sought but were unable to find effects of EF or MF exposure.
3. Effects reported but data insufficient to calculate magnitude of effect.
4. EF or MF effects reported and data sufficient to calculate magnitude of effect.
5. Replications of earlier positive reports. These studies attempted to reproduce earlier reports of MF effects.

Value of studies for evaluation of possible power-frequency magnetic field health effects

Project reports in the first and third categories have limited value for evaluation of MF health effects. The second category contains projects which showed no EF or MF effects at the time of review. Many of the EMF-RAPID projects, instead of being well-defined studies to replicate earlier positive claims, investigated new biologic end points. Some of the reports available to the committee do not give the rationale for the research, and most of these studies had negative results. In the case of the fourth category, in which results were reported with supporting data sufficient to estimate magnitude of effect, the committee is unaware of replications of these studies in other laboratories. Because the existence of any biologic effects of low-level, power-frequency MFs is still in question, the fifth category, consisting of attempts to replicate previously reported positive effects, has been the most important part of the EMF-RAPID program.

It should be noted that normal exposures in the domestic setting are of the order of 0.1–0.2 μT. "High" exposures in epidemiology are > 0.4 μT. On that basis, biologic effect studies in the EMF-RAPID program used "high" exposures. Much of the program

employed fields 3 to 4 orders of magnitude greater than those which the general human population normally experiences.

Important findings

The NIEHS biologic-research program made two important contributions that reduce somewhat the concern about whether the use of electric power might have adverse health effects. The first contribution was the effort to replicate previous reports of extremely-low-frequency (ELF) MF biologic effects, mostly through *in vitro* studies. All the attempted replications in the EMF-RAPID program have had negative or equivocal results. Because these replications were conducted in an environment of increased concern for field characterization and protocol development, their results are persuasive.

The second important contribution was the completion of several investigations of the relationship between MF exposure and cancer through controlled laboratory experiments in animal models. Nearly all the animal studies relevant to the EMF-cancer issue had negative results, even at field levels that were orders of magnitude greater than the levels typical of human exposure, including two of singular importance: the IIT Research Institute life-span exposure study examining cancer initiation by ELF MFs (NTP 1998a), a large screening study funded by NIEHS outside the EMF-RAPID program; and the EMF-RAPID-funded Battelle study on breast-cancer promotion in rats by ELF MFs (NTP 1998b), a replication of work by Loescher (Loescher and others 1993) which had previously reported positive findings. The outcomes of the animal experiments completed under EMF-RAPID, like those conducted elsewhere, do not support the hypothesis that MF exposure is involved in the carcinogenic process.

In vitro studies

Evaluation of the question of possible health effects of power-frequency MFs is handicapped by the absence of any robust effect that can be reproduced consistently from one independent laboratory to another. The EMF-RAPID *in vitro* replication studies further illustrate this problem. Their findings demonstrate that, without independent confirmation, caution must be exercised with regard to the weight that can be given to reports of effects, even if the effects appear to be large.

The *in vitro* results, for the most part, do not show effects that can be demonstrated as resulting from MF exposures at the field intensities that were explored. Few studies showed effects; the few reported effects were small and their connection to disease processes are speculative at best and irrelevant at worst. The results of several *in vitro* replication studies on gene expression were important in that they failed to support previous indications of a MF effect.

Many of the *in vitro* studies described did not develop surveys that permit generalization of any positive correlation between MFs and biologic response. The cell lines or the gene-expression assays were usually few and limited in scope or sensitivity. Some papers reported to be submitted or in preparation have not appeared, raising concerns about the reproducibility or quality of their data.

Is cancer a possible MF health effect?

The EMF-RAPID biologic research contributed little evidence to support the hypothesis that a link exists between MF and cancer. The results of the *in vitro* studies do not support an MF effect on cancer initiation, promotion, or progression, and they should be recognized as important studies in the overall evaluation of potential carcinogenic effects of MFs. Attempts to study the relationship between MFs and cancer in rodents have comprised more than a dozen studies including the EMF-RAPID-funded project at Battelle (NIEHS 1998a). The results of this latter study were negative in spite of the exposure of the animals in these experiments to extremely high MFs for long periods. The largest fields were 5,000 μT, which is more than four orders of magnitude greater than the field levels found in typical homes.

In contrast with the laboratory research, some epidemiologic studies have reported differences in the incidence of cancer associated with MF exposures that differ by as little as 0.2 to 0.4 μT. Estimates of MF exposures in epidemiology are crude at best. Because there is no support for a MF-cancer link in animal experiments where very large, carefully monitored fields have been used, occasional suggested epidemiologic associations between MFs and cancer are not supported by the EMF-RAPID animal data. It may be that the observed epidemiologic associations either are too weak to be significant or could be attributable to one or more confounding variables that have not been identified.

When the EMF-RAPID program began, emphasis was placed on two important phenomena—cancer promotion and gene-related effects *in vitro.* Experiments supported by EMF-RAPID provided some evidence to support, and considerable evidence to refute the view that power-frequency MFs can have biologic effects. Evidence of any robust and replicated effects on the development of cancer is lacking. That leaves the database slightly larger and the conclusions essentially unchanged from the Research Council's most recent review (NRC 1997).

Funding mechanism

The committee concludes that the NIEHS EMF-RAPID biologic research program would have benefited from a contract-funding approach with a requirement for complete reports and/or peer-reviewed publications at program's end. The investigator-initiated grant approach is excellent for basic research, but it is not effective for dealing with a time-limited, focused research program involving an applied-research question. The grant mechanism offers investigators freedom to change the focus of their research, provides too little opportunity for program management, and does not require timely, detailed reporting of results. As previously noted, the lack of complete reports and limited availability of published journal articles at the time the program ended made it difficult to judge the quality, completeness, or significance of the biologic studies funded by the EMF-RAPID program. At a minimum, complete, detailed, and accurate project reports should have been required of the investigators at program's end.

EMF-RAPID communication program

The communication effort initiated by EMF-RAPID is reasonable. The two booklets and the telephone information line are useful, as is the EMF-RAPID Internet site. There are two limitations to the effort. First, it is largely passive, responding to inquiries and providing information, rather than being active. Second, much of the information produced is in a scientific format not readily understandable by the public.

The three NIEHS review symposia (NIEHS 1997; NIEHS 1998b; NIEHS 1998c) provided an additional forum for communication among scientists and engineers interested in MF and health. A fourth review symposium presented projects completed in the EMF-RAPID engineering program (NIEHS 1998d). The committee concludes that the most important accomplishment of the three biology review symposia was to educate newcomers who were brought into the risk-assessment process being considered by NIEHS. The scientific value of the literature reviews produced by meetings is less than that of the 1997 Research Council report (NRC 1997), the NIEHS working-group report (NIEHS 1998a), or other published reviews.

The NIEHS working group[2] produced an extensive, updated review of the entire literature (NIEHS 1998a) related to all aspects of research on the effects, if any, of MFs—a useful accomplishment that unfortunately was overshadowed by the use of the International Agency for Research on Cancer (IARC) method to review the status of MFs as a potential human carcinogen. Labeling power-frequency magnetic fields a class 2B human carcinogen (possible human carcinogen) conveys to the public a conclusion that our committee believes is not supported by the underlying research. The committee notes that no working-group members voted that MFs belonged in the "carcinogenic" classification (IARC 1) and no members voted for the "probably carcinogenic" classification (IARC 2A).

The Electric and Magnetic Fields Research and Public Information Dissemination program, in its relatively brief existence, has achieved a number of important objectives. There has been an increase in the research activity devoted to possible adverse effects of exposure to MFs on human health. An effort was made to ensure that this research activity was coordinated and targeted to produce answers to a number of important questions raised in the Energy Policy Act of 1992. From a technical perspective, the EMF-RAPID program has helped in an incremental manner to reduce uncertainty, strengthening the conclusion that power-frequency MFs are unlikely to have significant adverse effects on public health. The engineering studies underscore the fact that time-averaged MF exposures in a wide variety of occupations are remarkably similar, which has implications for the interpretation and design of epidemiologic investigations. Good science and good engineering make it essential to distinguish between repeatable results that correspond to testable hypotheses and empirical observations that are not predicted and not reproducible. Large amounts of data do nothing to strengthen claims of cause and effect that are fundamentally weak. The literature on laboratory studies of this

[2] NIEHS was directed by Congress to submit an evaluation of the potential human health effects of ELF-EMF exposure. A subcommittee began reviewing the literature and completed a first draft of a literature review in December, 1997. NIEHS selected 31 scientists in and outside EMF research to make up a Working Group which met 16–24 June 1998 in Brooklyn Park, MN to review the published information on possible EMF health effects. Using International Agency for Research on Cancer classifications, the working group produced a report identifying EMF as a "possible human carcinogen".

subject contains many conflicting claims. One way to deal with the situation is to subject the most promising positive reports to multiple independent replications. EMF-RAPID made a substantial start on that task. The largely negative results of the replication studies reduce the credibility of many of the original claims of MF effects.

The committee observed that several aspects of the national EMF research plan were not addressed, especially in epidemiologic studies and policy analysis. The lack of meaningful efforts in these fields (only one project was funded in each) probably was due to the lack of adequate time and to funding limitations.

An earlier Research Council assessment of the available body of information on biologic effects of power-frequency magnetic fields (NRC 1997) led to the conclusion "that the current body of evidence does not show that exposure to these fields presents a human health hazard. Specifically, no conclusive and consistent evidence shows that exposures to residential electric and magnetic fields produces cancer, adverse neurobehavioral effects, or reproductive and developmental effects". The new, largely unpublished contributions of the EMF-RAPID program are consistent with that conclusion. We conclude that no finding from the EMF-RAPID program alters the conclusions of the previous NRC review on the Possible Effects of Electromagnetic Fields on Biologic Systems (NRC 1997). In view of the negative outcomes of EMF-RAPID replication studies, it now appears even less likely that MFs in the normal domestic or occupational environment produce important health effects, including cancer.

RECOMMENDATIONS

The results of the EMF-RAPID program do not support the contention that the use of electricity poses a major unrecognized public-health danger. Basic research on the effects of power-frequency magnetic fields on cells and animals should continue, but a special research funding effort is not required. Investigators should compete for funding through traditional research-funding mechanisms. If future research on this subject is funded through such mechanisms, it should be limited to tests of well-defined mechanistic hypotheses or replications of reported positive effects. If carefully performed, such experiments will have value even if their results are negative. Special efforts should be made to communicate the conclusions of this effort to the general public effectively.

The following recommendations are made by the committee:

1) The committee recommends that no further special research program focused on possible health effects of power-frequency magnetic fields be funded.
2) If, however, Congress determines that another time-limited, focused research program on the health effects of power-frequency magnetic fields is warranted, the committee recommends that emphasis be placed on replications of studies that have yielded scientifically promising claims of effects and that have been reported in peer-reviewed journals. Such a program would benefit from the use of a contract-funding mechanism with a requirement for complete reports and/or peer-reviewed publications at program's end.

3) The committee recommends that no further engineering studies be funded unless a biologic effect that can be used to plan the engineering studies has been determined.
4) NIEHS should collect all future peer-reviewed information resulting from the EMF-RAPID biology projects and publish a summary report of such information periodically on the NIEHS Web site.
5) The committee recommends that further material produced to disseminate information on power-frequency magnetic fields be written for the general public in a clear fashion. The Web site should be made more user-friendly. The booklet *Questions and Answers about EMF* should be updated periodically and made available to the public.

INTRODUCTION

The use of electricity in residential and occupational settings benefits society. The ever-expanding use of electricity has not, however, come without some risks, most notably the potential for shocks and bums from contact with energized electrical conductors. *Vital Statistics of the U.S.* (DHHS 1992) reported that 525 deaths in the United States in 1992 were caused by accidental electrocution; that amounts to an annual risk of two fatalities per 1,000,000 population per year.

Public concern has grown in recent years over the possibility that more subtle or delayed adverse health effects might result from exposure to power-frequency magnetic fields surrounding transmission and distribution lines and the electrical devices that have become common in residences and workplaces. Concern over the possible health effects of exposure to low-intensity, 60-hertz (60-Hz) power-frequency magnetic fields was a driving force in setting research agendas for government and private organizations and led to a series of workshops held in 1990–1992 with participation by representatives of the Department of Energy (DOE), the National Institute for Occupational Safety and Health, the Environmental Protection Agency, the Electric Power Research Institute, public utilities, state governments, and the scientific community. The workshops were designed to elicit strategies for research in the biologic effects of magnetic field (MF) exposure, and various methods of disseminating research findings to the public were considered. The workshops provided the basic framework for establishment of a national program in electric and magnetic field research that was ultimately authorized by Congress in the Energy Policy Act of 1992 (Public Law 102–486). This program is commonly called EMF-RAPID.

CONGRESSIONAL HEARINGS

Two congressional hearings also were instrumental in developing the Energy Policy Act of 1992 and in implementing the research program established under the act. The first was held before the Subcommittee on Natural Resources, Agriculture Research, and Environment of the House Committee on Science, Space, and Technology. The hearing, held on July 25, 1990, was chaired by Rep. James H. Scheuer (New York). Testimony was presented by members of Congress and federal agencies, academic scientists, and representatives of electric power companies and commercial businesses with a strong interest in the outcome of research on the human health effects on MFs. The testimony presented at the heating was important in developing the goals and implementation strategy of the Energy Policy Act.

After passage of the Energy Policy Act, a second hearing was held before the Subcommittee on Energy and Power of the House Committee on Energy and Commerce. The hearing, held on April 1, 1993, was chaired by Rep. Phillip R. Sharp (Indiana). It involved testimony by officials of DOE and the National Institute of Environmental Health Sciences (NIEHS) and three scientists with expertise in epidemiology, risk analysis, and basic science related to MF effects on human health. The primary objective of this heating was to impress on DOE and NIEHS that members of Congress had a strong interest in the outcome of research funded through the Energy Policy Act.

THE ENERGY POLICY ACT OF 1992

In item 303, section 2118, the act outlined a national program—the Electric and Magnetic Fields Research and Public Information Dissemination (EMF-RAPID) program—intended to be a partnership between government and industry. Three main directives were given: to determine whether exposure to 60-Hz MFs produced by the generation, transmission, and use of electric energy affects human health; to carry out research in and development and demonstration of technologies that could mitigate any adverse human health effects; and to provide for dissemination of information related to possible human health effects of MF exposure. The legislation also called for establishment of a National EMF Interagency Committee (IAC) and a National EMF Advisory Committee (NEMFAC) to guide these efforts. The legislation directed the secretary of energy to enter into an agreement with the National Academy of Sciences (NAS) whereby NAS would evaluate the research activities completed under the program and report its findings to DOE, IAC, and NEMFAC.

ELECTRIC AND MAGNETIC FIELDS RESEARCH AND PUBLIC INFORMATION DISSEMINATION PROGRAM

The Electric and Magnetic Fields Research and Public Information Dissemination program, in its relatively brief existence, has achieved a number of important objectives. There has been an increase in the research activity devoted to possible adverse effects of exposure to MFs on human health. An effort was made to ensure that this research activity was coordinated and targeted to produce answers to a number of important questions raised in the Energy Policy Act of 1992 (Public Law 102–486):

"(1) Determine whether or not exposures to electric and magnetic fields produced by the generation, transmission, and use of electrical energy affect human health;
(2) carry out research, development, and demonstration with respect to technologies to mitigate any adverse human health effects; and
(3) provide for dissemination of information . . . to the public".

The act further specifies that the program shall provide for:

"(1) the collection, compilation, and dissemination of scientifically valid information on

(A) possible human health effects of electric and magnetic fields;
(B) the types and extent of human exposure to electric and magnetic fields in various occupational and residential settings;
(C) technologies to measure and characterize electric and magnetic fields; and
(D) methods to assess and manage exposure to electric and magnetic fields.

(2)

(A) research on mechanisms by which electric and magnetic fields interact with biological systems; and
(B) epidemiologic research on the possible human health effects of electric and magnetic fields; and

(3) research, development, and demonstration with respect to

(A) technologies to improve the measurement and characterization of electric and magnetic fields; and
(B) techniques to assess and manage exposure to electric and magnetic fields".

The act directs that the Secretary of Energy "shall enter into appropriate arrangements with the National Academy of Sciences under which the Academy shall periodically submit to the Interagency Committee and the Advisory Committee reports that evaluate the research activities under the program. The report shall include recommendations to promote the effective transfer of information derived from such research projects, including the transfer of information to representatives of State regulatory agencies, State health agencies, electric utilities, electrical equipment manufacturers, labor unions, and the public. The Secretary shall be responsible for expenses incurred by the NAS in connection with the preparation of such reports".

According to the act, the Director of the National Institute of Environmental Health Sciences (NIEHS) shall report to the National EMF Interagency Committee (IAC) and National EMF Advisory Committee (NEMFAC). The IAC, in consultation with NEMFAC, shall report to the Secretary of Energy and Congress in a final report "stating the IAC's findings and conclusions on the effects, if any, of electric and magnetic fields on human health and remedial actions, if any, that may be needed to minimize any such health effects".

BACKGROUND

Humans evolved in an environment including natural electric and magnetic fields of several types. The natural electromagnetic spectrum common to our environment covers a broad range of frequencies and wavelengths. These vary from the quasi-static geomagnetic field to low-frequency emissions of a few hertz (Hz) to a few thousand hertz associated with lightning storms. However, in the last 100 yrs, a number of human-made electromagnetic frequencies have been added to the environment. Radio transmitters and microwave ovens contribute high-frequency components to our electromagnetic environment. The transmission, distribution, and use of electric power contributes at the extremely-low-frequency (ELF) end of the frequency spectrum (the term extremely low frequency is commonly used to refer to frequencies of under 300 Hz).

Power frequencies are 60 Hz in the United States and 50 Hz in Europe. The biological effects of electric and magnetic fields vary greatly depending on their frequency and field strength. The EMF-RAPID program has been concerned almost entirely with magnetic fields.

It is in this context that considerable controversy was created within the scientific community when it was asserted that exposure to powerline fields was associated with increased incidence of disease. Wertheimer and Leeper (1979) reported that an increase by a factor of 2–3 in the incidence of childhood cancer was associated with residence in houses that had electrical wiring configurations that were thought to be associated with higher currents and thus higher than usual MFs. Their findings were unexpected and could not be explained by known interactions of power-frequency magnetic fields with biologic systems.

Many epidemiologic studies have since evaluated associations of a number of cancers, particularly leukemias and brain tumors, with estimated or measured exposures to electric fields (EFs) and MFs. Studies of cancer in children have focused on residential power-frequency magnetic field exposure; both residential and occupational exposures of adults have been examined. The reported associations are inconsistent from study to study, and effects range from none to weak. With the passage of time, such studies have generally improved in quality with respect to exposure assessment, population size, and outcome assessment, but this has not resulted in greater consistency of results, stronger associations, greater acceptance, or greater consensus about interpretation.

Epidemiology can be a powerful tool for identifying potential risk factors when there is a strong correlation between increased risk of disease and specific environmental conditions. Epidemiologic studies also have been effective in identifying relatively weak associations between putative risk factors and some cancers. Epidemiology is most successful in cases where there are large differences in exposure, where the adverse effects are not rare, and when large samples can be studied prospectively. However, when association is weak, interpretations are more difficult, and conclusions concerning risk less convincing. Epidemiologic studies are at a serious disadvantage if they are used in an effort to prove that weak associations exist or do not exist.

Recent epidemiologic studies of power-frequency MFs and cancer have been conducted in larger populations and with more rigorous methods, but they have not produced evidence that argues persuasively for a quantitative relationship between increased exposure to power-frequency MFs and increased risk of any particular form of human cancer (NRC 1997).

The results of epidemiologic studies of the association between ELF-MF exposures and cancer are difficult to interpret for a number of reasons:

- There is considerable uncertainty in exposure assessment. Measurements are usually made after the time period of interest, and the relevant exposure metric is not known.
- Little is known about the risk factors for different leukemias and central nervous system cancers; therefore, possible confounders cannot be identified, measured.
- There is no accepted mechanism that can plausibly account for the causality of any association.
- The cancer outcomes identified are rare, as is high-MF exposure in a population; detection of a causal relationship between exposure and health effects at a level of high statistical significance therefore is difficult to achieve.

For all the above reasons, quantitative estimates of the relationship between exposure level and excess cancer risk are not persuasive. People evaluating epidemiologic findings in this field can arrive at different conclusions, depending on their starting viewpoints. Those concerned about protecting public health might lean toward acceptance of a possible association between MFs and cancer risk, whereas others might reject such an association based on the lack of a plausible mechanism and the inability to identify possible confounders. All will agree that the evidence supporting an association is limited.

An important requisite for the credibility of epidemiologic findings of weak associations between surrogate estimates of MF exposure and excess cancer risk is assessment of the evidence that supports the biologic plausibility of such an association. Results of the laboratory experiments that have sought to link MF exposure and processes associated with any biologic precursors to carcinogenesis strongly suggest that ELF MFs do not cause cancer promotion and do not affect progression (NRC 1997; NIEHS 1998a). Some laboratory studies have reported evidence of biologic response after exposure to MFs, but they have not been independently confirmed in the peer-reviewed literature. Most of the unconfirmed biologic effects have not been conclusively associated with detrimental health effects. Although the history of study of the responses of biologic systems to exposure to power-frequency magnetic fields is extensive, no conclusive evidence of the potential for such fields to cause detrimental health effects has been produced, other than effects caused by direct contact with electrical conductors.

Public alarm about the possibility of adverse health consequences of exposure to MFs associated with electric-power transmission, distribution, and use is increased by scientific uncertainty. The tragedy of cancer often provokes in a family, or a patient, a strong need to understand the cause. Many cancer patients and their families worry about the possibility that the disease might arise from previous exposures to power-frequency magnetic fields. Accounts in the mass media offer examples of "clusters" in which a small group of people exhibits an apparently high frequency of cancer. It then is a simple step for the public to draw an association between MF exposure and cancer, even though such clusters are sometimes expected as statistical artifacts. When serious uncertainties in interpretation of available evidence arise in a subject in which one or another interpretation would have serious technical and economic consequences, it is important for the government to help to resolve the issues.

As noted, there has been extensive study of the response of biologic systems to exposure to MFs, but there is still no conclusive scientific evidence that such fields cause detrimental health effects. Literature reviews have been undertaken by the Oak Ridge Associated Universities (ORAU 1992), working under the sponsorship of the Committee on Interagency Radiation Research and Policy Coordination; by the Environmental Protection Agency (EPA 1990); by the National Radiological Protection Board of the United Kingdom (NRPB 1992, 1994); by the government of Australia (Peach and others 1992); by the National Research Council (NRC 1997); and by NIEHS (NIEHS 1998a). With one exception, these reviews have come to the same general conclusion: there is little or no evidence that ELF-MF exposure leads to an increased incidence of cancer. The exception is the previously noted NIEHS working-group report (NIEHS 1998a) which, using strictly defined International Agency for Research on Cancer (IARC) guidelines, placed ELF MFs in the "possibly carcinogenic" classification.

EMF-RAPID PROGRAM RESEARCH STRATEGY

In 1993, the Department of Energy (DOE) published a document that recommended activities that should be considered for the following 5 yr in four related program subjects: scientific research, engineering research, communication, and policy support. The document (DOE 1993), entitled *The National Electric and Magnetic Fields Research and Communication Program: Draft Strategic Plan*, is the national EMF research plan referred to in the charge to the present EPACT Committee. The plan outlined specific

goals and objectives for the four major program components: The EMF scientific-research component would seek to determine whether human health effects result from exposure to power-frequency magnetic fields; research activities were to include epidemiologic, cellular, molecular, and large-scale animal studies. The EMF engineering-research component was to characterize the MF exposure of various residential and worker groups and to develop a range of options for managing MF exposure. EMF communication activities were to improve understanding of MF issues by seeking input from concerned citizens and other interested groups, by improving discussion between communities and agencies, by investigating means to improve the communication process, and by providing the public with balanced and credible information on which to base public-policy decisions and individual judgments. EMF policy support was to include "research and analysis to understand the societal, ethical, economic, and legal implications of the MF issue and provide government and business decision makers with a wide range of policy options".

Specific objectives were identified for each of the four components; these are paraphrased below from the *National Electric and Magnetic Fields Research and Communication Program: Draft Strategic Plan* (DOE 1993).

The stated objectives of the scientific research component were to:

- determine the biologic effects of electric and magnetic fields on humans, animals, tissues, and cells;
- conduct replication studies designed to duplicate previous research methods in an attempt to resolve conflicting research results and confirm key research findings;
- determine the underlying causes of any biologic effects;
- establish quantitative dose-response or other quantitative relationships between exposure and effect; and
- determine whether an association exists between EMF exposure and human health effects using well-designed epidemiologic studies.

Objectives of the EMF Engineering Research Program Component were:

- development and evaluation of instrumentation and techniques for measuring various types of electric and magnetic fields and assessing personal exposure;
- assessment of exposure of various residential and worker groups in terms of the various types of electric and magnetic fields;
- development and evaluation of the costs, benefits, and effectiveness of options for managing EMF exposures from a variety of sources;
- development of equations and methods (computer simulations) for estimating electric and magnetic field strengths and power-frequency magnetic field exposures in situations where direct measurements are not feasible;
- development of standardized procedures for EMF exposure measurements to facilitate comparisons between research findings; and
- development of equations and methods (computer simulations) that relate external (outside the body) measurements of EMF exposures to internal (inside the body) power-frequency magnetic field doses experienced by the biologic system.

Objectives of the EMF Communication Component were:

- plan, support, and conduct communication research to improve understanding of how various groups perceive the EMF issue, to evaluate their needs and utilization of information, and to determine more effective methods of communication;
- educate the public, workers, government officials, policy makers, and other interested parties by establishing appropriate channels of communication and providing materials and services that respond to their communication and information needs;
- improve coordination and communication within the national and international MF scientific community. Provide referral services for the public, government, scientists, and businesses to make research findings more widely and readily available; and
- encourage communication from the public decision-makers to those who plan scientific studies. This information could help identify areas of conflicting findings that require further research.

Objectives of the Policy Support Component were:

- improve understanding of the possible health risks, economic effects, and value judgments that must be considered when formulating power-frequency magnetic field policy or regulation;
- improve understanding of how economic costs related to power-frequency magnetic field concerns are affecting citizens, utilities, manufacturers, and other interested parties;
- analyze the potential effects of EMF concerns on the safety, availability, reliability, and costs of electric power and electrical equipment;
- develop and evaluate various regulatory and policy instruments that could be implemented; These instruments may differ depending on the power-frequency magnetic field sources, exposures, and potential health impacts;
- involve the various interested parties in activities related to EMF policy analysis so that individuals or groups can gain an appreciation of trade-offs inherent in various decisions and policies; Comments from interested parties will also assist policy makers in identifying, evaluating, and formulating policy choices;
- develop potential frameworks, including guidelines, criteria, and computer simulations, to assist regulatory bodies in making logical, responsible decisions; and
- ensure that policy research and analysis encompass a broad range of options to account for regulatory and related policy decisions that are made at various levels.

Three implementation plans were published in 1994 to further define the health-effects research and risk communication (DOE 1994a), the engineering research (DOE 1994b), and the communication components of the EMF-RAPID program (DOE 1994c).

EMF-RAPID FUNDING

This committee has not received a formal, complete accounting of EMF-RAPID income and expenses. However, on the basis of preliminary figures received from DOE and

NIEHS, we estimate that a total of about $41 million was spent on the program; estimated expenditures are summarized as follows:

Estimated EMF-RAPID expenditures

Activity	Amount, in thousands of dollars	Percent of total dollars spent
Biologic research	25,553[a]	62
Estimated indirect costs for biologic research (38%)	9,710	24
Engineering projects	2,670[b]	6
Communication	3,350[c]	8
Total	41,283	100

[a] Total from appendix A.
[b] Total from appendix B.
[c] Total from appendix C.

Nearly all the biologic research was carried out under National Institutes of Health (NIH) grants, which normally are described in terms of "direct cost" dollars. Universities separately negotiate reimbursement of "indirect costs" with the government. To complete an estimate of the indirect costs associated with these direct costs, we assumed an average indirect cost rate of 38%. The engineering and other external activities were conducted under contracts, which include direct and indirect costs in the total amount. The Battelle MF-cancer-promotion biologic study was also conducted under a contract.

Despite the uncertainty in the figure for total EMF-RAPID expenditures, it is clear that the amount spent is much less than the $65 million authorized by the enabling legislation. About $20.5 million was actually provided from federal sources. If funded as planned, there would have been $13 million per year for 5 yr. Because a 50% matching with nonfederal dollars was required and because less than $32.5 million was allocated by federal sources, the total budget ($41 million) was 37% less than the $65 million planned.

Because the effective life of EMF-RAPID was four yr, annual funding averaged $10 million per year. (Funding came from FY 1994, 1995, 1996, 1997, and 1998, suggesting a 5-yr program. However, FY 1994 funds were committed late in September 1994, and EMF-RAPID activities ended on December 31, 1998, in effect producing a 4-yr program). Before 1992, when EMF-RAPID was authorized, DOE, the Electric Power Research Institute, and a number of utilities were supporting a major research program on MF bioeffects. Although this committee does not have data on the total funding available at that time, EMF-RAPID might not have represented the major increase in funding that was expected when the authorizing legislation was approved.

The goal of EMF-RAPID was to conduct a special, focused program to provide the public with answers to the general question: "The matter having been intensively

investigated to reduce uncertainty, has scientific concern about the possibility of unrecognized adverse health effects of the use of electric power increased or diminished?" Answers are being offered as a result of EMF-RAPID. However, given the shortened time available (4 yr instead of 5 yr), the less-than-requested funding support ($41 million instead of $65 million), and the use of grants rather than contracts for the biology program, it is not surprising that EMF-RAPID was unable to provide a more definitive answer.

BIOLOGIC RESEARCH

According to NIEHS, EMF-RAPID funded 61 biologic research projects (appendix A), providing a total of $25,553,000 in direct cost support. Funding began in FY 1994 with $4,743,000, peaked in FY 1997 with $7,101,000, and ended in FY 1998 with $2,239,000. The average grant was $419,000; the smallest was $5,000 (supplementing other funding), and the largest was $1,837,000; these three figures are direct-cost totals. Seven investigators each received two grants, and a total of 54 investigators were funded. Twenty-nine projects (48%) began with FY 1994 money, 6 (10%) with FY 1995 money, 3 (5%) began with FY 1996 money, and 20 (33%) began with FY 1997 money.

ENGINEERING PROJECTS

EMF-RAPID also funded 12 engineering projects; 11 final reports arrived in time for the EPACT Committee to review. Support for these 12 projects totaled about $2,670,000 (appendix B). The committee assumes that because these projects were funded by contracts, overhead costs are included in that amount.

PROGRAM MANAGEMENT AND RISK ASSESSMENT

EMF-RAPID committed $3,350,000 to biologically-oriented non-research activities (appendix C). A small contract provided a database of MF publications. NIEHS reports spending a total of $718,000 for program administration; this is a small percentage (1.7 %) of the total EMF-RAPID effort. Three-fourths of the funding in this class of activities—$2,480,000—was for the entire process of information gathering and exchange, including the three workshops, the completion of the working-group report, the public reviews of the working-group report, and preparation of the NIEHS report to Congress; this is 6% of all EMF-RAPID funding.

SUMMARY OF EPACT COMMITTEE INTERIM REPORT

The interim report of the EPACT Committee, EMF Research Activities Completed Under the Energy Policy Act of 1992 (NRC 1995), briefly discussed the status of research related to the biologic effects of MF exposure. A review of the research strategy adopted by the EMF-RAPID program (including program strengths and limitations) discussed work initiated under the EMF-RAPID program, reviewed the one project that had been completed at the time the report was written, and presented the conclusions and recommendations. A brief summary of each of these components of the interim report follows.

STATUS OF RESEARCH RELATED TO BIOLOGIC EFFECTS OF POWER-FREQUENCY MAGNETIC FIELD EXPOSURE

The biologic-effects portion of the interim report began with a description of the risk-assessment process, which appeared to be a central focus of the EMF-RAPID program. Although expressing some doubts that the three goals of the risk-assessment process (characterization of toxicity, definition of hazard, and conduct of risk assessment) were achievable in the time frame of the EMF-RAPID program, the committee noted that *in vitro* and *in vivo* studies have an intrinsic value in that "the determination of biologic sensitivity to EMF exposure should be considered as an important component of toxicology, independent of the direct application to risk assessment".

The biology portion of the research effort was just getting started at the time of the interim report; research results were for the most part not available, so they were not evaluated by the committee. The *in vitro* and *in vivo* components of the program were described.

In vitro studies

The following goals of the *in vitro* studies were identified in the interim report:

- Replication of studies that had previously indicated a cellular response to power-frequency magnetic field exposure.
- Identification of one or more cell systems that produce a robust response. It was emphasized that such systems are needed "to characterize those components of power-frequency magnetic field that are essential to elicit response, as well as to determine temporal patterns of the response".
- Identification and characterization of possible mechanisms that would lead to the establishment of clear hypotheses for biologic effects of power-frequency magnetic fields.

In vivo studies

The committee observed that *in vivo* studies complement and bridge information obtained from *in vitro* and epidemiologic studies. It noted that the following points should be considered if *in vivo* data are to be used in a risk-assessment context:

- The experimental animal must be an appropriate surrogate for human response to the tested agent.
- The ability to detect small toxic effects can be severely limited by the number of animals that can be assayed.
- Chronic toxic effects must be interpreted in animal studies through a knowledge of the dose-response relationships for the toxic effects of concern.

REVIEW OF RESEARCH STRATEGY ADOPTED BY EMF-RAPID PROGRAM

The interim report noted that the research strategy of the EMF-RAPID program attempts to balance breadth and depth within a limited budget and schedule. The committee found no glaring omissions in the program but recommended that it "include mechanisms for seeking rapid confirmation of important observations and for the rapid implementation of studies that seek to test new hypotheses that appear especially relevant".

Strengths and limitations of the program were noted. Of the three specific goals stated in the Research Agenda and Communication Plan, EMF-RAPID Program (DOE 1994a), the committee expressed doubts that the first goal, determination of the health effects of MF exposure, could be definitively reached within the limitations of the 5-yr program. It noted that the second goal, development of techniques to mitigate any adverse health risks, seemed premature. The third goal, dissemination of scientifically valid information to the public, was considered appropriate and a clear strength of the program. Program weaknesses cited by the committee included the absence of a clearly defined methodology to be used in risk determination. Another shortcoming noted by the committee was the decision to conduct all biology and health-related research through the NIH grant process. The committee strongly recommended that a special study section be formed within the EMF-RAPID program to evaluate new proposals and competing renewals of program projects, particularly with a view to bringing the program to closure in some reasonable period. It was also recommended that the program office consider selected use of cooperative agreements to allow more-focused studies to be performed when needed.

The interim report commented on the EMF-RAPID program strategy and tactics, citing the emphasis on replication studies and the fact that the broad approach for cultured-cell systems was combined with a more specific focus on copromotion-cocarcinogenesis and melatonin effects in the animal studies. The committee felt that the strategy represented a solid compromise based on intriguing data and reasonable hypotheses but that it was unlikely over the program's lifetime to produce a database sufficient to support a formal risk analysis.

DESCRIPTION OF WORK INITIATED UNDER EMF-RAPID PROGRAM

The interim report noted 16 current and 10 expected engineering projects, 10 communication projects, 14 *in vitro* biology projects, and seven *in vivo* biology projects. Some proposed engineering and communications projects were eventually canceled because of budget cuts. The number of EMF-RAPID-funded NIEHS *in vivo* and *in vitro* projects, however, increased to a total of 61 projects.

REVIEW OF COMPLETED PROJECT

The only EMF-RAPID project that had been completed at the time of the interim report was the booklet *Questions and Answers About Electric and Magnetic Fields Associated with the Use of Electric Power* (DOE 1995). The booklet was judged by the committee to present objective responses to a variety of questions that might be asked by a concerned public. The answers were for the most part accurate and presented in nontechnical language. It was noted that the booklet contained an excellent discussion of the epidemiologic data that had caused public concern. Although the booklet noted the importance of statistical uncertainty, the committee concluded that the tables should have included confidence limits. The committee also noted that the booklet should have made clear that the associations being considered were, for the most part, with surrogate measures of MF exposure, such as job titles, and that associations with measured fields were not made. Several technical errors were pointed out, but it was thought that they would not substantially mislead the public. The committee concluded that more booklets of this sort should be published and suggested that it would be useful to prepare a more comprehensive guide that would include biologic effects observed in the laboratory from exposure to power-frequency magnetic fields.

CONCLUSIONS OF THE INTERIM REPORT

In general, the interim report concluded that the EMF-RAPID program had several commendable components including identification and quantification of appropriate environmental exposure characteristics, reproducibility of crucial biologic experiments, a commitment to reduce experimental uncertainty through a team approach to experimental design, and emphasis on good laboratory practices.

Regarding the research strategy and agenda, the committee noted that it would be difficult to obtain definitive results on demand from a program of investigator-initiated basic research. The situation was complicated by the fact that the program got a late start: the first research grants were funded a year after congressional authorization. Projects were then funded at various times throughout the program. The lack of a specific, defined method for undertaking risk assessment also was cited as posing a difficulty in judging the ability of the program to meet its risk-assessment goal.

RECOMMENDATIONS OF THE INTERIM REPORT

Risk assessment

The interim committee report recommended that the EMF-RAPID program develop the process by which data would be incorporated into a formal risk analysis and make that process known to the program managers as a guide to the research-planning effort. [The present EPACT Committee notes that a working group was convened to produce an informal assessment of hazard to humans from MF exposure. On the basis of IARC guidelines, a vote was taken by the NIEHS working group and ELF-MF were placed in the classification of "possibly carcinogenic" (NIEHS 1998a). A formal risk analysis had not been done at the time of this review].

Focused research

The interim report recommended that a special NIH study section be used to evaluate new proposals and competing renewals. This study section should include people with a broad and specific knowledge of MF research. In addition, a funding mechanism should be included to allow for the rapid implementation of studies that seek either to replicate important findings or to test new hypotheses derived from continuing work. The selected use of cooperative agreements or supplementary applications was recommended to allow a more timely performance of highly focused studies.

Research management

The interim report noted that knowledge of mechanisms of MF effects was lacking and that such knowledge would be needed to provide efficient program direction. In general, a focused characterization of environmental exposure as it might be related to biologic effects was urged. No specific recommendations were made. [A 1,000 person evaluation of environmental exposure was completed within the engineering program at a later date].

Field mitigation

A primary goal identified by the EMF-RAPID program was to examine techniques to mitigate risks posed by exposure to power-frequency magnetic fields. The interim report recommended that task be delayed until the risk factors had been defined better. [After the interim report, one study on risk mitigation was completed (IIT 1997)].

Program extension

The interim report urged Congress to consider a 2-yr extension of the EMF-RAPID program. [After receiving input from many sources, Congress granted a 1-yr extension of the EMF-RAPID program to December 31, 1998].

Program completion

The interim report recommended that the EMF-RAPID program include a formal administrative mechanism to determine whether the data taken as a whole support the concept that a significant risk is or is not posed by ELF MFs. The intent of the recommendation was to provide a mechanism to determine when an adequate answer was at hand and to suggest that further research in this field should be curtailed. [The EMF-RAPID program later funded an NIEHS working group, which, using IARC classifications, concluded that power-frequency magnetic fields are a possible human carcinogen].

Information dissemination

Regarding information booklets, the interim report recommended that efforts after publication of *Questions and Answers* (DOE 1995) be reviewed by experts in engineering, physics, and biology. It also recommended that another booklet be issued for the lay public, expanding the discussion to include laboratory studies and providing a "relatively complete listing of appropriate scientific literature" for "the more interested reader".

A second booklet, *Questions and Answers about EMF in the Workplace* , produced and distributed by the EMF-RAPID program after the interim report, includes laboratory studies and provides a "relatively complete listing of appropriate scientific literature". The authors note that the booklet was reviewed by experts in federal and state agencies, academic institutions, national laboratories, citizens groups, labor organizations, and industry.

EPACT COMMITTEE REVIEW OF COMPLETED PROJECTS

DOE ENGINEERING PROJECTS

The present EPACT Committee received 11 of 12 engineering reports funded by EMF-RAPID as contracts in time for inclusion in the committee's final report. The 11 engineering reports are listed in table 1.

Table 1—EMF-RAPID Funded Engineering Projects Reviewed by EPACT Committee

#	Organization	Title	Work Done
1	Electric Research & Management, Inc.	"Development of Recommendations for Guidelines for Field Source Measurement"	Identification of set of MF characteristics that can be measured; development of protocols for measurements of fields from appliances on a laboratory test rig and from on-site measurements in complex field environment; gathering of data for specific appliances and environments
2	Magnetic Measurements Co.	"Recommendations for Guidelines for Environment-Specific Magnetic Field Measurements"	Identification of set of MF characteristics that can be measured; development of protocols for characterizing human activity patterns and using information to estimate personal exposures in defined areas; application of protocol in pilot studies
3	Enertech Consultants	"Environmental Field Surveys"	Surveys of MF levels in various environments
4	T. Dan Bracken, Inc.	"Recommendation for Guidelines for EMF Personal Exposure Measurement"	Identification of set of MF characteristics that can be measured; development of measurement protocols
5	T. Dan Bracken, Inc.	"Development of an EMF Measurements Database"	Development of database to serve as repository for MF exposure data
6	Enertech Consultants, Inc.	"Survey of Personal Magnetic Field Exposure"	Survey of average field exposures of 1000 randomly selected people in the United States
7	National Institute for Occupational Safety and Health	"Hazard Surveillance for Workplace Magnetic Fields"	"Walkaround" surveys of MF characteristics in large number of workplace environments

#	Organization	Title	Work Done
8	IIT Research Institute and Commonwealth Associates	"Evaluation of Field-Reduction Technologies"	Evaluation of field-reduction strategies for several kinds of sources, including cost estimates for various strategies for each kind of source
9	University of Washington	"Characterization of Exposures to Extremely Low Frequency Magnetic Fields in the Office Environment"	Spot and personal exposure-meter measurements of MFs in office environments and homes
10	EM Factors	"Assessment of Human Exposure to Magnetic Fields Produced by Domestic Appliances"	Comparison of information from questionnaires with data gathered from personal exposure meters for a group of 40 women in England to determine degree of correlation
11	Center for Risk Management, Resources for the Future	"Risk Dimensions of the EMF Problem"	Views of author on nature of power-frequency magnetic field risk [Note: although funded through the EMF-RAPID engineering program, this project did not involve actual engineering research]
12	T. Dan Bracken, Inc.	"Source and Exposure Prediction Model Development"	Project not completed in time for committee review

Committee evaluations of the projects follow:

Project 1: "Development of Recommendations for Guidelines for Field Source Measurement" (Electric Research and Management, Inc).

This project (ERMI 1997) involved identifying the set of field characteristics that should be measured for interpreting the results of biologic and human-exposure studies and for focusing any future attempts at field management. The investigators also proposed methods for characterizing MF sources on the basis of MF strength at a fixed distance, dominant field components, intermittency, spatial attenuation, and polarization. In addition, the report describes protocols for measurements of fields from appliances and for on-site measurements of fields in a complex exposure environment, such as an office or factory. Examples of these measurement protocols were provided, and useful data were presented on the MFs measured in the vicinity of 20 appliances commonly used in homes and offices.

Project 2: "Recommendations for Guidelines for Environment-Specific Magnetic-Field Measurements" (Magnetic Measurements Co).

This study (Magnetic Measurements 1998) attempted to anticipate every aspect of power-frequency MFs that might be related to biologic or human health effects and suggested the equipment, measurement protocols, data-management and analysis procedures, quality-control measures, and reporting procedures that should be used for characterizing the MF environment in any given occupational, public, or residential setting. Methods are described for characterizing human activity patterns and for using that information to estimate personal exposures to sources in a well-defined area. For that purpose, each study area is to be divided into sharply defined microenvironments within which the fields and activity patterns can be characterized with reasonable precision. The protocol was tested in three pilot studies involving a day-care center, a metal fabrication plant, and a grocery store. The field-characterization procedures described in the report would be extremely difficult and expensive to perform on a large number of people in any specific occupational or public environment. In addition, the results of other studies have not shown a clear correlation between activity patterns and MF exposure from appliances (see report of project 10).

Project 3: "Environmental Field Surveys" (Enertech Consultants)

The objective of this project (Enertech Consultants 1996) was to perform preliminary surveys of the levels and characteristics of MF exposures in residential, public, and occupational environments. Measurements were made of time-weighted average 60-Hz MFs and harmonic fields in grocery stores, schools, office buildings, hospitals, and machine shops. For each type of environment, four sites were studied; 11 sites were in California, and nine were in Massachusetts. Area surveys of the MFs indicated an approximately three-fold variation in the average exposure levels in the five types of environment; the measured values being 0.193 microtesla (μT) in grocery stores, 0.142 μT in machine shops, 0.127 μT in hospitals, 0.083 μT in schools, and 0.072 μT in office buildings. The highest occupational exposures were found for welders in machine shops (0.52 μT), butchers in grocery stores (0.41 μT), and clerks and cashiers in grocery stores (0.40 μT). Exposures were about the same for students, visitors in hospitals, and

professionals in office buildings—all 0.08–0.09 μT. The main sources of area fields were found to be net electrical currents in wiring, office equipment, milling and welding equipment, fluorescent lights, electrical panels in machine shops, and powerlines. It also was observed that DC and AC fields generally are not aligned (either parallel or perpendicular) to each other, third and fifth harmonics of MFs from various sources are generally the largest (with amplitudes that are, respectively, about 30% and 10% of the 60-Hz primary field amplitude), and the polarization of MFs is generally random. Funding limitations, and the unwillingness of people at some sites to participate reduced the type and number of sites surveyed. Apparently because of an agreement with site-owners and operators not to identify the sites, there is a minimal description of the sites. For example, there is no indication of whether the facilities were modern or old, and no information on the types of hospitals or office buildings.

Project 4: "Recommendations for Guidelines for EMF Personal Exposure Measurement" (T. Dan Bracken, Inc).

The report on this project (T. Dan Bracken 1997a) described protocols for an exhaustive assessment of personal exposures to power-frequency fields. An extensive discussion is given of potentially relevant field parameters, measurement equipment, technical problems associated with MF measurements, measurement protocols, time-activity monitoring, data management and analysis, and quality control. The report recommends that MF measurements record the resultant field (the square root of the sum of the squares of three orthogonal field components) rather than the magnitude of the field (which includes phase information but is more difficult to measure). For EFs, the investigators regard measurements at the body surface as having reasonable precision, but they recognize that the magnitude of a field depends in a complex manner on the orientation of the subject relative to the source of the field. The report also discusses the onerous and expensive nature of time-activity recording in diaries carried by the study participants. Some limited pilot results were obtained by using high-school physics students and employees at an instrument-manufacturing facility as subjects, but there were not enough data to assess the value of time-activity recording.

Project 5: "Development of an EMF Measurements Database" (T. Dan Bracken, Inc).

This project (T. Dan Bracken 1997b) involved the development of an MF measurements database that can serve as a repository for data and reports generated in a wide variety of studies on this subject. An Internet site was established to make the data readily available to users. Three types of data can be entered into the database: a "metadata" file that describes the origin, development, and physical content of a data set, a "data products" information base that contains actual measurement data and a "reports information" base that contains the text, tables, and figures describing the results of a study. The functions of the MF database were illustrated by entering a small set of data on 20 persons, 18 of whom were federal office workers. Although the report clearly describes the procedures for recording MF exposure data and making them available to users, there have apparently been no efforts to use the procedures for archiving the data obtained in large surveys of personal MF exposure, such as project 6, below. There is no information as to how much the database has been used, how satisfied any users are, and whether any problems have been encountered in its use.

Project No. 6: "Survey of Personal Magnetic Field Exposure" (Enertech Consultants)

The goal of this project (Enertech Consultants 1998a,b), which was the most comprehensive study undertaken as part of the EMF-RAPID engineering program, was to analyze average exposures to power-frequency MFs (and harmonics up to 1,000 Hz) of the US population on the basis of a randomly selected cross section of 1,000 people. The study used a combination of information obtained by questionnaires and by 24-h continuous measurements recorded with a compact MF exposure meter (the EMDEX). Exposures of people in all the major geographic regions of the United States at home, work and school and during travel were measured using a study design that was balanced on the basis of the gender and age of the participants. Before the main study, a pilot study (phase I) was performed with about 200 participants. The results of the phase I study formed the basis of a number of important decisions on the phase II study protocol and the personal exposure meter to be used (the EMDEX-MATE with permanent memory and 10-min data summaries). The primary findings of the large phase II study with approximately 1,000 participants were:

- The geometric mean value (and 95% confidence interval) recorded for a 24-h exposure is 0.089 (0.085–0.093) μT, with a lognormal distribution of data over the range 0.03–0.30 μT. Percentages of the population exposed to 24-h average field levels greater than 0.2, 0.3, 0.5, and 1.0 μT are 14.3%, 6.3%, 2.4%, and 0.5%, respectively. Those percentages are higher by about 35% than those observed in the previous Electric Power Research Institute 1,000-home study, in which "spot measurements" of MF levels were taken in various rooms of the homes (usually at the center of a room). It is reasonable that the personal exposure meters used in the present study would give higher average exposure levels in that the people wearing the exposure meters often came into contact with or were close to appliances that generated relatively large power-frequency MFs. It should be noted that 24-h exposure includes occupational exposures, which can be higher than residential ones.
- Little difference was observed in MF exposure between men and women, and the highest exposure was of working-age people (0.097 μT), followed by retirees and preschool children (0.080 μT) and school-age children (0.076 μT).
- Little geographic dependence was found in the average MF exposure, with the largest geometric mean value being observed in the Northeast (0.100 μT), followed by the West and Midwest (0.087 μT) and the South (0.086 μT).
- About 25% and 9% of the population were exposed to fields greater than 0.4 μT and 0.8 μT, respectively, for more than 1 h per day.
- About 1.6% of the population were exposed to fields greater than 100 μT at least once in a 24-h period.
- The highest average exposure occurred "at work" (0.103 μT), followed by "on travel" (0.096 μT), "at home not in bed" (0.080 μT), "at school" (0.064 μT), and "at home in bed" (0.052 μT). The average field exceeded 0.2 μT for 21%, 14%, and 3.5% of the people in the categories "at work", "at home not in bed", and "at school", respectively.

- For the "at work" period (8 h averages), the highest exposures were among electrical workers (0.16 μT), followed by food, cleaning, health, and protective service workers (0.16 μT), technical, sales, and administrative workers (0.11 μT), management and professional specialty workers (0.10 μT), precision production, crafts, equipment-repair workers, operators, fabricators, and laborers (0.09 μT), and farming, forestry, and fishing workers (0.05 μT).
- For the "at home" period, the highest average exposures were experienced by people living in standard (fewer than 5 floors) apartment buildings (0.11 μT) and duplexes (0.10 μT), followed by tall (more than 5 floors) apartment buildings (0.09 μT), single-family homes (0.07 μT), and mobile homes (0.05 μT). The highest average exposures were in small (less than 1,000 ft^2) dwellings (0.08 μT), followed by medium (1,000–2,000 ft^2) dwellings (0.07 μT), and large (more than 2,000 ft^2) dwellings (0.06 μT). Bedroom exposures were greatest when the bedroom was on the second or higher floors (0.06 μT), followed by the first floor (0.05 μT) and the basement (0.05 μT). Higher average exposures were observed in dwellings with metal pipes (0.08 μT) than with plastic pipes (0.05 μT).
- "At home" average exposures were inversely related to the distance of the nearest overhead powerline (less than 25 ft, 0.09 μT; 25–50 it, 0.08 μT; 50–150 ft, 0.06 μT; and more than 150 ft, 0.06 μT). Exposure also varied with the type and number of powerlines; the highest exposures were associated with transmission lines (0.1 μT) and two three-phase primary distribution lines (0.11 μT). Lower exposures were associated with a single-phase primary line (0.07 μT) and a two-phase primary line (0.05 μT).
- Many sudden field changes were recorded where the field value was more than 50% different from the average of two consecutive readings. The percentage of people experiencing more than 10 sudden field changes of over 1.0 μT, over 0.5 μT, and over 0.25 μT are over 30%, over 50%, and over 90%, respectively. Those data undoubtedly reflect intermittent exposures from local sources (such as appliances) or other types of power switching in the environment of the exposed person.

Three aspects of the study design reduce the ability to generalize from the results that were obtained:

- A low participation rate (28.4%) based on consent forms returned relative to the number of initial telephone contacts.
- The percentage of those age 17 yr or under studied in this project (8.2%) is only onehalf the percentage of those age 17 yr or under in the US population (16.6%).
- All measurements were made in the coldest months of the year (November to March).

Project 7: "Hazard Surveillance for Workplace Magnetic Fields: I. Walkaround Sampling Method for Measuring Ambient Field Magnitude and II. Field Characteristics from Waveform Measurements" (National Institute for Occupational Safety and Health).

This study (NIOSH 1998) provided a description of procedures for characterizing occupational MF exposures with a portable data logger (the EMDEX-II) and a waveform-capture system that enables evaluation of the field magnitude, frequency spectrum,

polarization, spatial orientation, and total harmonic content. The walkaround surveys with the portable exposure meter were conducted in 62 facilities, ranging from a small print shop to a large oil refinery. The results of the surveys demonstrated two aspects of workplace exposures: the electric-power consumption in a given facility *cannot* be used reliably as an indicator of worker exposures to MFs, and the Standard Industrial Classification is *not* a reliable tool for predicting worker exposures.

The waveform-capture system was used in six diverse industries: aluminum extrusion, aluminum-framed filters preparation, plastic-polymer production, liquid air separation, cement production, and pharmaceutical manufacturing. A problem that was encountered during these measurements was an effect on the waveform resulting from motion of the field probe. An algorithm was developed to correct for this motion, but the algorithm was not very reliable. On the basis of 59 waveform measurements, the recorded fields showed significant second, third, and fifth harmonics, with a total harmonic distortion of about 15%.

Project 8: "Evaluation of Field-Reduction Technologies" (IIT Research Institute and Commonwealth Associates)

This study (IIT 1997) involved an in-depth evaluation of exposure-mitigation procedures for nearly all common sources of human exposure to power-frequency MFs, including powerlines and substations, electric-power service connections in homes and businesses ("customer-side" power distribution), appliances and machine tools, and electric transportation systems. Four types of reduction were considered: self-cancellation methods, such as split currents moving in opposite directions or magnetic dipoles with oppositely directed vector orientations; active cancellation using bucking coils; field cancellation by inducing eddy currents in nearby metal structures; and shielding with ferromagnetic materials. For the various field-reduction methods, cost estimates were provided on the basis of required materials and labor, project costs (including land purchase, permits and licenses, and engineering surveys), and life-cycle costs (management and operations, interest on leases, property taxes, and insurance). The conclusions of this study were as follows:

- For powerlines, unbalanced current is the main source of MFs. This is the case for the MFs from distribution lines and for household wiring. A variety of field-reduction methods can be used, including balancing the current load, using splitphase configurations, compacting conductor bundles, placing cables underground, and decreasing the current while increasing the voltage to maintain the same load.
- Customer-side power distribution sources that were evaluated included electric service panels, transformers, switchgear, and wiring. Field-reduction methods include correcting the return-current imbalance and avoiding ground-current loops, using metal conduits, installing shielding for panels and switchgear, the use of shielded and twisted-pair wiring, and using three-conductor wires. The overall cost of upgrades in wiring can be 50% to 100% greater than the cost of standard wiring.
- In appliances and machinery, the main sources of MFs are small motors, resistive heating elements, meters, transformers, and wiring. A variety of methods are generally available to reduce a stray field at little cost, including split-return currents, shunt connections, and toroidal coil winding in transformers. However, some

machinery, such as welding and melting machines and electric furnaces, pose difficult problems in achieving field reduction.

- For electric transportation systems, the main sources of stray MFs include motors and unbalanced currents. These sources can lead to very high MF levels in passenger cars (1.0–10.0 μT at 60 Hz). However, significant field reduction can be achieved by using dual overhead-trolley connections, return current wires that are close to the supply wires, and DC currents. Shielding with ferromagnetic materials is not practical, because of the added weight.

Project 9: "Characterization of Exposures to Extremely Low Frequency MFs in the Office Environment" (University of Washington Master's Thesis in Environmental Health prepared by P. Hogue).

The purpose of this study (Hogue 1995) was to characterize exposures to power-frequency MFs in an office environment on the basis of data obtained from 70 workers in a single company at 12 sites. Comparisons were made between spot measurements of fields in the work location and exposure data obtained with a personal exposure meter, the EMDEX Lite. Exposure measurements were made for 24 h, thereby obtaining additional useful information on nonwork exposures of each subject. The primary findings in this study were as follows:

- The arithmetic mean value of the MF measured with a personal exposure meter for the office environment was 0.17 μT; for nonwork exposures (mostly at home), it was 0.14 μT. From the cumulative data, the average office exposure during a typical workday contributed about 35% of the total average 24-h exposure (8-h average).
- For office workers, the within-day variability was greater than the between-day variability. The greatest variability in exposure levels was observed between subjects.
- The exposure data were found to be quite stable when measurements were collected at time intervals separated by up to 62 d.
- No significant variation in the office exposure levels was observed as a function of time of day.
- Spot measurements of the MF levels were found to correlate well with measurements made with the EMDEX Lite personal exposure meter; spot measurements were able to account for about 65% of personal work-exposure variability.

Project 10: "Assessment of Human Exposure to Magnetic Fields Produced by Domestic Appliances" (EM Factors)

The primary purpose of this study (EM Factors 1996) was to assess the reliability of estimating MF exposure with questionnaire data on electrical-appliance use in the home. Predicted exposures based on questionnaire data and measurements of the MFs produced by various appliances were compared with personal-exposure data acquired with an EMDEX-II meter worn at the waist. The study, conducted in Avon, England, involved 50 women; 805 measurements were made on fields from 50 types of household electrical appliances. The following is a summary of the major findings in this study:

- No correlation was found between measurements of fields produced by appliances and actual exposures measured with an EMDEX meter.
- The personal-exposure data correlated reasonably well with an exposure model that included measured average fields in the kitchen and bedroom, independently of appliance contributions to the variability in the measured fields. Similarly, peak exposures were unrelated to the use of any appliance.
- The results of this study indicate that questionnaire data on the amount of time that various appliances are used cannot be relied on as a basis for estimating exposure to the power-frequency MFs emanating from household appliances.
- A model was developed that accounts for the effects of some commonly used appliances on the 90th percentile of peak exposures. Three appliances that were used more than 15 min/d at operating distances of less than 100 cm and that fit this model were a microwave oven, a conventional oven, and an electric cooker. Electric blankets were not included because only four of the 50 subjects used them. The model also was found to be applicable to characterizing exposures to fluctuating MFs at the 90th percentile of peak values.
- The median exposure of the subjects in this study was one-fourth to one-third of the exposures found in a previous large study of a comparable nature in the United States. This difference is probably related to the use of 240-V line voltages in the UK rather than the 120-V used in the United States, with correspondingly lower currents that give rise to lower MFs. Also, the report notes that electricity in the UK is quite expensive, and therefore is used more sparingly than in the United States.

Project 11 "Risk Dimensions of the EMF Problem" (Center for Risk Management, Resources for the Future)

The report of this project (Florig 1995) was delivered to the committee in connection with the engineering program, but it is actually a risk-analysis report rather than an engineering report. The objective of the project was to use epidemiologic information available up to 1995 to put the potential cancer risk posed by MF exposure into the broader context of risks posed by other environmental agents. The report is the opinion of one person, who also attempted to analyze the impact of information on EMF-exposure health risks on public policy and regulatory restrictions on exposure. The author apparently believes that power-frequency magnetic fields pose a childhood health hazard and that MF studies might be biased toward null results. He criticizes expert panels and government agencies in their handling of MF issues. This committee notes that the literature base on which this report was developed is now out of date, and therefore questions the utility of the conclusions of the author on cancer risk related to MF exposure.

Summary

EMF-RAPID committed about $2.7 million to engineering studies an amount that is 6.6% of the total budget of $41 million. The overall value of what has been accomplished in the 11 engineering projects funded as part of the EMF-RAPID program is questionable. The projects were commissioned without any convincing evidence of specific linkages between low-level MF exposure and human health effects. As a result, the engineering projects were designed to establish field-measurement and management

technologies for ill-defined possible future discoveries of biologic effects of power-frequency fields. There is a considerable degree of overlap and repetition among several of the individual projects. Many of the projects have "the cart before the horse", in the sense that they anticipate all possible field parameters of potential relevance, without good reason to focus on any specific one. A considerable amount of money has been spent to fund work that will probably never be used. Furthermore, the work was done concurrently with other EMF-RAPID studies, so the results of the engineering projects could not be used in the biology projects.

Three projects (projects 1, 2, and 4) had as goals the establishment of MF measurement methods and protocols. In the absence of real knowledge of what field properties might be of concern, a large number of possible field metrics were evaluated in these studies. A large amount of detail was provided about how to characterize a wide variety of field properties. However, in the absence of any established health effects associated with EMF exposure, it is not evident which, if any, of the measured field parameters are relevant. A fourth project (project 5) was concerned with the establishment of a database to serve as a "repository" for data generated in engineering studies of MF environments. Again, a significant effort has gone into the creation of the structure of this database without knowledge of the specific issue that the data will address. In addition, the large sets of individual exposure data obtained under funding from the EMF-RAPID program (projects 3, 6, 7, 9, and 10) have not been entered into the database at the time of this review. The measurement protocol and database projects probably will never be needed. At the least, this work would have been much more efficiently carried out after the establishment of a specific biologic effect.

The five individual-exposure data projects (projects 3, 6, 7, 9, and 10) involved determinations of levels of MF exposure in a variety of specific environments (household, work, office and so on). A large amount of detailed data was collected, but it is not likely that the bulk of it will ever be used. The overall conclusion from this work is that field exposures do not vary a great deal from one type of environment to another. On the basis of personal-exposure measurements, the time-weighted-average (TWA) MF levels to which most members of the US population are exposed are in the range of 0.1–0.2 μT. In that range, exposures at work and in some transportation vehicles are generally greater than those experienced in the home. TWA exposures above 0.2 μT are relatively infrequent among the general population, although occupations that involve working in close proximity to industrial machinery and business machines can lead to TWA exposures in excess of 0.4 μT.

Of the 11 projects, only one (project 8), which addressed field-reduction methods for a variety of sources and made comparisons of costs for various levels of reduction, provides information on what can be done to mitigate MF exposure if it is ever found necessary. This work could also be of some value with regard to field-reduction applications unrelated to health effects. Some of the methods described for reducing fields from powerlines are being used in new installations. It was also noted by the committee that EPRI has funded work on methods for reducing fields from powerlines and other sources.

It is not difficult to envision MF measurement studies that could be done to provide large volumes of data that might be useful if some causal effect is determined to exist. But to provide substantial funding for such studies without specific guidance from

documented and replicable biologic effects makes little sense. In order to do good science and good engineering, it is essential to distinguish between repeatable results that correspond to testable hypotheses and empirical observations that are not predicted and not reproducible. Large amounts of data do nothing to strengthen claims of cause and effect that are fundamentally weak.

Without a much more compelling case than has been made to date, future engineering studies of the kind that were funded in the EMF-RAPID program are not recommended.

NIEHS BIOLOGY PROJECTS

The Energy Policy Act of 1992 directed that research be carried out to "determine whether or not exposure to EMFs produced by the generation, transmission, or use of electrical energy affects human health". The biologic-research portion of the EMF-RAPID program was to address mechanisms by which MFs interact with biologic systems and to conduct epidemiologic research on the possible health effects of MFs. A decision was made early in the EMF-RAPID program to de-emphasize the epidemiologic effort, possibly because of funding restrictions and the existence of a number of epidemiologic studies already funded by other sources. Most of the EMF-RAPID-funded biology projects were intended either to investigate ELF-MF effects on biologic processes related to cancer or to fundamental cellular processes, such as signal transduction and gene expression. Most important, efforts were made to have independent investigators repeat previous experiments that reported MF effects. The EMF-RAPID program funded projects that examined the interactions of MF exposure with initiation and promotion of cancers by using established animal carcinogenicity models. These experiments were intended to serve as controlled laboratory tests of the carcinogenicity implied by the epidemiologic studies that reported associations between measurements assumed to indicate increased MF exposure and increased occurrence of cancer. The EMF-RAPID program also funded a number of studies that were designed to provide specific information on, or at least reduce the uncertainties about, the interaction of MFs with biologic systems and ultimately reduce uncertainties about adverse effects of MFs on human health. Because the possible mechanisms of MF interaction that could have carcinogenic effects are unknown, the relevant exposure metric cannot be determined with confidence.

Scientific data of relevance to the question of possible health effects can be obtained from laboratory studies involving animals and studies involving cells in culture. Two activities in the program were designed to ensure that *in vivo* and *in vitro* research funded under this program would have the benefit of accurately determined exposures. Grantees were provided with a site-visit team that inspected and calibrated exposure facilities. Another activity established four regional exposure facilities that would be available for experimentation under the EMF-RAPID program: such facilities were established at the Food and Drug Administration (Washington, DC), at the National Institute for Occupational Safety and Health (Cincinnati, Ohio), at the Pacific Northwest National Laboratory (Richland, Washington), and at Oak Ridge National Laboratory (Knoxville, Tennessee). The goal was to have standard facilities available for replication of important experiments. These facilities were primarily used by researchers working at

the four sites. It can be assumed that these two measures assisted in ensuring a more uniform and higher quality of MF research conducted under the EMF-RAPID program.

Most of the biologic research under EMF-RAPID was funded through NIH research grants, a mechanism that seeks investigator-initiated research-grant applications. In this case, such applications were produced in response to Requests for Applications (RFAs) describing the subjects of interest and the types of applications that the agency (NIEHS) desired to review and fund. In the NIEHS EMF-RAPID research program, 49 applicants were funded from proposals received in response to RFAs—approximately a 25% success rate. In addition, 12 projects were funded in-house at NIEHS with EMF-RAPID funds and were not competitive responses to RFAs. NIH grantees briefly report their progress in non-competing renewal applications and peer-reviewed publications.

The biology projects included screening studies, tests of formal hypotheses, and replications of previous claims of effect. The committee would have preferred to see more studies directed at replication of published claims of effects and formal hypothesis testing and fewer studies directed at screening for possible effects. Without development and testing of specific, well-defined hypotheses, the ability to draw firm conclusions regarding the biological interactions and potential health effects of power-frequency fields is very limited.

The importance of the NIEHS biologic research effort lies in the general observation that the results to date of this special, focused, 4-yr research effort tend to diminish, rather than increase, scientifically-based concern that use of electric power entails serious adverse health effects. Many of the investigations showed that the *in vitro* effects of MF exposure reported in the literature could not be replicated, and no link has been established between laboratory MF effects on a particular cellular process and the occurrence of adverse human health effects. Efforts to examine promotion by MF in animal cancer models did not detect increases in cancer incidence or tumor growth rates.

In an effort to evaluate MF health effects, EMF-RAPID funded 61 biologic studies. At the time of this committee's assessment, few of the studies had been published in the peer-reviewed literature. The committee was furnished with detailed and complete reports of the DOE engineering studies, but the brief project summaries of the bioeffects program supplied to the committee contained little quantitative information. Without extensive data on the magnitude of the effects and their reproducibility, it was difficult to evaluate the biologic studies adequately or to assess the program's impact on the existing body of knowledge related to the bioeffects of electric and magnetic fields[3].

The results of all 61 biologic studies funded by EMF-RAPID are summarized in the tables beginning on page 39. For the purposes of the committee's review, the biologic studies were grouped into five categories:

1. No MF results reported in project summary. These are projects that at the time of reporting had not produced either positive or negative findings.
2. No MF or EF effects reported. These are studies in which the investigators sought but were unable to find effects of EF or MF exposure.

[3] Bioeffects research supported by EMF-RAPID has been concerned almost exclusively with the effects of power-frequency MFs. Only two studies involved direct exposure to electric fields. Only two MF studies used frequencies other than 60 Hz.

3. Effects reported but data insufficient to calculate magnitude of effect.
4. EF and MF effects reported and data sufficient to calculate magnitude of effect.
5. Attempts to replicate earlier positive reports. These studies attempted to reproduce earlier reports of MF effects.

In about one-quarter of the preliminary reports, positive findings were indicated. In these cases, the responsible investigators were invited to supply supporting data. On the basis of their replies, it was possible to estimate the *magnitude* of the effects that are shown in the tabular summaries. Some of the investigators did not reply, and in some cases the information supplied could not be interpreted quantitatively. The 36 project summaries classified into the first three categories are of limited value at this time for determination of the possible health effects of electric and magnetic fields. If the investigators reported effects but did not provide supporting data, the committee could not evaluate the magnitude of the reported effect.

Even Category 4 (effects reported and information sufficient to calculate magnitude of effect), when placed in the context of the long history of investigations in this field, has limited value. Of the hundreds of claims of biologic effects of ELF MFs, only a few have been independently confirmed; in these cases, there has usually been a rudimentary understanding of the mechanisms of action of the fields. In contrast, a number of claimed effects have failed the test of independent replication. The reports of MF health effects available to the committee do not always give the rationale for the work, but most of the projects were probably extensions of earlier investigations. In light of the history of this field of investigation, these results, without independent confirmation, have little value in answering the basic question of whether there are biologic effects of low-level power-frequency MFs.

Category 5 (replications of earlier positive reports) has been by far the most valuable part of the EMF-RAPID program. Evaluation of the question of possible health effects of power-frequency MFs is handicapped by the absence of robust effects that can be reproduced consistently from one independent laboratory to another. No serious progress on understanding of MF health effects, if they exist, can be made until such reproduction occurs. Conventional funding mechanisms discriminate against applications that propose to test whether some other investigator's findings are valid but requests for proposals from the EMF-RAPID program deliberately encouraged replications.

Although many unconfirmed claims of biologic effects have been made during the course of more than 2 decades of effort, very little of the work to date has been mechanism-based research. If any of these effects turn out to be valid, they could provide the much-needed starting point for such systematic research. That is why replication studies are important at this point in the development of MF bioeffects research. If carefully performed, these experiments have value, even if their results are negative. All of the replication studies performed under EMF-RAPID had either negative or equivocal results.[4]

Biology Tables

The results of the 61 biologic studies commissioned by EMF-RAPID have been summarized in a series of tables (2.1–2.5). For the purposes of the Committee's review, the biologic studies fall into five categories:

2.1 No MF results reported in project summary (18 projects).
2.2 No MF or EF effects reported (10 projects).
2.3 Effects reported but data insufficient to calculate magnitude of effect (8 projects).
2.4 EF or MF effects reported and data sufficient to calculate magnitude of effect (7 projects).
2.5 Attempts to replicate earlier positive reports. This category includes studies that attempted to reproduce earlier reports of MF effects (18 projects).

Categories 4 and 5 have been subdivided into *in vivo* and *in vitro* studies.

Blank cells in the tables indicate that information was not available. The magnitude of a reported effect (tables 2.4a & b) is a number obtained by dividing the difference between exposed and sham samples by the standard deviation of the effect. Thus, a magnitude less than unity indicates that the effect is less than the standard deviation. The magnitude of a reported effect provides some perspective on whether the claimed effect is real and how important it could be from a biologic point of view. Effects that are small relative to experimental variability are difficult to establish experimentally and often are regarded as unimportant biologically. Projects in tables 2.4a and 2.4b reported at least one effect with data sufficient to estimate the magnitude of the effect. Unless otherwise indicated the frequency of the exposure is 60 Hz. When appropriate, additional information is provided as text describing the tabled material.

[4] The Committee is aware of an unpublished series of replications that has taken place under other sponsorship. Three replication studies support the observation by Liburdy and co-workers that low-intensity 60 Hz MFs eliminate the slight inhibitory effects of melatonin and tamoxifen on the growth of tumor cells *in vitro.* This might constitute the kind of confirmation that has been needed, but it will be necessary to evaluate the replications after their publication in peer-reviewed journals.

Table 2.1 lists project summaries that reported no MF results at the time of the EPACT Committee review (July - October 1998). No evaluation of the projects in this category, other than the descriptive material presented in the table, is possible at this time.

Table 2.1—No MF Results Reported in Project Summary

PI	Topic	Exposure	Result	Funded (FY)	Rationale
Astumian Univ. of Chicago	Nonlinear mechanisms of field effects on cells-entirely theoretical	None	Theoretical study, no MF results	1997	Author proposes to "develop theories of biophysical mechanisms that deal with biologically relevant MF exposure conditions"
Barrett NIEHS	Effects of melatonin on cell proliferation	No MF exposure	No MF results. Melatonin does not inhibit estrodiol-induced MCF-7 and BG-1 tumor cell proliferation	1994	Some previous reports indicated that melatonin can reduce cell proliferation
Bilski NIEHS	Study of reactions of biologic, transient neutral free radicals and radical ions that might be affected by MF exposure	Exposure facilities not available at time of report	No MF results reported	1993	Recent speculation regarding prolongation of free-radical life span by MF exposure as a mechanism of MF effects
Binninge Florida Atlantic Univ.	Effects of MFs on gene expression in yeast	20 μT, 60 Hz AC; exposure duration not reported	No results reported	1994	Historical interest in MF-induced gene expression based on results of Goodman and others
Blumenthal NIEHS	Model of melatonin production, distribution and elimination	None	Development of physiologically based pharmacokinetic model for melatonin; no MF results	1994	Pharmacokinetics of melatonin might be relevant to potential MF effects

PI	Topic	Exposure	Result	Funded (FY)	Rationale
Chignell NIEHS	Rate constants of melatonin reactions with free radicals and singlet oxygen	None	No MF exposure involved, so no MF results; indoles reacted rapidly with free radicals	1993	Previous indications of MF effects on melatonin concentrations and melatonin's action as a free-radical scavenger
Craviso Univ. of Nevada	MF effects on calcium in excitable cells	~1 mT	No MF results reported, "data being evaluated"	1997	General interest in intracellular calcium as function of several MF measures
Griffin Oak Ridge National Laboratory	MF effects on cell-cell communication in rat liver cell line	8–50 μT, 45 Hz; 37 μTDC parallel; <0.2 μT perpendicular	No MF results reported; "delay in start of funding"	1997	Replication study of observations by Benane and by Blackman of MF effects on cell-cell communication (Blackman and others 1993; Benane and others 1996)
Hahn Virginia Medical Center	Brain tumors in mice exposed to 60-Hz MFs	1.4 mT, 18 h/d from wk 4 until death or age 29 mo	No results reported; study not completed at time of committee review	1997	Some epidemiologic studies link MF exposure to increased brain-cancer incidence in humans

PI	Topic	Exposure	Result	Funded (FY)	Rationale
Harry NIEHS	Alterations in GAP-43 mRNA in rats after exposure to MFs	2, 200, and 1000 μT for 18.5 h/d continuously and 1,000 μT for 18.5 h/d intermittently (lh on and 1 h off); throughout both pregnancy and postnatal period	No results reported; study not completed at time of committee review	1996	Authors state that project addresses possible effects of MF during neonatal period; a few studies suggest MF effects on neural development
Litovitz Catholic Univ.	Mechanisms of MF-induced bioeffects	Exposure not described	No results reported; study not completed at time of committee review	1995	Investigation and characterization of mechanisms by which cells detect and respond to weak MF
Mandeville Univ. of Quebec	MF effects on brain-tumor promotion in rats [ENU initiation]	< 0.02, 2, 20, 200, and 2,000 μT for 20 h/d applied from 18 d prenatal to 60 wk postnatal	No results reported, study not completed at time of committee review	1994	Certain epidemiologic research suggests MFs might act as promoter in carcinogenesis, including development of brain cancer
McCormick IIT Research Institute	Potential health effects of MFs on pineal function in rats and mice	0.2 mT, 60 Hz with transients added, intermittent fields, and 60-Hz fields with added harmonics; 4 wk of exposure	No results reported, study not completed at time of committee review	1997	Considerable past research on MFs and melatonin in rats, including speculation on role of transients

PI	Topic	Exposure	Result	Funded (FY)	Rationale
Murphy NIEHS	Ion changes in apoptosis as possible mechanism of MF effects	No MF exposure	No MF results	1993	Some studies have suggested changes in Ca^{2+} transport with MF exposure; author hypothesizes that altered Ca^{2+} homeostasis enhances neoplastic progression
Murphy NIEHS	Signal-transduction pathways responsible for oncostatic properties of melatonin; use of BG1 cells	No MF exposure	No MF results	1993	Elucidation of signaling pathways involved in oncostatic action of melatonin
Putney NIEHS	Effects of MFs on calcium signaling in S49 and Jurkat cells	"No MF exposure" (Walleczek 1992 used 6 mT)	No MF results	1994	Putney proposed to replicate a report on calcium signaling in immune-system cells (Walleczek 1992)
Sheppard Loma Linda Univ.	Analysis of epidemiologic studies	Epidemiologic studies; no exposure involved	No results reported	1997	Combined analysis of 13 epidemiologic studies of childhood leukemia to estimate fraction of cases of childhood leukemia attributable to MFs

PI	Topic	Exposure	Result	Funded (FY)	Rationale
Travlos NIEHS	Effects of nocturnal melatonin on progression of breast cancer induced by methyl nitrosourea (MNU) in F344/N rats	None	Although light-burst treatment affected melatonin, no clear relationship between melatonin and cancer induction by MNU was found; not an MF study, therefore no MF results	1997	Earlier suggestions that melatonin affected development of breast cancer

Table 2.2 lists project summaries that report no effect of EF or MF exposure

Two of the studies (Hei and Glickman) investigated mutational effects. Hei reported on the comutagenicity of MFs and gamma radiation; the results indicated that MFs did not have the capacity to enhance the cytotoxicity or mutagenicity of gamma radiation. Glickman investigated both the potential comutagenicity of MFs and $NiCl_2$ at the *lacI* locus in the transgenic *R2LIZ* rat fibroblast cell line and the potential mutagenic effect of MFs at the *lacI* locus in the Big Blue^T transgenic mouse. Glickman reported no MF effect on *R2LIZ* cell survival. No mutation results had been reported at the time of this review.

Hong investigated the role of tyrosine phosphorylation in response to 60-Hz MF exposure. The data showed no change in the activity of the epidermal growth factor (EGF) receptor after MF exposure of A431 cells. It is relevant to this study, however, that A431 cells have an extremely high concentration of the EGF receptor, which makes them a useful source of this protein tyrosine kinase receptor but might not make them a useful test system for studying the influence of a weak upstream signal. It should be noted that the negative results regarding the EGF receptor, despite the concerns about the validity of A431 cells as a model system, are in sharp contrast with the alleged MF effects on activity of the *Lyn* kinase in B-cell lymphomas (see Uckun, table 2.3).

Reiter tested the possibility that MF exposure increases free-radical longevity, resulting in increased damage to DNA. Rats were treated with safrole, a carcinogen that increases free-radical production *in vivo*, and liver concentrations of 8-hydroxyguanosine and average number of micronuclei per cell were measured 8 h after exposure; these indirect measures of free-radical damage were increased by the safrole treatment. Other rats were given safrole and then exposed to a 0.1-mT MF for 8 h. MF exposure had no detectable effects on concentrations of 8-hydroxyguanosine and number of micronuclei greater than those produced by safrole. These observations do not substantiate any MF-induced increase in radical half-life.

In the study by Marino on immune-system changes in mice no overall consistent effect of MFs was apparent to the committee.

Kripke noted that it was "too early to form a basis for positive or negative conclusions" in a study on melatonin concentrations in elderly human volunteers.

No effects were reported for EFs on yeast H+ATPase (Astumian), or for MFs on p53 expression in normal human lymphoblastoid or ataxia telangiectasia cells (Loberg), maternal toxicity in study using rats (Ryan), and on a variety of end points in brain-cell cultures obtained from embryonic mice (McMillian).

Table 2.2—No EF or MF Effects Reported

PI	Topic	Exposure	Result	Funded (FY)	Rationale
Astumian Univ. of Chicago	Sensitivity of yeast H^+ATPase to EFs	1 mV/m to 100 V/m, 1–100,000 Hz	No effects of applied EFs on yeast H^+ATPase; reference is made to a doubling of NaK-ATPase response, in which theory suggests a much larger effect	1994	PI hypothesizes that H^+ATPase will show EF dependence similar to that seen with Nak-ATPase, in which both frequency and amplitude optimums have been observed
Glickman Univ. of Victoria	MFs, chemical toxicity, and comutagenesis *in vitro* MF mutagenesis *in vivo*	2 mT for 120 h 3 mT for 8 h/d for 12 wk	Nickel toxicity not enhanced by MF exposure No mutation data on MF exposure at time of this report	1997	Mutagenesis thought to be prominent in mechanisms of carcinogenesis
Hei Columbia Univ.	Comutagenicity at SI and *hgprt* loci in AL cell line after MF and gamma-radiation exposure	1.5 or 3 Gy followed by 50 and 60 Hz, 100 μT for 1–7 d	MFs did not enhance cytotoxicity or mutagenicity of gamma irradiation	1997	Mutagenesis thought to be prominent in the mechanisms of carcinogenesis
Hong NIEHS	MF effects on tyrosine phosphorylation in A431 cells *in vitro*	0.1 mT for 0.5–8.0 h	No MF effects revealed in experiments conducted in two laboratories (Environmental Protection Agency and University of North Carolina)	1994	Tyrosine phosphorylation as mechanism of signal transduction and carcinogenesis

PI	Topic	Exposure	Result	Funded (FY)	Rationale
Kripke Univ. of California, San Diego	MF effects on melatonin in elderly volunteers	Personal exposures up to 3 μT, with median at 0.05 μT	No effect of MF exposure on melatonin concentrations	1997	Interest in MF effects on melatonin concentrations, which are reduced in elderly
Loberg IIT Research Institute	MF effects on gene regulation in ataxia telangiectasia and normal lymphoblastoid cell lines	10 μT and 1 mT for 1, 3, 6, or 24 h	No MF effect on p53 expression in normal or AT cells	1997	Testing hypothesis that MFs can modulate cellular responses to agents that damage DNA via effects on cell regulatory pathways
Marino Louisiana State Univ. Medical Center	MF-induced changes in immune system of mice	0.5 mT for 1–49 d in one experiment and 175 d in another	In three replicate experiments, T cells, B cells, and corticosterone were assayed; corticosterone concentrations were sometimes increased and sometimes decreased in MF groups relative to controls; no overall consistent effect apparent	1995	Testing hypothesis that exposure to environmental power-frequency magnetic fields can impair immunosurveillance
McMillian NIEHS	Evaluation of MF effects on neuronal development	0.002, 0.2, and 1 mT intermittently, or 1 mT continuously, for 18.5 h/d	"Correlations with EMF dose-exposure were generally lacking"	1993	Epidemiologic suggestion of increase in brain tumors associated with MF exposure

PI	Topic	Exposure	Result	Funded (FY)	Rationale
Reiter Univ. of Texas Health Science Center	MF effects on DNA damage in rats as determined by 8-hydroxyguanosine and micronuclei formation	0.1 mT for 8 h	No statistically significant increase in 8-hydroxyguanosine or micronuclei after MF exposure	1997	To test hypothesis that MFs increase half-life of free radicals, thereby increasing probability of DNA damage
Ryan IIT Research Institute	Developmental toxicology of MF exposure in rats	Dams were exposed to 0.2 mT during gestational days 6–19 for 18.5 h/d or to third harmonic (180 Hz) or playback of 20 recorded transient events. Harmonics and transients were superimposed on 60 Hz	Maternal toxicity not observed; no results available for fetuses	1997	Hypothesis that transients of MF exposure and harmonics might adversely affect development of fetus

Table 2.3 lists project summaries that report MF effects but in which the information provided is insufficient to calculate the magnitude of the effect. Project evaluations, other than the brief descriptions presented in table 2.3, are not warranted. Some comments on methodology are noted below.

The Luben project to study membrane receptor function was based on results from a previous collaboration with Uckun (Uckun and others 1995), in which it was reported that 0.1-mT (60-Hz) MFs activate the *Lyn* kinase in B cells. The data on *Lyn* kinase and tyrosine phosphorylation in the Uckun paper (used as a rationale for the present EMF-RAPID project) appear to be adequate and reasonably well controlled. The data on phosphokinase C (PKC), however, are limited in that the studies on PKC activity were restricted to assays of membrane fractions for phosphorylation of a peptide substrate. The use of protein kinase inhibitors allegedly specific for PKC is the only evidence that the activity measured was due to PKC. Rinehart reports that MF exposure enhances the growth of some human epithelial cultures, although supporting data are minimal. The project also investigated gene expression with endometrial stromal fibroblasts. Studies on gene expression of the type described have major limitations in that they focus on a narrow repertoire of messenger RNAs. *C-myc* and *gro* do not adequately cover the spectrum of possible changes in gene expression. Studies by Woloschak on MF that used a differential display method did detect changes in gene expression; genes were both induced and repressed after 1.0-mT exposures. However, the changes were small, and the significance of this effect can be assessed only after the results are published.

Table 2.3—Effects Reported, but Information Insufficient to Calculate Magnitude of Effect

PI	Topic	Exposure	Result	Funded (FY)	Rationale
Costa Univ. of Washington	Investigation of MF effects on proliferation of mitogen-stimulated human astrocytoma cells	0.06–0.12 mT; exposure duration not provided	Increased cell proliferation in human astrocytoma cells	1997	Suggestion in some epidemiologic studies of increase in brain tumors associated with MF exposure
Grissom Univ. of Utah	Effects of DC fields on enzyme reactions	1.0 mT to 1.0 T; exposure duration not provided	Small effects on enzyme rate constants at very high DC MF levels.	1997	Some historical interest in possibility that MF can moderate enzyme reaction rates
Luben Univ. of California	MF effects on membrane receptor function	0.1 mT; exposure duration not provided	Description of first-yr results appears generally consistent with earlier, related experiments	1994	Earlier reports of PI and others that MFs affect concentration of PKC and cellular pathways related to it
Pennypacker NIEHS	MF effects on proto-oncogene-DNA binding during brain development	2, 200, and 1,000 μT, continuous exposure, or 1 h on and 1 h off, for 18.5 h/d during gestation and 3 d postnatal	AP-1 binding reportedly lowered by exposure, but no data provided; AP-1 binding assumed to be indicator of early brain development	1994	Hypothesis that MF affects early brain development and results in neurobehavioral dysfunction
Rinehart Univ. of North Carolina at Chapel Hill	Evaluation of transforming potential of MF	0.01–0.2 mT, short-term exposure for 1 h, chronic exposure for 30 min, 3 times/wk	No effects of 1-h exposure seen on *c-myc* and *gro* gene expression or in cell cycle; intermittent long-term exposures accelerated aging; anchorage-independent proliferation of some cancer cell lines increased	1994	Previous work by other investigators that suggested MF effect on *c-myc* or *gro* messenger expression

PI	Topic	Exposure	Result	Funded (FY)	Rationale
Sisken Univ. of Kentucky	Effects of MFs on calcium entry in cultured cells	0.3 and 50 mT; exposure duration not provided	Data from oral presentation show calcium increases of around 10%, but data insufficient to determine statistical significance	1997	Previous studies suggesting that changes in Ca^{2+} transport with MF exposure affect cellular proliferation
Uckun Univ. of Minnesota	Stimulation of protein tyrosine kinases (PTK) in human B-cell lymphocytes by MFs	1–1,000 μT; exposure duration not provided	Stimulation of PTK reported, but no data provided	1995	MF exposure of lymphocytes might stimulate tyrosine kinases, which are implicated in progression of leukemias and lymphomas (Luben, Byus, and others have reported MF effects on tyrosine kinases)
Woloschak Argonne National Laboratory	Changes in gene expression accompanying exposure to MFs	0.1 and 1 mT for 24 h	Preliminary data show "modest induction of a few genes" at exposures of 1 mT for 24–72 h	1994	Historical interest in MF-induced gene expression based on results of Goodman and others

Table 2.4a lists project summaries that report *in vitro* EF or MF effects and contain sufficient information to estimate magnitude of effect.

The study by Goodman on the copromotion of cancer by MF was directed largely at gene expression of *c-myc* and p53 in cells. Although Goodman reports no publications from the grants supported by the EMF-RAPID program, the group has five publications related to MF effects (Goodman and others 1989; Goodman and Shirley-Henderson 1990; Goodman and others 1992; Lin and others 1994; Goodman and Blank 1998). These mainly involve a study of effects of MF exposure on gene expression—for example, of the *myc* gene—or in the induction of heat-shock proteins. It is an enigma why the results in the Goodman publications on MF and heat-shock proteins disagree with other studies supported by the current program, which find no changes in gene expression or heat shock protein expression, for example, Saffer and Thurston 1995 and Owen 1998 (see table 2.5a).

Aaron presents preliminary data on increased glycosaminoglycan content per milligram of tissue on days 7 and 9 of MF exposure but not on days 3, 5, and 11. A significant increase is observed at 0.07 and 0.1mT but not at other doses. Aaron concludes that the 60-Hz field accelerates chondrogenic differentiation and synthesis of cartilage. He suggests further that the data indicate that Tumor Growth Factor- (TGF) responses are a possible mechanism of the observed increases in differentiation. In 1998, the investigator has one paper in press and two others in preparation that involve these studies on differentiation and on TGF synthesis. The author hypothesizes that MF exposure alters endochondrial ossification, a process central to skeletal embryogenesis.

Blank and colleagues suggest that stress responses in cells might be measured by determining changes in cytochrome oxidase function and the rate of electron transport. They conclude that 60-Hz MFs increase the oxidation rate constant of cytochrome oxidase by 20–30% at field strengths below 3 μT and by a factor of about 2 between 6 and 10 μT. Those data on MF effects on cytochrome oxidase are similar to effects on Na^+/K^+-ATPase reported earlier by Blank. One paper on these experiments has been submitted for publication. The committee questions the rationale that cytochrome oxidase is an indicator of stress in cells but notes that the results appear to be significant if the conclusions are limited to the studies on enzyme reaction rates.

Liburdy presents an extensive report on preliminary studies on the influence of MFs on signaling processes; the investigator describes a number of measures for the study of mitogen-activated calcium transport in rat lymphocytes. The preliminary conclusions suggest that MFs increase intracellular calcium and enhance signal transduction, but not to the extent that cell viability is affected. The investigator also suggests that MFs act synergistically with an activating agent, such as anti-CD3 antibody, to enhance signal transduction in lymphocytes. The objective was to test the hypothesis that time-varying (AC) MFs interact with biologic systems in a manner that depends on the presence of static DC MFs. The specific aims were to determine whether particular AC-DC combinations increase or decrease calcium signaling in mitogen-activated thymocytes and, if so, to determine whether the changes increase or decrease cell viability or proliferation. The PI indicates that MF exposure can increase intracellular calcium in Jurkat cells activated with antibody to the CD3 cell surface receptor. Scatchard analyses indicated that binding was increased by 25–30% after brief (10–15

min) MF exposures. The PI regards this as biologically relevant. A dose-response study at 100, 1,000, or 10,000 μT indicated a monotonically increasing effect.

McLeod and co-workers reported small effects on cell proliferation, alkaline phosphatase concentrations, and cell shape and orientation when bone cells were exposed *in vitro* to ELF MFs of around 2 mT. They hypothesize that these effects are the result of the action of EFs induced in the medium by the MFs rather than direct action of the MFs on the cells.

Motivated by suggestions in their earlier studies that 30-Hz EFs of about 1 mV/m countered the osteoporosis normally associated with bone disuse in experimental animals, McLeod and colleagues (1993) studied the effects of large MFs (about 2 mT) on cell proliferation and alkaline phosphatase activity of bone-related cells *in vitro.* In the entire study, involving several combinations of exposure time and cell plating density, three statistically significant results were reported: cells at one plating density exposed for 72 h had a 20% ± 10% (mean ± SE) lower proliferation rate, alkaline phosphatase activity in those cells *increased*, and cells at a higher plating density exposed for 12 h also had higher alkaline phosphatase activity. Although many individual samples were pooled to obtain the statistically significant end points, the investigators did not perform a separate study to confirm their findings. A related study (McLeod, table 2.4a) funded by EMF-RAPID found *reduced* alkaline phosphatase activity in another line of osteoblast-like cells.

The general report of the McLeod EMF-RAPID project describes two exposure systems. One produces MFs, which of course induce EFs in samples placed within a solenoid. The other produces pure EFs by way of electrodes introduced into the sample media. Although pure EFs could easily be used to test directly the suggested physical mechanism of the action of MFs in these effects, no report of such tests is described in the materials supplied to the committee. If the hypothesis is correct, biologic effects can occur at EFs as small as 1 mV/m. The general report briefly mentions a study of effects of pure EFs on the orientation of cells. However, a paper in press by Lee and McLeod (In press) describes only the use of MFs in this work. Rubin and colleagues (1996) report inhibited proliferation of osteoclast cells. However, the effect is lower by only 8% at 30 Hz than at 60 Hz, whereas the EF was lower by half.

In view of the apparent inconsistencies and/or small magnitudes of these reported effects, it will be necessary to have both internal and independent confirmation before the results can be used to guide animal studies, which would be necessary before evaluation of the implications for human health effects.

Table 2.4a— EF or MF Effects Reported in vitro, Information Sufficient to Calculate Magnitude of Effect

PI	Topic	Exposure	Result	Funded (FY)	Magnitude of effect	Rationale
Aaron Rhode Island Hospital	MF effects on chondrogenesis in developing bone cells (*in vivo/in vitro* study)	0.1 mT, 7 d for 7 h/d	Increased glycosaminoglycans in days 7 and 9 but not days 3, 5, and 11; 60-Hz field accelerates chondrogenic differentiation and synthesis of cartilage	1995	~2	To test hypothesis that MF exposure produces alterations in endochondral ossification
Blank Columbia Univ.	MF effects on cytochrome oxidase function	60 Hz, 0–10 μT; exposure duration not provided	Reaction of cytochrome C with ascorbate is accelerated by MF exposure when basal rate of reaction is low (Blank and Soo 1998)	1997	~2	Use of cytochrome oxidase-ascorbate reaction rates as a measure of stress response to MF exposure
Goodman Columbia Univ.	MF and copromotion of neoplastic transformation using C3H 101/2 cells	0.8–800 μT for 4–60 min and 1–7 h	Activation of transcription factor enhanced; cells undergoing neoplastic transition are more sensitive to MFs than normal cells; cells undergoing suppression or induction of neoplastic transformation display more pronounced response (in gene expression) to intermittent MF exposures	1997	Insufficient data	To test hypothesis that intermittent and transient MFs act as copromoter in carcinogenesis
		8 and 80 μT for 5–40 min	Increases in heat shock protein in human breast cancer cells (Han and others In press)	Up to 5		

PI	Topic	Exposure	Result	Funded (FY)	Magnitude of effect	Rationale
Goodman (cont.)		8 μT for 20–40 min	Increased protein-DNA binding (Lin and others 1998a)		Up to 10	
		8 μT for 20 min	Myc-mediated transactivation of heat shock protein (Lin and others 1998b)		~3	
Liburdy Lawrence Berkeley National Laboratory	MF effects on intracellular calcium content	100 μT, 60 Hz plus 40 μT DC	Cells in MFs take up more calcium than controls after activation with anti-CD3	1994	2	To test hypothesis that specific AC-DC field combinations National increase or decrease calcium signaling in mitogen-activated thymocytes according to Lednev parametric theory (Lednev 1991)
McLeod State Univ. of New York	Effects of EFs on bone cells *in vitro*	> 100mV/m	Bone cells show dose-response with threshold near 100 mV/m; transformed and nontransformed cells respond differently	1993	Insufficient data	Hypothesis that magnetic fields act indirectly on cells through induced electric fields
		2.5 mT (1 mV/m), 30 Hz for 4–64 h	McLeod gives example of about 20% reduction in alkaline phosphatase activity after 16 h exposure; evidence of EF versus MF effect not clear (Note: McLeod (McLeod and others 1993) showed increased alkaline phosphatase activity)		Insufficient data	

PI	Topic	Exposure	Result	Funded (FY)	Magnitude of effect	Rationale
McLeod (cont.)		0.7 mT (0.2 mV/m) for 24 h	Exposed cells showed changes in shape (Lee and McLeod In press)		~0.1 length, 0.2 area	
		1.6 mT, 0.5 mV/m, 30 Hz; 1 mV/m, 60 Hz; for 7 d	Rubin (Rubin and others 1996) reports inhibited proliferation of osteoclast cells; effect is lower by only 8% at 30 Hz than at 60 Hz although EF was lower by half		~0.7	
		1.8 mT, 0.6 mV/m, 30 Hz, 12 and 72 h	McLeod (McLeod and others 1993) reports increased alkaline phosphatase activity in cells plated at high density, but not in cells at low plating density		0.5	

Table 2.4b lists project summaries that report *in vivo* MF effects and contain sufficient information to estimate magnitude of effect.

Behavioral experiments conducted by Lai (1996) indicated that exposure to a 0.75-mT 60-Hz MF for 45 min immediately before training in a 12-arm radial maze retarded initial training but not asymptotic performance. In another experiment, adverse effects on Morris water-maze performance were observed (Lai and Carino 1998). In these experiments, the effects of several MF intensities and duration were assessed. These results, suggesting interference with memory, are potentially important. The committee believes that evaluation of potential health effects other than cancer and birth defects is appropriate. Other work by those and other authors also suggests that strong MFs can affect neurologic mechanisms and produce slight behavioral alterations. If such effects are confirmed, the public-health implications of small changes in performance of laboratory tasks caused by acute exposure to very strong MFs are unknown. Lai also reported in this project that small changes in performance of laboratory tasks were associated with MF-reduced high-affinity choline uptake in the frontal cortex and hippocampus of rats; opiate-receptor antagonists eliminated the effect (Lai and Carino In press). The data suggest an intensity times duration interaction; no effects were observed at 1 h and less than 2 mT, or at 1 mT and less than 1.5 h (Lai and Carino In press).

In another project of Lai (Lai and Singh 1997), rats were exposed to 0.1, 0.25, or 0.5 mT and 60 Hz for 2 h, and then DNA-strand breaks were measured in isolated brain cells. Exposure to 0.01 mT for 24 or 48 h induced strand breaks, again suggesting an (intensity x duration) dose metric. The finding of single- and double-strand DNA breaks after MF exposure is highly controversial. The energy in ELF MFs is very low and the energy deposited will not break chemical bonds. DNA strand-breaks occurred at a maximum level approximately 4 h after MF exposure. This fact suggests that the breaks were not induced directly by the MF exposure, but occur due to secondary processes. Lai observes that some DNA damage is a consequence of free-radical formation, a normal process of many metabolic events (Lai and Singh 1997). The working hypothesis is that MF exposure increases the very brief duration of free radical survival, thereby increasing the resulting damage. This hypothesis has some support in magneto chemistry with very high MF strengths, but its relevance to biologic systems at lower field strengths is at best uncertain. The authors also report DNA-protein and DNA-DNA cross-linking after MF exposure (Singh and Lai 1998). As a whole, these observations could be seminal or wrong. The experiments provide an example of the dictum, "extraordinary claims require extraordinary proof". If further replication studies are funded, the Lai and Singh studies could be candidates for consideration.

Table 2.4b—MF Effects Reported in vivo, Information Sufficient to Calculate Magnitude of Effect

PI	Topic	Exposure	Result	Funded (FY)	Magnitude of effect	Rationale
Lai Univ. of Washington	MF effects on behavioral and cholinergic activity in brains of rats	0.75 mT for 45 min 2 mT for 1 h	MF effect on cholinergic system induced spatial "working" memory deficit (Lai 1996) Radial arm maze (Lai and Carino 1998)	1994	2 1	Suggestion by this group that MFs affect cholinergic mechanisms in brain
		0.5 mT for 3 h 2 mT for 1 h	MFs reduced high-affinity choline uptake in frontal cortex and hippocampus in two experiments; opiate-receptor antagonist eliminated effect (Lai and Carino In press)		2 1	
		1 mT for-90 min	Reduced cholinergic activity (Lai and Casino In press)		1	
Lai Univ. of Washington	Evaluation of DNA-strand breakage and DNA cross-links in rat brain after MF exposure	0.5 mT for 2 h 0.5 mT for 2 h	Lai and co-workers report DNA strand breaks (Lai and Singh 1997) DNA-DNA cross-links, and DNA-protein cross-links (Singh and Lai 1998) in brain cells isolated from rats exposed to MFs *in vivo*	1997	2 1	PI hypothesis that MF exposure affects free-radical kinetics and results in DNA-strand breaks and cross-links

Table 2.5a lists project summaries that report *in vitro* experiments conducted as efforts to replicate previous reports of EMF effects.

Most of the outright replications of *in vitro* studies shown in table 2.5a were straightforward, and most turned out to be negative. Some are rather striking. In an original study by Rodemann and others (1989) one of the strongest published effects of MFs (magnitude of about 10) was reported, and the 6-mT fields used in the study were large. Nuccitelli attempted to replicate the work of Rodemann indicating that MFs affect protein synthesis in fibroblasts and keratinocytes. He also attempted to replicate a report by Goodman and Blank (1998) that MFs induce heat-shock proteins in HL-60 cells. Nuccitelli did not observe effects reported by Rodemann and by Goodman, even though the experimental conditions were carefully replicated.

A number of EMF-RAPID projects attempted to replicate positive studies on gene expression—all with negative results. Two studies by Balcer-Kubiczek investigated various aspects of gene expression which have been of interest since earlier studies (Goodman and Shirley-Henderson 1990) suggested changes in gene expression after MF exposure. The studies of MF effects on expression of 11 genes conducted by Balcer-Kubiczek involved the use of northern blots and a technique based on the polymerase chain reaction (PCR). With those techniques, no MF effects on expression of these genes were noted in a series of four experiments. At the time of the Balcer-Kubiczek study, PCR was perhaps the technique of choice because of its high sensitivity for detection of changes in messenger levels in cells responding to extracellular stimulation. The rapid development of new chip technology and the use of new genomic data on gene expression could facilitate further studies of this nature. Studies like those carried out by Balcer-Kubiczek might have further value if replicated with the new technology.

A study by Lieberman noted no MF effects on gene expression, failing to reproduce preliminary experiments performed in Goodman's laboratory. The Lieberman studies on yeast transcription are so briefly described that one cannot be certain about whether the measurements were sufficiently sensitive to detect subtle changes.

Owen looked at expression of the *c-myc* proto-oncogene in promyelogenous leukemia cells (HL-60) and examined omithine decarboxylase (ODC) activity in mouse L929 cells (Cress and others, In press). In an attempt to replicate the expression of *c-myc* in HL-60 cells reported by Goodman and others, the PI attempted to use serum lots, cell types, and procedures as used by Goodman and co-workers. One of the core exposure facilities was used in some of the studies. MF exposure did not increase *c-myc* expression (Owen 1998). No statistically significant effects on ODC activity were observed.

Miller investigated oncogenic transformation after MF exposure. No effect was seen in the 10T1/2 transformation system; preliminary indications of copromotion were noted in a study with late gestational Syrian hamster fetuses exposed in utero.

In an attempt by McDonald to replicate the induction of heat-shock proteins in human lymphoblasts, the PI was unable to show that the expression was a function of exposure to MFs as reported by Goodman and others.

In another published study, Saffer and Thurston (1995), using great care in their replication efforts, were also unable to show that the *c-myc* proto-oncogene expression in HL-60 was altered by exposure to 60-Hz EMFs. Differential-display PCR did not indicate that any other genes in HL-60 were affected. Using the JB6 cell line, already

initiated but not fully transformed, Saffer was also unable to demonstrate transformation over a wide range of MF exposures (Saffer and others 1997).

McCormick also attempted replication of the findings of Goodman and Henderson. In two replication studies conducted independently by different investigators in the McCormick laboratory, no MF-induced increases in *c-myc* expression in HL-60 cells were noted, either in basal conditions or when stimulated by TPA. McCormick also reports that exposure to MFs for 20 min to 24 h had no effects on cell proliferation or on expression of cancer-associated genes (*c-myc*, p53, or HER-2/neu) in either estrogen-receptor-positive or -negative human breast epithelial cells. MF exposure also had no interactive effects with *c-myc* expression stimulated by TPA or p53 expression stimulated by mitomycin C.

Williams, in his report outlining preliminary work on gene expression, notes that HL-60 cells do not appear to up-regulate *c-myc* mRNA in response to the five MF exposure conditions he tested. Williams also was unable to replicate a previous report of up-regulation in *c-myc* mRNA in the human T-cell leukemic cell line CEMCM3 after MF exposure. An investigation of MF effects on cellular responses to DNA damage was also negative.

A focused replication effort by S.C. Miller of previous work by Uckun and others (Uckun and others 1995) using the DT-40 cell line and selected DT-40 mutants from the Uckun laboratory showed no effect on inositol 1,4,5-phosphate (IP3) production with 0.1-mT 60-Hz MF exposure. Miller failed to find any effects on NFkB- or AP-1-dependent reporter-gene expression in a human leukemia cell line. Miller also reports a failure to find an effect on phosphotyrosine profiles after MF exposure.

The project summary by Hui and colleagues presents an inquiry into the response of lymphoblastoid cells to 0.1- to 0.4-mT MF exposure. Attempts to reproduce the results of Phillips (Phillips and others 1992), who reported that the expression of *c-fos* and c-myc proto-oncogenes was affected in lymphoblastoid cells exposed to 0.1-mT 60-Hz MFs, were unsuccessful even after exhaustive attempts at replication. Quantification of proto-oncogene expression was normalized to the expression of a housekeeping gene, G3PDH, a step not taken in the original experimentation by Phillips and co-workers. The investigators also used a transformation model (INIT C3H 10T1/2 cells transformed with methylcholanthrene but controlled with retinyl acetate) to test for promotional effects of EFs and MFs. No promotional effects were found. Hui and co-workers also noted that exposure to 0- to 100-mV/cm EFs does not produce changes in internal calcium concentrations. In summary, Hui did not find any effects that could be attributed to MF exposure regarding gene expression, transcription rates, transcript levels, c-myc levels, proliferation rates of initiated cells, or intracellular Ca^{2+} concentrations in this careful study.

Lotz conducted studies (at the NIOSH regional exposure facility) to replicate the experiments of Lindstrom and colleagues (1995a, b) who reported that transient changes in intracellular free-calcium concentrations were induced in the human leukemic Jurkat lymphocyte cell line by exposure to a weak MF at 50 Hz. In the intracellular-calcium study, no significant differences were found in incidence of Ca^{2+} concentration transients during exposure to a 50-Hz, 0.15-mT MF. Another replication by Lotz attempted to confirm the findings of R.W. West (West and others 1994, 1996) that exposure to ELF MFs significantly increases colony-forming efficiency in soft agar, an event associated

with neoplastic transformation in these cells (anchorage-independent proliferation). In the cell-proliferation study, the NIOSH data indicate that exposure of JB6 cells to a 0.1-or 1.0-mT, 60-Hz field does not alter anchorage-independent proliferation, and exposure does not increase the effect of TPA or alter anchorage-independent proliferation. In the Lotz replication studies, the importance of continuing consultation with the original investigators was apparently recognized. Collaboration with the original investigators appears to have been a part of the two replication efforts, and extensive efforts were made to achieve close replication of the original experimental conditions.

Table 2.5a—In vitro Experiments Conducted as Efforts to Replicate Previous Reports of MF Effects

PI	Topic	Exposure	Result	Funded (FY)	Replication
Balcer-Kubiczek Univ. of Maryland at Baltimore	MF effects on gene expression in various cell lines *in vitro* in relation to exposure parameters	Typically 2 mT for 3 h	No MF effects on expression of 11 genes in a series of four different experiments	1994	Historical interest in MF and gene expression based on results of Goodman and others
Balcer-Kubiczek Univ. of Maryland at Baltimore	MF effects on gene expression *in vitro* with PCR-based method	2-mT, 60-Hz square wave for 3 or 24 h	When mRNAs in exposed and control HL-60 cells were compared, one differentially expressed cDNA clone was found among. 1,000 cDNAs (no internal confirmation of observation)	1997	To test hypothesis that exposures to MFs with higher-frequency components "alter expression of immediate early genes"
Hui Roswell Park Cancer Institute	Effects of MF exposure on expression of proto-oncogenesin lymphoblastoid cells	0.1 mT, 60 Hz; duration not reported	Failure to replicate observation that MF exposure of lymphoblastoid cells affects expression of *c-fos* and *c-myc* proto-oncogenes or intracelluar Ca2+ concentration	1994	Attempt to replicate results of Phillips (Phillips and others 1992) indicating that MF exposure of lymphoblastoid cells affected expression of *c-fos* and *c-myc* proto-oncogenes
Lieberman Columbia Univ.	MF effects on gene expression in yeast	80 µT, 20 min	No MF effect on gene expression	1997	Lieberman observation in preliminary experiments in Goodman's laboratory that selected genes were turned off in cells exposed to MFs

PI	Topic	Exposure	Result	Funded (FY)	Replication
Lotz National Institute for Occupational Safety and Health	MF effects on transient changes in intracellular free calcium in human leukemic cell cultures	0.15 mT, 50 Hz for 8–16 min	MF effects reported by Lindstrom not found	1995	Attempt to replicate results of Lindstrom (Lindstrom and others 1993), who reported MF induction of transient changes in intracellular free calcium (Lindstrom and others 1995a)
	Anchorage independent proliferation of promotion-sensitive JB6 cells in soft agar (transformation assay)	0.1 and 1.0 mT for 10-14 d	MF effects reported by West not found		Anchorage independent proliferation of promotion-sensitive JB6 cells in soft agar (West and others 1994; Lindstrom and others 1995b; West and others 1996)
McCormick IIT Research Institute	MF effects on expression of *c-myc* gene in HL-60 promyelocytic leukemia cells	1–1,000 µT	No MF effects on *c-myc* expression in HL-60 cells in two replication studies by different investigators in laboratory	1994	Attempts to replicate, in two independent studies, expression of *c-myc* in HL-60 cells as reported by Goodman and Shirley-Henderson (1990)
McDonald IIT Research Institute	MF effects on heat-shock protein expression in human cell lines	0.01, 0.1, and 1 mT for 1, 4, or 24 h	No MF effects observed	1997	Evaluation of possible MF effects on stress responses as judged by induction of heat-shock proteins
Miller, R.C. Columbia Univ.	Oncogenic transformation in C3H 10T1/2 cells exposed to MFs, TPA, and x rays	0.2 and 1.0 mT, 24 h., TPA at 0.1 mg/ml for 8 wk, 3-Gy x rays	No effect of magnetic field on C3H 10T1/2 cell transformation	1994	Interest in MF exposure and carcinogenesis; transformation models used here are thought to be indicators of carcinogenic potential
	Transformation in Syrian hamster embryos exposed in utero to MFs, TPA, and x rays	2.5 mT, 48 h, TPA at 0.1 µg/ml, 1-Gy x rays	Indications of copromotion in late-gestational-age embryos		

PI	Topic	Exposure	Result	Funded (FY)	Replication
Miller, S.C. SRI International	MF effects on IP-3 production in DT-40 cell line	0.1 mT, 60 Hz for 24 h	Failure to find MF effect on IP-3 production as reported by Uckun	1994	Careful replication of MF effects on IP-3 production reported by Uckun (Uckun and others 1995)
Nuccitelli Univ. of California, Davis	MF effects on protein synthesis in human keratinocytes and fibroblasts	8 mT, 20 and 60 Hz for 6 h/d for 7, 14, or 21 d	Failure to find increase in protein synthesis as reported by Rodemann and by Goodman	1994	Exact replication of study by Rodemann (Rodemann and others 1989), who reported one of strongest published effects of MFs (magnitude, 10), an increase in protein synthesis rates in human fibroblasts
	MF effects on heat-shock proteins (HSPs) in human keratinocytes	0.1 mT for 5 min, 20 min, 2 h, and 24h	No effects on HSPs observed		Reports from Goodman of effects on HSPs (Goodman and Blank 1998)
Owen Food and Drug Administration	MF effects on gene expression in HL-60 promyelogenous leukemia cells and ornithine decarboxylase activity in mouse L929 cells	6 μT, 60 Hz for 20 min or 6 μT, 60 Hz for 4 h	MF exposure did not increase *c-myc* expression, and no statistically significant effects on ODC activity were observed	1994	Attempt to replicate expression of *c-myc* in HL-60 cells as reported by Goodman and other investigators (Byus and others 1987; Goodman and others 1989; Litovitz and others 1991; Goodman and others 1992; Lin and others 1994; Lin and Goodman 1995; Litovitz and others 1995; Jin and others 1997; Litovitz and others 1997)

PI	Topic	Exposure	Result	Funded (FY)	Replication
Saffer Battelle Pacific Northwest National Laboratory	MF effects on gene expression in HL-60 cells	6–1,000 μT for 20–60 min	No MF effects on *c-myc* expression; no indication of increased gene expression from differential-display PCR (Saffer and Thurston 1995); a major replication study involving 15 tests of claims of effects varying by factors of 1.3–4.5	1994	Attempt to replicate expression of *c-myc* in HL-60 cells as reported by Goodman and other investigators (Byus and others 1987; Goodman and others, 1989; Goodman and Shirley-Henderson 1990; Litovitz and others 1991; Goodman and others 1992; Phillips and others 1993; Litovitz and others 1995; Uckun and others 1995; Jin and others 1997; Litovitz and others 1997)
		100–1,000 μT for 20–60 min	No indication of cell transformation in initiated JB6-cells cells (Saffer and others 1997)		Attempt to replicate indications of MF promotional effect on initiated JB6 (Litovitz and others 1991; Fitzsimmons and others 1992; Phillips and others 1993; West and others 1994; Uckun and others 1995; Litovitz and others 1995; West and others 1996)
Williams Johns Hopkins Univ.	MF effects on gene expression and interaction of fields with mutagens in HL-60 and lung-cancer cells	100 μT, 60 Hz for 20 min; 100 μT, 60 Hz for 72 h	No reproducible patterns of gene expression observed after any MF exposure investigated	1994	Attempted to replicate expression of *c-myc* in HL-60 cells, as reported by Goodman and co-workers (1990)

Table 2.5b lists project summaries that report *in vivo* replication studies.

In general, the *in vivo* replication studies (table 2.5b) funded by EMF-RAPID did not confirm the positive results of the original experiments. Two replication studies investigated the possibility that MFs act as promoters in carcinogenesis. The study by Anderson and co-workers attempted to replicate the results of Loescher and colleagues, who reported that 50-Hz MF exposure promoted mammary-tumor development in Sprague Dawley rats given dimethyl-[a]benzanthracene (DMBA); melatonin concentrations also were studied. Four papers by Loescher and colleagues, (Loescher and others 1993; Mevissen and others 1993; Loescher and others 1994b; Baum and others 1995) describe their work. Promotional effects and melatonin suppression were observed in some of their experiments.

To evaluate the potential of 50- or 60-Hz MFs to promote breast cancer in female Sprague Dawley rats treated with DMBA, several experimental protocols were followed by Anderson's group. In each of the protocols, groups of 130 rats were used for each exposure level of 0.1 mT at 60 Hz and 0.1 and 0.5 mT at 50 Hz, with and without administration of DMBA by gavage in sesame oil. Animals were exposed to MFs for 13 wk or 26 wk, including sham-exposed and vehicle-control groups. During the MF exposure period, all animals were evaluated for mammary-gland tumors by palpation; at the end of the MF exposure period, tissues from all animals were evaluated histopathologically. The first 13-wk, 20 mg DMBA study and the 26-wk, 10 mg DMBA study showed that 90% of the rats developed multiple mammary carcinomas; this limited the sensitivity to a possible promotional effect of MFs. Therefore, the second 13-wk study was carried out at a reduced DMBA dose of 8 mg. In this study, 40% of the animals developed mammary cancers, thus providing enough sensitivity to detect effects reported by Loescher. In addition, a 26-wk study With 10 mg of DMBA was completed in which there was no evidence of early onset of mammary gland tumors as a result of magnetic field exposure.

This project, using a proven and well-established protocol, found no evidence of any promotional activity of MFs of 0.1 and 0.5 mT at 50 Hz or 0.1 mT at 60 Hz in the Sprague Dawley rat. The study also found no evidence of a melatonin-suppression effect. Possible differences in the replication study include the age of the rats and DMBA purity; the DMBA lot at Battelle produced tumors at a lower concentration than the lot used by Loescher and colleagues. Independent evaluation of the weak positive promotional results reported by Loescher and others was an important objective of the EMF-RAPID program. The study by Anderson and colleagues was one of several EMF-RAPID biology projects funded by a contract mechanism. Because the contract mechanism was used, a complete peer-reviewed report (NTP 1998a) for Anderson's project was available to the committee at the completion of the EMF-RAPID program. The second group of investigators (Byus and others 1987) received support to test claims that MFs and TPA can act as copromoters of DMBA-initiated epidermal tumors. Two Sencar mouse experiments involving DMBA initiation, TPA promotion, and 2-mT field exposure were completed; they yielded contradictory results. The PI is convinced that the best chance of detecting a copromotional effect of MFs occurs with low doses of TPA, at which tumor response is low and statistical power is highest.

The difference between groups was not statistically significant until between weeks 30 and 43. The PI feels that this "late" effect is important and possibly reflects the

response of a subset of tumor types. However, experiment 2 did not show a clear copromotional effect. The author discusses possible reasons for the different outcomes, emphasizing that in experiment 2 the overall tumor response to the same dose of TPA was greater. Also, the response in experiment 2 was "early" rather than "late". In both experiments, ornthine decarboxylase (ODC) was measured in a variety of tissues; no MF-related increases in ODC were observed. The report supplied to the committee on this project is difficult to evaluate, but it does not establish robust effects.

Three projects tested various aspects of the relationship between MF exposure and melatonin concentrations in humans. A preliminary reanalysis of existing data (Burch and others 1998) by Yost reports a statistically small effect ($P < 0.04$) on melatonin concentrations at night in electrical-utility workers. In an analysis of one of their earlier studies of human subjects, Graham and others (1996) found that melatonin concentrations in men with low pre-existing melatonin were affected by exposure to large MFs under controlled conditions in a laboratory setting. Under EMF-RAPID sponsorship, they tested these findings in a replicate experiment with men and in a similar experiment with women as subjects; both experiments produced negative results.

Reiter conducted a series of about 12 experiments on melatonin in rats using the Yellon exposure paradigm (Yellon 1994), which involves a single 30-min exposure to 60-Hz and 0.1 mT beginning 2 h before lights off. The Reiter experiments used rats as the animal model; the Yellon studies used a djungarian hamster model. Species differences in melatonin responsiveness to MF exposure are a possibility. Reiter reports uniformly negative results. Later, he conducted five experiments with the exposure paradigm of Selmaoui and Touitou. This protocol involves 12 h of exposure, beginning in light and extending into darkness; again, melatonin was assessed on the first night of exposure. This also was an acute experiment, ignoring evidence from rats that the melatonin-suppression effect develops over days to weeks of chronic day-night exposure (Wilson and others 1986; Kato and others 1994). Selmaoui and Touitou (1995) had reported weak evidence of a melatonin-suppression effect; Reiter reports uniformly negative results with the Selmaoui and Touitou exposure paradigm.

Table 2.5b—In vivo Experiments Conducted as Efforts to Replicate Previous Reports of MF Effects

PI	Topic	Exposure	Result	Funded (FY)	Replication
Anderson Battelle Pacific Northwest National Laboratory	Effect of MFs as promoters of DMBA-initiated mammary-tumor development in Sprague Dawley rats	0.1 and 0.5 mT at 50 Hz, 0.1 mT at 60 Hz, 13 and 26 wk	Anderson and colleagues unable to replicate reports by Loesher and co-workers that MF exposure promotes mammary-tumor development in DMBA-treated rats (NTP 1998a)	1996	Attempt to replicate observation by Loescher and co-workers that MF exposure promotes mammary-tumor development in DMBA-treated rats (Mevissen and others 1993; Loescher and others 1994a; Loescher and others 1994b; Baum and others 1995)
Byus Univ. of California, Riverside	MFs and TPA as copromoters of DMBA-initiated epidermal cancer in Sencar mouse	2 mT	One experiment indicated significant copromotional effect on skin carcinogenesis after 30 wk of treatment; second experiment did not show copromotional effect	1992	Positive indication of copromotion in ODC transgenic K2 mice (Stuchly and others 1992)
Graham Midwest Research Institute	MF effects on melatonin and immunity in humans	20 μT	One study failed to confirm hypothesis that MFs suppress nocturnal melatonin in men with pre-existing low melatonin; second study failed to show MF effect on melatonin in women	1994	Replication of previous observation (Graham and others 1996) that, in men with low existing melatonin, MF exposure further suppressed production

PI	Topic	Exposure	Result	Funded (FY)	Replication
Reiter Univ. of Texas Health Science Center	MF effects on pineal melatonin in rats	0.025, 0.05, and 0.1 mT continuously and intermittently for 12 h	No statistically significant effects on pineal melatonin in 17 experiments conducted with Yellon or Selmaoui and Touitou acute exposure protocols	1994	Attempt to verify MF effects on melatonin as mechanism of MF health effects with multiple acute MF-exposure protocols
Yost Univ. of Washington	MF effects on melatonin in utility workers	Environmental fields of 0.1–0.3 [.muT measured with personal exposure meters for reanalysis of data of Butch and colleagues (1998)	Trend of decreased nocturnal melatonin after increased MF exposure during workday; weaker correlation when compared with h mean exposures, suggesting a confounder; results have borderline statistical significance	1997	Reanalysis of data from study by Burch and co-workers reporting an association between MF exposures of utility workers and lowered melatonin (Butch and others 1998)

Biology Summary

The first three categories of biology projects are of limited use for the evaluation of health effects at the present time. The majority of the information was provided to the committee in the form of 2–3 page project summaries. It was not always clear whether the work was hypothesis driven or "screening for effect" investigations. If published in peer-reviewed journals the hypothesis-driven studies could have value even if they report negative results. Category 4 projects provided sufficient information, either in the project summaries, or in solicited material sent to the committee, to estimate the magnitude of the reported effect. The reports of effect in this category are unconfirmed. Category 5, the replication category, is an important classification in the committee's judgement. This final category includes a wide scope of replication studies, ranging from "exact replications" to attempts to replicate general effects (transformation for example). The results of these replication studies are almost entirely negative.

Discussion

From a technical perspective, the EMF-RAPID program has helped incrementally to answer the basic question of whether environmentally relevant power-frequency MFs can produce biologic effects. The engineering studies underscore the fact that time-averaged MF exposures in a wide range of occupations are remarkably similar. That has implications for the interpretation and design of epidemiologic investigations. The literature on laboratory studies of this subject is full of conflicting claims. The only responsible way to deal with the situation is to subject the most important positive reports to multiple independent replication. EMF-RAPID made a substantial start on replication, which is an important contribution. The replications conducted under the program have had almost entirely negative results and thus have reduced the credibility of many of the claims of biologic effects of power-frequency MFs.

If it can be shown unequivocally that low-level power-frequency MFs do produce biologic effects, and if the effects are robust enough for the scientific community to reproduce the phenomena routinely, the underlying biophysical mechanism will eventually be established. However, the EMF-RAPID program has shown that much of the literature on MF bioeffects is questionable, in that it is not easily replicated. No finding from the EMF-RAPID program substantially contradicts the conclusions of the earlier National Research Council committee report *Possible Health Effects of Exposure to Residential Electric and Magnetic Fields* (NRC 1997).

INFORMATION-DISSEMINATION PROJECTS

The Energy Policy Act of 1992 specified that the EMF-RAPID program should "provide for dissemination of information . . . to the public". Two of the four objectives of the National Electric and Magnetic Field Research and Communication Program: Draft Strategic Plans[5] were not met:

- "Plan, support, and conduct communication research." The committee is unaware of any communication research funded under EMF-RAPID.
- "Encourage communication from public decision-makers to those who plan scientific studies". The committee found little evidence of such encouragement, although it is not clear what was intended by the objective, and the interagency committee might be seen as fulfilling this aim.

Information-Dissemination Booklets

Two booklets were published as part of the EMF-RAPID communication effort. The first, *Questions and Answers About EMF: Electric and Magnetic Fields Associated With the Use of Electric Power* (DOE 1995) was reviewed in the committee's interim report. The present EPACT Committee concurs with the original assessment on page 20 of this report. According to information provided by NIEHS, about 180,000 copies of the booklet have been dispersed, half going to utilities for distribution to customers and the remainder going to state and local governments and to fill requests from the public. An additional 20,000 copies of the booklet were printed in Spanish; about 16,000 copies have been dispersed. The committee, in its interim report, concluded that more booklets of this sort should be published and suggested that it would be useful to prepare a more comprehensive guide, which would include biologic effects observed in the laboratory and an extended reference section for the more technically interested reader.

A second booklet, *Questions and Answers EMF in the Workplace*, was produced by EMF-RAPID. This booklet included some of the same information as the first booklet, but it also included chapters on human health studies (epidemiology) and biologic research (animal and cell biology). Information was presented on MF measurements, and examples of MF exposure in the workplace were included. It identifies other information sources and includes an extended reference section. The booklet was printed in the United States and Canada, and NIEHS has estimated that 65,000 copies were distributed in the United States. It meets the recommendations of the interim EPACT Committee report.

EMF InfoLine

The Environmental Protection Agency (EPA) initially operated a toll-free telephone EMF-information line jointly funded by EPA and EMF-RAPID. In 1998, oversight of the line was assumed by NIEHS. The information line responds to public inquires about both 60-Hz MFs and radio-frequency radiation, and it refers callers to appropriate resources. The persons who answer calls also take orders for the two booklets described above. Calls to the line seem to be handled responsibly. The EPACT Committee has no information on funding support for this seemingly useful activity.

EMF-RAPID Web Site

The NIEHS EMF-RAPID Web site (http://www.niehs.nih.gov/emfrapid/home.htm) contains a number of documents available to any member of the public who has access to the Internet. The number of requests for downloads averages 161 per day. For the period

[5] For communication objectives see page 16 of this report

March 1, 1997, to June 30, 1998, a total of 78,128 files were downloaded from the site. Items are added and occasionally removed from the site, but a menu existing in August 1998 illustrates the type of information that is available:

- Overview and program focus: a one-page description of the program.
- Program organization, staff, and components.
- EMF annual reports: NIEHS reports for years 1994–1996 with updates for 1996 and 1997.
- EMF-RAPID interim report to congress, December 1995.
- Research information: short (two or three page) project summaries of the 61 projects funded by EMF-RAPID and some projects funded by other means. Some of the project summaries included on the Web site have many of the same shortcomings as those in the project summary books provided to the committee. Data sometimes were incomplete, absent, or not current. Occasionally, cited figures and tables are not present. It sometimes appears that publications cited as resulting from projects predate the projects or are not related to them. Some funding information and contact information on the principal investigators are provided.
- EMF regional magnetic field exposure facilities: brief descriptions of the four facilities designed to provide uniform MF exposures for the EMF-RAPID program, links to the four institutions (Food and Drug Administration, National Institute for Occupational Safety and Health, Oak Ridge National Laboratory, and Pacific Northwest National Laboratory), and an e-mail contact for each program.
- EMF-science review symposia and meetings: information from the three NIEHS symposia and the Department of Energy engineering symposium. The discussion of the DOE engineering component was fragmentary and incomplete at the time this report was written.
- *Questions and Answers about EMF*: this booklet can be accessed directly or downloaded from the Web site.
- *EMF in the Workplace-Questions and Answers*: can be accessed directly or downloaded from the site.
- EMF measurements database: "The purpose of this project is to make measurements of EFs and MFs publicly available". A small amount of information from the engineering symposium is available here. Three data sets had been entered at the time of committee review. The database is not judged to be user-friendly.
- Other MF information sources: directs the users to other sources MF information.
- Working-group report: available in PDF and HTML versions.

Miscellaneous

An EMF "sourcebook" was created in a hard copy version and on the Internet. The hard copy version of the sourcebook consists of materials similar to those appearing on the EMF-RAPID Web site (described previously). Two travel grants were awarded to allow representatives from citizen groups concerned about EMFs to attend the 1995 annual DOE contractors' meeting in Palm Springs, CA.

Summary

Regarding a third objective of the draft strategic plan—"improve coordination and communication with the national and international scientific community. Provide referral services . . ."—the scientific symposia (discussed in the next section of this report) did meet the objective of improving communication among the scientific community. The committee finds the scientific and technical quality of the information to be acceptable. The objective to "provide referral services" is partially met by the Web site described above, and referral services were also provided by the EMF-RAPID information line. If data were regularly entered into the database, progress toward meeting this objective would be improved.

Finally, the fourth objective of educating the public and others is addressed by many of the activities listed above. However, much of the material is in a format or a language directed at the technical community. The first booklet was written for the general public. The committee recommends that NIEHS work to make the Web site easily accessible for the general public.

EMF SCIENCE-REVIEW SYMPOSIA

NIEHS organized three EMF science-review symposia that were intended to review the literature on several major power frequency magnetic field research subjects. The first covered theoretical mechanisms and *in vitro* research, the second covered epidemiologic research, and the third covered clinical and *in vivo* laboratory research. The meetings were open to the public. The "breakout group" reports of the meetings are available as NIEHS publications (NIEHS 1997; NIEHS 1998b,c) and also are available to the public on the EMF-RAPID Web site. The reports reasonably summarize the meetings. However, despite the hard work of many participants, the meetings did not constitute a systematic, comprehensive review of the literature.

The most important accomplishment of the three biology-review symposia might have been to educate newcomers brought into the risk-assessment process being considered by NIEHS. For example, discussion groups attempted to answer specific questions posed by NIEHS. Some of these questions were related to summaries of the state of the science, and other questions were related to hazard identification and risk assessment. However, on-site ad hoc efforts to review a selected subset of extensive and complex scientific literature in a few hours in a large public meeting did not provide an effective and satisfying product. Thus, the scientific value of these meetings is less than that of the 1997 National Research Council committee report (NRC 1997), the 1998 NIEHS working-group report (NIEHS 1998a), or other published reviews. Furthermore, with respect to communication among members of the bioelectromagnetics community, the three NIEHS biology review meetings were supplementary efforts added to the two prime scientific meetings, the DOE contractors' conference and the Bioelectromagnetics Society meeting, which have been held annually for at least 2 decades. The NIEHS working group did not use the three EMF science-review symposium booklets in a formal way. It is not known whether they will be used by NIEHS in the preparation of its final report.

A fourth symposium on the engineering component of the EMF-RAPID program, sponsored by DOE, allowed principal investigators who had completed detailed engineering-project reports to present their methods and findings publicly, and discuss them with interested participants (NIEHS 1998d).

EMF-RAPID WORKING-GROUP REPORT

The working-group meeting, held June 16–24, 1998, in Brooklyn Park, MN, produced an NIEHS report titled *Assessment of Health Effects from Exposure to Power-Line Frequency Electric and Magnetic Fields* (NIEHS 1998a). A press release described the essential findings of the report, and the report was made available for public review (hard copy and CD-ROM available by mail) and placed on the EMF-RAPID Web site in several formats. A period for public review and comment was designated from August 10, 1998, through October 9, 1998. The public was encouraged to comment on the report by mail or in person at three locations: Washington, DC, on September 28, 1998; San Francisco, CA on October 1, 1998; and Chicago, IL, on October 5, 1998. A fourth opportunity for public comment occurred on the afternoons of September 14 and 15, 1998, at the annual EMF contractors' meeting sponsored by DOE in Tucson, AZ. Records of the public comments are available to the public at various sites in the United States.

Under the EMF-RAPID program, NIEHS established the working group to assess health effects of exposure to power-frequency magnetic fields. The working group, consisting of 29 voting members, met on June 16–24, 1998, in Brooklyn Park, MN. Twelve of the participants contributed to first-draft documents before the meeting.

As in the three biology symposia, the working group largely considered published findings. Papers and reports that had not been published but that provided enough detail, including results of *in vivo* studies funded by RAPID, were considered. Although this rule was not always strictly adhered to, it tended to eliminate current EMF-RAPID research from consideration or discussion. The NIEHS working group reviewed essentially the same epidemiology that was reviewed by the Research Council committee on Possible Health Effects of Exposure to Residential Electric and Magnetic Fields (NRC 1997), adding the literature accumulated from 1996 to 1998.

The two reviews differed in a number of important ways. Perhaps the most important were the time available for arriving at the conclusions and the process of arriving at the wording of the conclusions. The Research Council committee functioned for several years and had intensive discussions over the course of many meetings. The NIEHS working group as a whole was operational for 10 d, and most of the time was devoted to arriving at the final language of the literature review. The discussions in which conclusions were reached occurred at the end of the meeting and were very limited in time. The Research Council committee developed its conclusions, after multiple discussions among the whole committee, in the form of a consensus report agreed to by all participants. The NIEHS working group was directed to follow the process used by IARC. The participants answer a set of predefined questions in successive votes. The questions cannot be modified during the process, and the weight of the participants' opinions is equal for all questions and votes, regardless of their disciplines and expertise. No effort was made to reach consensus nor to identify and explain differences in opinion.

Much of the working group's time was spent in small groups as subcommittees worked to write specific sections of the literature review. Although plenary sessions were held, these usually were attended only by groups that wrote the text or by individuals from closely related fields of expertise.

The process used by the Research Council committee involved long and repeated discussions in which the expertise of the participants could be considered in arriving at a consensus. The findings and conclusions were framed in ways that allowed a consensus to be developed. Furthermore, they reflected nuances based on the context of the weight of evidence that was discussed in many sessions in which all members took part. This negotiated consensus was a set of conclusions arrived at by all the participants after multiple sessions of open discussion. The process put a premium on the persuasiveness of the evidence and on the ability of participants of one discipline to persuade participants from other disciplines about the value of different lines of evidence.

The value of the IARC-based process is its following of an established process used extensively in the evaluation of the carcinogenicity of hundreds of compounds. The IARC process leads to a definite result—the evaluation of the human carcinogenicity of an agent. Because an agent to be evaluated with the IARC process needs to be a suspect carcinogen and because the process is conservative in the prescribed steps, it is not surprising that IARC evaluations are extremely likely to result in a finding of possible carcinogenicity.

The IARC process is guided by the epidemiologic evidence in humans which can be "sufficient", "limited" or "inadequate". Animal evidence can be "sufficient", "less than sufficient", "limited", and "inadequate". The final characterization of the exposure can then be Group 1 "carcinogenic" (human:sufficient, animal:sufficient), Group 2A "probably carcinogenic" (human:limited, animal:sufficient), Group 2B "possibly carcinogenic" (human:limited, animal:less than sufficient), Group 3 "not classifiable" (human:inadequate, animal: inadequate or less than sufficient), and Group 4 "probably not carcinogenic" (human:evidence suggesting lack of carcinogenicity, animal:evidence suggesting lack of carcinogenicity) or (human:inadequate, animal:lack of carcinogenicity). The process does not recognize lack of carcinogenicity in animals except in Group 4, and that would require a finding that the human evidence was inadequate.

Both reviews (NRC 1997; NIEHS 1998a) had the benefit of meta-analysis of epidemiologic findings, and much the same approach was used in both meta-analyses. The meta-analyses were carried out on the basis of published data; considerable differences existed in the design and execution of the studies. Characterization of the exposure to EMFs varies widely in different studies, and it is not possible at this time to identify the most relevant metric for characterizing exposure. The appropriateness of converting wire codes into assigned levels of MFs on the basis of the few simultaneous observations of wire codes and direct measurements in homes may be a questionable undertaking but it is necessary to link different studies. Many of the meta-analyses were based on categorical estimates of exposure; few analyses addressed exposure estimates of a continuous nature. The meta-analyses in both reports contain numerous cautions as to many inherent weaknesses, but they then proceed to present the combined results of a large number of analyses. One purpose of the meta-analyses is to see whether the combined statistical power of several studies provides more significant associations. The

meta-analyses have not increased the strength of the association, although one does get the expected increase in statistical significance.

The Research Council committee report and the NIEHS working-group report reviewed much of the same epidemiology. The latter group had the ability to review literature published in 1996–1998, although no definitive or extraordinary epidemiologic studies were published during the 2-yr period. The conclusions are not greatly dissimilar, but the two processes resulted in differently worded statements. The Research Council committee report (NRC 1997) concluded that;

- Living in homes classified as being high in the wire-code category is associated with about a 1.5-fold excess of childhood leukemia, a rare disease.
- MFs measured in the home after diagnosis of disease in a residence have not been found to be associated with an overall excess incidence of childhood leukemia or other cancers.
- Studies have not identified the factors that explain the association between wire codes and childhood leukemia.
- Taken together, epidemiologic evidence does not support possible associations of MFs with adult cancers, pregnancy outcome, neurobehavioral disorders, and childhood cancers other than leukemia.
- MF exposures at 50–60 Hz delivered at field strengths similar to those measured in typical residential exposures (0.01–1.0 μT) do not produce any significant *in vitro* effects that have been replicated in independent studies.
- Reproducible changes have been observed in the expression of specific features in the cellular signal-transduction pathways for MF exposures at about 100 μT and higher.
- There is no convincing evidence that exposure to 60-Hz power-frequency magnetic fields causes cancer in animals.
- There is no evidence of any adverse effects on reproduction or development in animals, particularly mammals, from exposure to power-frequency 50- or 60-Hz EFs and MFs.
- There is convincing evidence that low-frequency pulsed MFs greater than 0.5 mT are associated with bone-healing responses in animals.

A number of additional conclusions and recommendations in the Research Council committee report referred to findings and recommendations about research needs.

The final summary and evaluations of the NIEHS working-group report (NIEHS 1998a), offer the following statements:

- The working group concluded that ELF MFs are "possibly carcinogenic" in humans (supported by 19 members; eight members considered the evidence as not allowing a classification as to carcinogenicity, one member considered the evidence as indicating noncarcinogenicity in humans, and one member abstained from voting).
- Of 26 working-group members voting on the question, 20 concluded that there was limited evidence that residential exposure to ELF MFs is carcinogenic in children on the basis of the results of epidemiologic studies of childhood leukemia; the remaining six voting members concluded that there was inadequate evidence.

- Of 25 working-group members voting on the question, 14 concluded that there was limited evidence that occupational exposure to ELF MFs is carcinogenic in humans, primarily on the basis of results of studies of chronic lymphocytic leukemia; the remaining 11 voting members concluded that there was inadequate evidence.
- Of 25 working-group members voting on the question, 22 concluded that there was inadequate evidence of an association between occupational exposure to ELF MFs and the risk of cancers other than leukemia; two members concluded there was limited evidence, and one that there evidence for lack of an effect.
- Of 25 working-group members voting on the question, 24 concluded that there was inadequate evidence that residential exposure to ELF MFs is carcinogenic in adults; the other member concluded there is evidence for lack of an effect.
- All 25 working-group members voting on the question concluded that there was inadequate evidence of an association between exposure to ELF MFs and childhood nervous system tumors or childhood lymphoma.
- Of 27 working-group members voting on the question, 19 concluded that there was inadequate evidence in experimental animals of the carcinogenicity of exposure to ELF MFs; the remaining eight members concluded that there was evidence of lack of an effect.

It is worth noting that no working-group member voted for the conclusion that ELF MFs are "carcinogenic" or "probably carcinogenic". It is unfortunate that the summary statements focused so heavily on cancer. The extensive literature reviewed in the report addressed effects other than cancer.

When the working-group report is considered in more detail, the dramatic contrast apparent between the Research Council committee report (NRC 1997) and the NIEHS report (NIEHS 1998a)—"no effect" versus "possible carcinogen"—is reduced; and when the differences between the two evaluation processes that were used are taken into account, the difference in conclusions is understandable. The current committee concludes, however, that the conclusions of the 1997 Research Council committee report (NRC 1997) more accurately convey the health implications of the underlying research to the public.

Several national and international organizations are involved in developing exposure guidelines for EFs and MFs, and several such guidelines have been published for power frequencies. The predecessor of the International Commission for Non-ionizing Radiation Protection (ICNIRP) and the International Non-ionizing Radiation Committee (INIRC) of the International Radiation Protection Association (IRPA), published exposure guidelines for power-frequency EFs and MFs in 1990 (ICNIRP 1990; IRPA/INIRC 1990). These guidelines were recently updated by ICNIRP (ICNIRP 1998) and extended to include exposure to power-frequency magnetic fields with frequencies up to 300 GHz. Similar guidelines or standards have been developed by the American Conference of Governmental Industrial Hygienists (ACGIH 1998) and by the Institute of Electrical and Electronic Engineers (IEEE 1997). These guidelines are based on known acute effects of EFs and MFs. Although all those organizations are aware of the epidemiologic literature dealing with reported associations between EMF exposure and different cancer end points, the data from such experiments have not affected the recommended exposure guidelines. The reasons are the lack of quantitative data about

these associations, the lack of consistency in the reported outcomes, and the lack of adequate characterization of the exposures. It is not possible to determine how much protection can be obtained against undefined risks that might or might not exist at relevant exposures. In the absence of clear, reproducible effects at relevant EMF exposures, the tendency is often to limit exposures specific to the situation or to prescribe that exposures at new installations be held below levels experienced in existing installations.

DISCUSSION AND RECOMMENDATIONS

The results of the EMF-RAPID program do not support the contention that the use of electricity poses a major unrecognized public-health danger. Basic research on the effects of power-frequency magnetic fields on cells and animals should continue, but a special research funding effort is not required. Investigators should compete for funding through traditional research-funding mechanisms. If future research on this subject is funded through such mechanisms, it should be limited to tests of well-defined mechanistic hypotheses or replications of reported positive effects. If carefully performed, such experiments will have value even if their results are negative. Special efforts should be made to communicate the conclusions of this effort to the general public effectively.

The following specific recommendations are made by the committee:

1) The committee recommends that no further special research program focused on possible health effects of power-frequency magnetic fields be funded. Basic research on the effects of power-frequency magnetic fields on cells and animals should continue but investigators should compete for funding through traditional research-funding mechanisms.
2) If, however, Congress determines that another time-limited, focused research program on the health effects of power-frequency magnetic fields is warranted, the committee recommends that emphasis be placed on replications of studies that have yielded scientifically promising claims of effects and that have been reported in peer-reviewed journals. Such a program would benefit from the use of a contract-funding mechanism with a requirement for complete reports and/or peer-reviewed publications at program's end.
3) The engineering studies were initiated without the guidance of a clearly established biologic effect. The committee recommends that no further engineering studies be funded unless a biologic effect that can be used to plan the engineering studies has been determined.
4) Much of the information from the EMF-RAPID biology program has not been published in peer-reviewed journals. NIEHS should collect all future peer-reviewed information resulting from the EMF-RAPID biology projects and publish a summary report of such information periodically on the NIEHS Web site.

5) The communication effort initiated by EMF-RAPID is reasonable. The two booklets and the telephone information line are useful, as is the EMF-RAPID Internet site. There are two limitations to the effort. First, it is largely passive, responding to inquiries and providing information, rather than being active. Second, much of the information produced is in a scientific format not readily understandable by the public. The committee recommends that further material produced to disseminate information on power-frequency magnetic fields be written for the general public in a clear fashion. The Web site should be made more user-friendly. The booklet *Questions and Answers about EMF* should be updated periodically and made available to the public.

APPENDIX A: BIOLOGIC RESEARCH PROJECT FUNDING

Summary of EMF-RAPID Funding of Biologic Research Projects* (in thousands of dollars)

Proj.	P.I.	Project #	FY94	FY95	FY96	FY97	FY98	Total
1	Aaron	R01-ES07402	0	153	179	184	60	576
2	Anderson	N01-ES65397	0	0	805	1,004	28	1,837
3	Austumian	R29-ES06620	109	108	107	107	107	538
4	Austumian	R03-ES08913	0	0	0	77	77	154
5	Balcer-Kubiczek	R01-ES07120	231	195	225	0	0	651
6	Balcer-Kubiczek	R03-ES08898	0	0	0	72	72	144
7	Barrett	Z01-ES23019	10	120	54	70	22	276
8	Bilski	Z01-ES50138	0	10	0	0	0	10
9	Binninger	R01-ES07181	127	109	134	0	0	370
10	Blank	R03-ES08855	0	0	0	85	85	170
11	Blumenthal	Z01-ES90602	54	41	50	80	0	225
12	Byus	R01-ES06128	249	152	0	0	0	401
13	Chignell	Z01-ES50136	2	73	72	76	63	286
14	Costa	R03-ES08851	0	0	0	62	64	126
15	Craviso	R03-ES08903	0	0	0	72	72	144
16	Glickman	R03-ES08894	0	0	0	49	90	139
17	Goodman	R03-ES08867	0	0	0	85	85	170
18	Graham	R01-ES07053	281	296	354	364	0	1,295
19	Griffin	R03-ES08864	0	0	0	89	90	179
20	Grissom	R03-ES08896	0	0	0	72	75	147

Proj.	P.I.	Project #	FY94	FY95	FY96	FY97	FY98	Total
21	Hahn	R03-ES08895	0	0	0	57	58	115
22	Harry	Z01-ES21164	0	6	8	6	11	31
23	Hei	R03-ES08926	0	0	0	85	85	170
24	Hui	R01-ES07091	169	147	170	177	0	663
25	Hong	Z01-ES90083	0	0	59	60	15	134
26	Kripke	R03-ES08930	0	0	0	71	76	147
27	Lai	R01-ES06290	172	158	187	194	0	711
28	Lai	R03-ES08865	0	0	0	73	74	147
29	Liburdy	R01-ES06401	283	266	283	294	0	1,126
30	Lieberman	R03-ES08931	0	0	0	85	85	170
31	Litovitz	R01-ES06872	0	206	177	302	0	685
32	Loberg	R03-ES08921	0	0	0	106	108	214
33	Lotz	Y01-ES0032	0	118	184	193	83	578
34	Luben	R01-ES06410	235	240	238	249	60	1,022
35	Mandeville	R01-ES07049	151	109	78	0	0	338
36	Marino	R01-ES05928	0	223	167	172	0	562
37	McCormick	R01-ES07093	360	214	264	274	0	1,112
38	McCormick	R03-ES08854	0	0	0	106	0	106
39	McDonald	R03-ES08911	0	0	0	106	108	214
40	McLeod	R01-ES06287	179	151	0	0	0	330
41	McMillan	Z01-ES90067	15	30	0	0	0	45
42	Miller, R.C	R01-ES07124	226	162	181	188	0	757

Proj.	P.I.	Project #	FY94	FY95	FY96	FY97	FY98	Total
43	Miller, S.C	R01-ES07127	196	199	266	357	0	1,018
44 45	Murphy (Two Reports)	Z01-ES50156	2	68	68	47	25	210
46	Nuccitelli	R01-ES0713	231	193	235	235	0	894
47	Owen	Y01-ES40272	79	222	150	131	42	624
48	Pennypacker	Z01-ES90066	15	30	0	0	0	45
49	Putney	Z01-ES90087	19	43	40	46	0	148
50	Reiter	R01-ES07132	206	168	198	205	0	777
51	Reiter	R03-ES08890	0	0	0	60	64	124
52	Rinehart	R01-ES07145	231	185	222	0	0	638
53	Ryan	R03-ES08873	0	0	0	110	0	110
54	Saffer	R01-ES07122	378	324	355	0	0	1,057
55	Sheppard	R03-ES08920	0	0	0	63	62	125
56	Sisken	R03-ES08878	0	0	0	73	74	147
57	Travalos	Z01-ES21195	0	5	0	0	0	5
58	Uckun	R01-ES07175	0	152	145	0	148	445
59	Williams	R01-ES07076	383	299	352	359	0	1,393
60	Woloschak	R01-ES07141	150	128	160	0	0	438
61	Yost	R03-ES08877	0	0	0	69	71	140
		Totals	4,743	5,303	6,167	7,101	2,239	25,553

* All dollar amounts are direct costs

APPENDIX B: SUMMARY OF EMF RAPID ENGINEERING RESEARCH EXPENDITURES BY DOE

Summary of Funding for EMF RAPID Engineering Projects

Project number	Contractor	Amount (in thousands of dollars)	Title
1	ERM	120	"Development of Recommendations for Guidelines for Field Source Management"
2	Magnetic Measurements	123	"Recommendations for Guidelines for Environment-Specific Magnetic Field Measurements"
3	Enertech Consultants	230	Environmental Field Surveys"
4	T. Dan Bracken	110	"Recommendation for Guidelines for EMF Personal Exposure Measurement"
5a	T. Dan Bracken	100	"Development of an EMF Database"
5b	T. Dan Bracken	400	Maintain Data Base
6	Enertech Consultants	996	"Survey of Personal Magnetic Field Exposure"
7	National Institute for Occupational Safety and Health	200	"Hazard Surveillance for Workplace Magnetic Fields"
8	IIT Research Institute and Commonwealth Associates	123	"Evaluation of Field-Reduction Technologies"
9	University of Washington	20	"Characterization of Exposures to Extremely Low Frequency Magnetic Fields in the Office Environment"
10	EM Factors	60	"Assessment of Human Exposure to Magnetic Fields Produced by Domestic Appliances"
11	Center for Risk Management, Resources for the Future	50	"Risk Dimensions of the EMF Problem"
12	T. Dan Bracken	138	Project not received in time for review. ("Source and Exposure Prediction Model Development")
	Total	2,670	

APPENDIX C: SUMMARY OF EMF RAPID NON-RESEARCH EXPENDITURES BY NIEHS

EMF-RAPID Non-Research Expenditures (in thousands of dollars)

PI	Project	FY94	FY95	FY96	FY97	FY98	FY99	Total
Boorman	Administration	94	117	113	154	215	25	718
Goldberg	PR702671 Publication Database	0	0	0	63	0	0	63
Portier	Evaluation	0	0	155	620	1,516	278	2,569
Totals		94	117	268	837	1,730	306	3,350

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LIST OF ABBREVIATIONS

ACGIH	American Conference of Governmental Industrial Hygienists
BRER	Board on Radiation Effects Research
CLS	Commission on Life Sciences
DHHS	Department of Health and Human Services
DMBA	Dimethyl2-[a]benzanthracene
DOE	Department of Energy
EF	Electric field
EGF	Epidermal growth factor
ELF	Extremely low frequency
ELF MF	Extremely low frequency magnetic field
EMF	electric and magnetic field
EMF-RAPID	Electromagnetic Field Research and Public Information Dissemination
EPA	Environmental Protection Agency
EPACT	Committee to Review the Research Activities Completed under the Energy Policy Act of 1992
EPRI	Electric Power Research Institute
IAC	EMF Interagency Committee
IARC	International Agency for Research on Cancer
ICNIRP	International Commission for Non-ionizing Radiation Protection
IEEE	Institute of Electrical and Electronic Engineers
INIRC	International Non-ionizing Radiation Committee
IRPA	International Radiation Protection Association
MF	Magnetic field
NAS	National Academy of Sciences
NEMFAC	National EMF Advisory Committee
NIEHS	National Institute of Environmental Health Sciences
NIH	National Institutes of Health
NIOSH	National Institute of Occupational Safety and Health

NRPB	National Radiological Protection Board
ORAU	Oak Ridge Associated University
PI	Principal investigator
PKC	Phosphokinase C
TWA	Time weighted average