United States
Environmental
Protection Agency

Science Advisory
Board (A-101)

EPA-SAB-RAC-92-013
January 1992

EPA

AN SAB REPORT: POTENTIAL CARCINOGENICITY OF ELECTRIC AND MAGNETIC FIELDS

REVIEW OF THE ORD'S POTENTIAL CARCINOGENICITY OF ELECTROMAGNETICS FIELDS BY THE RADIATION ADVISORY COMMITTEE'S NONIONIZING ELECTRIC AND MAGNETIC FIELDS SUBCOMMITTEE

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 29, 1992

EPA-SAB-RAC-92-013

OFFICE OF
THE ADMINISTRATOR

Mr. William K. Reilly, Administrator
U.S. Environmental Protection Agency
401 M Street SW
Washington, DC 20460

Re: Potential Carcinogenicity of Electromagnetic Fields

Dear Mr. Reilly:

The enclosed is the report of the Nonionizing Electric and Magnetic Fields Subcommittee of the Science Advisory Board's Radiation Advisory Committee. The report has been endorsed by the Science Advisory Board on the recommendation of its Radiation Advisory Committee.

The Subcommittee was set up in response to the October 12, 1990, memorandum from the Directors of the Environmental Protection Agency's Offices of Health and Environmental Assessment (William Farland), Health Research (Ken Sexton), and Radiation Programs (Richard Guimond). The letter requested a peer review of the draft report Evaluation of the Potential Carcinogenicity of Electromagnetic Fields (EPA/600/6-90/005B).

The Subcommittee met three times. Its first meeting, on January 14-16, 1991, in Washington, D.C., elicited an uncommonly strong public participation: over 200 people, 19 formal and several informal presentations, and a lively debate between Subcommittee members (sitting as a panel) and members of the audience. Among the formal presentations were those made by Congressman Frank Pallone (Dem.-New Jersey), Mayor J. Connors (Scranton, Pennsylvania), Dr. D. N. Erwin of the United States Air Force Armstrong Laboratory for Human Systems, and Dr. Robert Adair, Sterling Professor of Physics at Yale University. At its second meeting on April 12-13, 1991, in San Antonio, Texas, the Subcommittee received preliminary drafts prepared by its three subgroups (on physics, biology, and epidemiology) and heard invited presentations by biophysicist Dr. Arthur Pilla of Mt. Sinai Hospital in New York City, biologist Dr. Russel Reiter of the University of Texas Health Science Center in San Antonio, and physiologist Dr. Asher Sheppard of the Pettis Memorial Veterans Hospital in Loma Linda, California. At its third meeting, July 23-25, 1991, in Washington, the Subcommittee reviewed a draft of the present report which was subsequently approved by mail with some amendments.

The charge to the Subcommittee was to review the document as to the accuracy and completeness of the information provided, as well as the interpretation of the scientific data. The EPA document has serious deficiencies and needs to be rewritten. As the result of many internal inconsistencies, it is often difficult to tell what the EPA's position is when reading the Evaluation of the Potential Carcinogenicity of Electromagnetic Fields. Portions of the draft lead to conclusions which are not the conclusions stated elsewhere in the document. Such inconsistencies appear not only between the body and the executive summary, but also between different pages of the document itself.

Consequently, the document requires a logical reorganization and complete rewriting with particular attention to careful and precise use of language. A simple editing of the present text would not be sufficient. The Subcommittee consciously refrained from providing a list of particular inconsistencies because it does not want to mislead the EPA into believing that editing alone will address the Subcommittee's concerns.

Six specific questions were posed in the charge to the Subcommittee. Before responding to these questions explicitly, the Subcommittee feels it important to express its viewpoint on three underlying scientific issues, concerning (a) epidemiology, (b) biological effects, and (c) carcinogenicity. These issues are critical for the understanding of scientific issues in research regarding electric and magnetic fields and must be addressed in any future EPA discussion of the potential carcinogenicity of electric and magnetic fields.

a. The Subcommittee concluded that some epidemiological evidence is suggestive of an association between surrogate measurements of magnetic-field exposure and certain cancer outcomes. In such studies, the existence of confounders is always a possibility, but since no common confounder has yet been identified, the existing evidence cannot be dismissed. In the absence of much better exposure information and an understanding of which exposures are significant, no precise exposure-response relationship has yet been adduced. This lack, together with limited understanding of possible biological mechanisms, prevents the inference of cancer causality from these associations at this time.

b. The Subcommittee accepts that effects on some biological systems have been shown to occur at moderate field intensities. (An example of such effects is the well-documented work on phosphenes.) However, the evidence for effects at very low field strengths is not so widely accepted. Even if effects on living systems at lower fields do occur, the assumptions leading to estimations of physical constraints thought to preclude effects on isolated small spherical cells without ferromagnetic structures may not be applicable to larger cells or cell systems such as neurons or neuronal networks. Many intervening steps must be clarified before the biological phenomena so far shown can be taken as direct evidence of health impairment or carcinogenesis in the human.

c. The EPA document does not present a holistic model of carcinogenesis within which the strength of existing evidence concerning the carcinogenic properties of electric and magnetic fields can be assessed. The revised document should do so. Low-frequency electric and magnetic fields do not carry enough energy to cause mutations directly. The Subcommittee recognizes that the incidence of cancer might well be affected by an agent that does not produce mutations. The known influence of factors such as hormonal imbalance and nutrition on cancer promotion is an example of epigenetic effects.

With respect to the Subcommittee's charge and the six questions that were posed, the Subcommittee responds as follows.

1. Is the interpretation of the human and animal evidence of carcinogenicity supported by the available information?

Currently available information is insufficient to conclude that the electric and magnetic fields are carcinogenic. Some human epidemiologic data report an association between surrogates for electric and magnetic field exposure and an increased incidence of some types of cancer, but the conclusion of causality is currently inappropriate because of limited evidence of an exposure-response relationship and the lack of a clear understanding of biologic plausibility.

2. Does the animal or biological effects information provide a basis for postulating that there is a human hazard from exposure to extremely low-frequency fields or either modulated or unmodulated radiofrequency radiation?

Some of the <u>in vitro</u> and <u>in vivo</u> data on unmodulated RF have suggested the existence of mechanisms by which human health

effects, but not carcinogenicity, may be inferred. Both unmodulated and extremely low frequency (ELF)-modulated radiofrequency (RF) fields of sufficient intensity can give rise to thermal effects. Nonthermal biological effects also have been reported in some animals exposed to RF fields. It is well established that some in vitro and in vivo experiments on ELF have shown nonthermal biologic effects at fields of moderate intensity, and there are some suggestive effects at lower levels. Furthermore, ELF-modulated RF fields assumed to be nonthermal can produce many of the biological effects of ELF fields alone. It should be noted that the distinction between biological effects and health effects is an important one. This is especially relevant in the context of the question of possible health effects from electric and magnetic field exposure. Hypothetical constructs relating observed biological effects to possible health effects (specifically, increased cancer risk) have been delineated. However, there are at present insufficient data on many of the critical steps in the linkage to infer causality on the basis of animal or cellular data.

3. Has the Agency properly evaluated the way in which the findings on biological effects and field-tissue interaction mechanisms affect the interpretation of the human studies?

No, the EPA has not evaluated how the findings on biological effects and nonionizing field and tissue interaction mechanisms relate to the interpretation of human studies. The strength of epidemiologic data depends on identification of supporting evidence from in vitro and in vivo data. This relationship has not been developed in the report. The critiques of studies of biological effects are contained in the discussions of the several chapters.

4. Is the choice of topics in Chapter 5 appropriate and is the interpretation of the biological effects literature as it relates to carcinogenesis supported by the available information?

The heading of chapter 5, "Supporting Evidence of Carcinogenicity," is inappropriate. The interpretation of the biological effects in the in vitro systems as presented by the report does not make a case for carcinogenicity. The Subcommittee found a lack of balance in the analysis and presentation of evidence in this chapter. Specific individual experiments need critical review.

5. Is the Agency's carcinogen classification system applicable to electromagnetic fields?

Nonionizing electric and magnetic fields should not be classified under EPA's chemical carcinogenesis system because of present major uncertainties. These involve an incomplete understanding of which aspects of field-tissue interactions give rise to biological effects. Properties of the various electric and magnetic fields such as phase angle, polarization, transients, and frequency range may contribute to different biological effects. For these reasons, the use of the EPA's classification scheme at this time would be inappropriate and confusing.

6. Does the information cited in the document support the conclusion that there is not enough information to designate specific values of magnetic field strength as being hazardous to human health?

Yes, there is insufficient information to designate specific values of magnetic-field strength that may be hazardous to human health, for two reasons.

a. There is insufficient evidence from the human epidemiology data and from animal/cell experiments to establish cause-and-effect relationships between low-frequency electric and magnetic field exposure and human health effects and cancer.

b. The precise nature of the environmental low frequency electric and magnetic field potentially related to human disease remains to be elucidated. In addition to field strength, parameters such as the time-varying nature of the magnetic fields and the relevant time/exposure parameters need to be determined.

The Subcommittee also wishes to express two specific policy recommendations that in its view follow inescapably from the scientific recommendations.

POLICY RECOMMENDATION #1: The Subcommittee is unanimous in its belief that the question of electric and magnetic field effects on biological systems is important and exceptionally challenging, and that the Subcommittee's advice to the EPA should be that the report should be rewritten by EPA, and then re-reviewed by the Science Advisory Board.

POLICY RECOMMENDATION #2: EPA should complete its efforts with regard to RF electromagnetic fields (including microwaves) and issue exposure guidelines independent of present issues pertaining to lower frequencies. The current EPA report inadvertently leads even the careful reader to conclude that the potential carcinogenicity of electric and magnetic fields of ELF (i.e., powerline) frequencies is the only--or at least the principal--subject of concern with regard to nonionizing fields. Such a conclusion would reinforce the skewed and somewhat sensationalized picture presented to the public in recent years by the news media and government agencies responding to this publicity. The report should therefore declare explicitly that the attention given to nonionizing electric and magnetic fields derives in the first place from long-standing concern over the hazards of RF (including microwave) radiation. EPA has expended substantial resources on the study of such radiation over a period dating back to the EPA's inception, and EPA should complete its efforts directed toward the issuance of RF exposure guidelines. RF fields present long-known and well-understood hazards such as temperature elevation in tissue and heat stress resulting from acute exposures against which users and the general public must be warned and protected. Any published exposure guideline should specifically identify the hazards from RF exposure.

The Science Advisory Board appreciates the opportunity to review issues of this importance and looks forward to a written response from the Agency concerning its schedule for revising the Evaluation of the Potential Carcinogenicity of Electric and Magnetic Fields and it's availability for subsequent Science Advisory Board review.

Sincerely,

Raymond C. Loehr, Chairman
Executive Committee
Science Advisory Board

Oddvar F. Nygaard, Chairman
Radiation Advisory Committee
Science Advisory Board

Genevieve M. Matanoski, Chairman
Nonionizing Electric and
Magnetic Fields Subcommittee
Radiation Advisory Committee

Dr. David V. Bates, Vice Chairman
Nonionizing Electric and
Magnetic Fields Subcommittee
Radiation Advisory Committee

NOTICE

This report has been written as a part of the activities of the Science Advisory Board, a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide a balanced, expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency; hence, the comments of this report do not necessarily represent the views and policies of the Environmental Protection Agency or of other Federal agencies. Any mention of trade names or commercial products does not constitute endorsement or recommendation for use.

ABSTRACT

This review constitutes comments by an Environmental Protection Agency (EPA) appointed subcommittee of seventeen experts in twelve disciplines to review a draft version of EPA's report Evaluation of the Potential Carcinogenicity of Electromagnetic Fields (EPA/600/6-90/005B). The reviewers suggest numerous changes in emphasis, coverage, and wording; comment on some policy considerations; and conclude that the draft report in effect will have to be rewritten if all of these suggestions and comments are to be taken into account. The Subcommittee also presents its conclusions on the substantive scientific questions discussed in the EPA report.

Keywords: electric, magnetic, electromagnetic, cancer

August 2, 1991

U. S. ENVIRONMENTAL PROTECTION AGENCY
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Harvard University, Cambridge, Massachusetts

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1.0 EXECUTIVE SUMMARY

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*

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2.0 INTRODUCTION

2.1 Background

At the request of the Environmental Protection Agency's Office of Radiation Programs, the Office of Health and Environmental Assessment prepared Evaluation of the Potential Carcinogenicity of Electromagnetic Fields. In January 1990, EPA staff requested orally that the Science Advisory Board (SAB) review this document. At its next meeting, in May 1990, the SAB's Radiation Advisory Committee (RAC) responded by establishing a Nonionizing Electric and Magnetic Fields Subcommittee under the chairmanship of RAC member Dr. Genevieve Matanoski. An earlier draft of the Evaluation was reviewed on June 23, 1990, by a panel chaired by Dr. Richard Griesemer of the National Institute of Environmental Health Sciences; this review was not a Science Advisory Board review.

After wide consultation and consideration of more than 250 scientists, the Director of the Science Advisory Board selected seventeen members for the Nonionizing Electric and Magnetic Fields Subcommittee:

Dr. A. Karim Ahmed, Princeton, New Jersey
Dr. David Bates,* University of British Columbia
Dr. Patricia A. Buffler, University of Texas Health Center in Houston, School of Public Health
Dr. Craig V. Byus, Biomedical Sciences and Biochemistry, University of California-Riverside
Dr. Kelly H. Clifton, Department of Human Oncology and Radiology, University of Wisconsin Clinical Cancer Center
Dr. John DiGiovanni, Department of Carcinogenesis, M.D. Anderson Cancer Center
Mr. William E. Feero, Electric Research and Management, State College, PA
Dr. Robert Harris, Department of Environmental Science and Engineering, School of Public Health, University of North Carolina
Dr. Clark Heath, American Cancer Society
Dr. Nan Laird, Department of Biostatistics, Harvard School of Public Health
Dr. Genevieve Matanoski,** School of Hygiene and Public Health The Johns Hopkins University
Dr. M. Granger Morgan, Department of Engineering and Public Policy, Carnegie-Mellon University
Dr. Mary Ellen O'Connor, Psychology Department, University of Tulsa
Dr. Donald Pierce, Department of Statistics, Oregon State University
Dr. Charles Susskind, College of Engineering, University of California-Berkeley
Dr. Bary Wilson, Battelle Pacific Northwest Laboratory

Dr. Richard Wilson, Department of Physics, Harvard University

*Vice Chairman of the Nonionizing Electric and Magnetic Fields Subcommittee.

**Chairman of the Nonionizing Electric and Magnetic Fields Subcommittee.

On October 12, 1990, the Directors of the Office of Health and Environmental Assessment, Health Research, and Radiation Programs formally requested SAB review of EPA's Evaluation of the Potential Carcinogenicity of Electromagnetic Fields and a related research agenda. (This memorandum is Appendix A.) The memorandum contained the charge to the Subcommittee. (The charge also appears in Section 2.2)

At its October 23-24, 1990 meeting, the Executive Committee accepted a workplan for the SAB which included four Fiscal Year 1991 meetings of the Subcommittee to undertake and complete its reviews of the carcinogenicity and research agenda documents.

The Federal Register published a notice December 18, 1990, announcing both the availability of the Evaluation of the Potential Carcinogenicity of Electromagnetic Fields and the first meeting of the Subcommittee. At the first meeting, January 14-16, 1991, in Washington, D.C., EPA staff and contractors briefed the Subcommittee on the document, the public provided more than a day of oral comment, and time was allotted for Subcommittee discussion. Before adjourning, the Subcommittee formed into three groups which would prepare papers for consideration by the Subcommittee at its next meeting. These groups were:

Physics: Mr. Feero, Dr. Susskind,* Dr. Richard Wilson
Biology: Dr. Ahmed, Dr. Byus, Dr. Clifton, Dr. DiGiovanni, Dr. O'Connor, Dr. Bary Wilson*
Epidemiology: Dr. Bates, Dr. Buffler, Dr. Harris, Dr. Heath,* Dr. Laird, Dr. Pierce

* Authored paper after discussion with group.

The Subcommittee met for the second time April 12-13, 1991, in San Antonio, Texas. The Subcommittee considered three group papers, heard three invited speakers (Dr. Russel Reiter of the University of Texas Health Science center at San Antonio, Dr. Asher Sheppard of the Pettis Memorial Veterans Hospital in Loma Linda, California, and Dr. Arthur Pilla of Mt. Sinai School of Medicine in New York City), listened to oral comment from three members of the public, and appointed a writing group to prepare a draft Subcommittee report for consideration at the Subcommittee's July 23-25, 1991, meeting in Washington, DC. (This July meeting also began the Subcommittee's review of the research agenda.)

During the course of its review, the Subcommittee received almost a thousand pages of written public comment from about three dozen individuals and organizations. The Subcommittee listened to oral comment from about 40 individuals. There was

some overlap between those providing oral and written public comments.

The Subcommittee edited this report at the July 23-25, 1991, meeting, subsequently approved it by mail, and forwarded it to the Radiation Advisory Committee. The Radiation Advisory Committee addressed the Subcommittee report at its September 18-20, 1991, public meeting and forwarded it to the SAB's Executive Committee to be considered at its October 29-30, 1991, public meeting. After approval by the Executive Committee and minor editorial corrections as suggested by the Executive Committee, the report was transmitted to the Administrator of the Environmental Protection Agency.

2.2 Charge to the Subcommittee

The Agency seeks the advice of the Board on the accuracy and completeness of the entire document and on the question of whether the interpretation of the available information reflects current scientific opinion. In addition, we would like the Board to address the following specific issues:

1. Is the interpretation of the human and animal evidence of carcinogenicity supported by the available information?

2. Does the animal or biological effects information provide a basis for postulating that there is a human hazard from exposure to extremely low frequency fields or either modulated or unmodulated radiofrequency radiation?

3. Has the Agency properly evaluated the way in which the findings on biological effects and field-tissue interaction mechanisms affect the interpretation of the human studies?

4. Is the choice of topics in Chapter 5 appropriate and is the interpretation of the biological effects literature as it relates to carcinogenesis supported by the available information?

5. Is the Agency's carcinogen classification system applicable to electromagnetic fields?

6. Does the information cited in the document support the conclusion that there is

not enough information to designate specific values of magnetic field strength as being hazardous to human health?

3.0 REVIEW OF THE DOCUMENT

3.1 Response to the Charge

The charge to the Subcommittee was to review the document as to the accuracy and completeness of the information provided, as well as the interpretation of the scientific data. The EPA document has serious deficiencies and needs to be rewritten. It is often difficult to tell what the EPA's position is when reading the Evaluation due to many internal inconsistencies. Portions of the draft lead to conclusions which differ from the conclusions stated elsewhere in the document. Such inconsistencies appear not only between the body and the executive summary, but also between different pages of the document itself.

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effects. For these reasons, the use of EPA's classification scheme at this time would be inappropriate and confusing.

6. **Does the information cited in the document support the conclusion that there is not enough information to designate specific values of magnetic field strength as being hazardous to human health?**

Yes, there is insufficient information to designate specific values of magnetic-field strength that may be hazardous to human health, for two reasons.

a. There is insufficient evidence from the human epidemiology data and from animal/cell experiments to establish unequivocal cause-and-effect relationships between low frequency electric and magnetic field exposure and human health effects and cancer.

b. The precise nature of the environmental low frequency electric and magnetic field potentially related to human disease remains to be elucidated. In addition to field strength, parameters such as the time-varying nature of the magnetic fields and the relevant time/exposure parameters need to be determined.

3.2 Comments on the Executive Summary

The executive summary of Potential Carcinogenicity of Electromagnetic Fields is not adequate. Special care should be taken to ensure that it reflects the contents of the revised report exactly, without drawing any conclusions not substantiated by the body of the report. Not a few readers (and most news media) are sure to give only cursory attention to the full 366-page text and to depend for the gist of it on the executive summary, so special care must be taken to make it readable and accurate.

3.3 Comments on Chapter 2

3.3.1 Electric and Magnetic Fields and Mechanisms for Biological Interactions

Chapter 2 attempts to do four things: describe the physical characteristics of electromagnetic fields; explain how fields couple with the body; quantify ambient exposures; and discuss mechanisms of biological interactions. A comprehensive treatment of these four areas would constitute a book-length text. The authors have compounded their difficulties by attempting to make the presentation relevant to the entire range of frequencies,

from ELF to microwaves. Trying to present all the above in less than forty pages was destined to result in a superficial and spotty treatment. The authors should reduce their scope to a more manageable level by emphasizing the lower frequencies, for which quasistatic analysis is appropriate. The report should not attempt to teach field theory. Instead, it should present material toward the physical understanding needed in later chapters. Simplified but logical and correct relationships must be drawn from the large body of knowledge that encompasses the theory of electricity and magnetism, together with the second law of thermodynamics. In particular, relationships of charges, forces, motion, and time rates of change should be presented for simple situations. It is an assumption, not yet disproved, that they also apply to more complex (biological) situations. The difficulties lie in calculating such complex situations and knowing the boundary conditions.

The draft report separates electric and magnetic fields according to frequency, but the way in which these fields are likely to differ is poorly described. The following should be highlighted.

a) Ionizing frequencies (e.g., gamma and x radiation): the product hf (Planck's constant times frequency) is above the ionization threshold, so that ionization and destruction of a simple cell are possible (even at low intensity, although with correspondingly lower probability).

b) High nonionizing frequencies (e.g., microwave and other radiofrequency radiation): hf is below threshold and no ionization takes place, but both electric and magnetic fields penetrate insulating and partially conducting bodies and can produce heating, as do microwave ovens.

c) Extremely low frequencies (e.g., powerline frequencies): electric fields are strongly attenuated in partially conducting bodies. The electric field E in such bodies derives primarily from changes in the magnetic field B, according to the equation $\text{curl } \mathbf{E} = -\partial \mathbf{B}/\partial t$, or in words, the spatial rate of change of the vector E equals the negative of the time rate of change of the vector B, so that it is not alone the magnitude of the magnetic field that is important, but also the rate at which it <u>changes</u> with time.

The draft report lacks a discussion of the actual parameters of the total electromagnetic fields that are likely to be important for subsequent chapters. There is no recognition that the effects on a system of charges (including the human body) are in <u>forces</u>, as summarized by the Lorenz force law

$F = q(E + v \times B)$, where v is the velocity vector and q is the charge; or in words, that the force consists of two components: (1) the product of charge and electric field, and (2) the product of charge and velocity times the magnetic field and sine of the angle between them. This point is not made in the draft report. There are many implications.

Under some circumstances charges in some bodies act coherently; this provides one potentially promising route for investigating mechanisms of biological interactions with electric and magnetic fields. Another route for investigation is the existence in biological tissues of permanent magnets, such as those found in some soil microorganism and in honey bees. In some circumstances these magnetic structures appear important to living organisms; however, there has not been systematic investigation of the prevalence of such structures or their importance.

3.3.2 Exposure

In the discussion of epidemiology, all mention of exposure is couched in the vague terms of "electromagnetic fields" or even "magnetic fields." The EPA's Human Health Assessment Group normally relates cancer incidence to a long-term average of some exposure parameter. Although that may be appropriate for most cancer-inducing agents, the averaging time may well be shorter for an agent that increases cancer in a new way. However, if there are risks, it is not clear which parameters of electric or magnetic fields will be the important ones. It is appropriate for the report to focus on the time-integrated exposure (or dose) metric, but it is important as well that other parameters be adequately treated.

Which critical parameter of the magnetic-field intensity H should be discussed? It could be dH/dt (the time rate of change of H), or dH/dt above some threshold applied randomly or in some particular sequence over some period of time. It could be $\int H(t)\,dt$ (the integral or sum of H over a time t), as implied by the draft report; or the amount above a threshold H_c, $\int [H(t) - H_c]\,dt$; or the amount with a saturation H_s, $\int H(t)\,dt$ (for $H < H_s$) and $\int H(t)\,dt + \int H_s\,dt$ (for $H > H_s$). It may not be feasible to be all-inclusive, but some discussion of the plausible possibilities is recommended.

The report also fails to discuss background fields other than fluctuations. If we accept there is no new force, the exposure parameter is $E + v \times B$; and inside the body, $\text{curl } E = -\partial B/\partial t$. One of the principal contributions to background exposure comes as we move with a velocity v through the earth's magnetic field B. For many of us, this component is vastly increased when v is the velocity of an aircraft. Yet the draft report is written as if the only background of importance

were the ambient 60-Hz field. That is clearly wrong and should be corrected. And of course this varying background is a source of confusion in any epidemiological study in ways that the draft report fails to discuss.

3.3.3 Models

The rather extensive discussion of models in the report should be reduced to a tabulation of the prevalent hypothesized models, with reference to when each was introduced and to what extent attempts to explain experimental findings by each have been successful. The strengths and weaknesses identified in the literature should be tabulated. For example, the cyclotron-resonance model has been criticized on two counts in a simple paper by John Sandweiss (Bioelectromagnetics 11: 203-205, 1990): (1) the cyclotron radius at the assumed field exceeds the size of the object, yet several revolutions inside are needed to get a resonance; and (2) the mean free path of an electron in the medium is so short that no resonance seems possible--a problem to which reference is made, but whose fundamental nature is not brought out.

3.3.4 Fluctuations

A graph on p. 2-15 of the draft report shows the current densities at which biological effects are expected, as well as the noise fluctuations. There are other papers on fluctuations. A recent publication by Robert Adair in the Physical Review (A43: 1039-1048, 1991), which also served as the basis of his presentation at the Subcommittee's 15 January 1991 meeting, is a good summary of the apparent points of conflict between the biological effects attributed to weak electric and magnetic fields and the constraints of known physical principles.

If a finding is repeatable but not explainable by existing physical theory, it must be clearly labeled as such. Hypothesized mechanisms in such cases are desirable and should be presented. However, they must be discussed in terms of strengths and weaknesses in predicting the observed phenomena, and the points at which they do not fit present understanding. For example, the calculation of thermal noise in a single cell would prove to be inapplicable if it could be demonstrated that the bodies under consideration are not isolated cells but agglomerations of cells of substantially larger dimensions than individual cells, so that calculations based on single cells would have to be revised; or if ferromagnetic materials are involved. An additional point is that biological systems are inherently nonlinear in hierarchies that extend from molecules to cells, to tissues, and finally to organs and organ systems, so that appropriate physical models must account for nonlinear behavior, as well as nonequilibrium physical characteristics, commonly seen at the atomic level rather than the molecular.

3.4 Comments on Chapter 3

3.4.1 Comments

The Subcommittee feels that the report's discussion of epidemiologic findings is seriously deficient, given the central importance of such data in evaluating possible human health risks in this perplexing field. Extensive revisions are therefore necessary both in Chapter 3 and in the report's Summary and Conclusions. Although the EPA report achieves nearly complete coverage of pertinent epidemiologic work published through 1989 and properly approaches workplace exposures separately from residential exposures, the manner in which these data are described and evaluated is inadequate in major respects.

a) In general, the report's review and analysis of epidemiologic findings is unfocused and diffuse. Its writing is often repetitive and imprecise, and descriptions of data are frequently mingled with interpretative comments. As a result, the report lacks cohesiveness, is difficult to read, and loses effectiveness in communicating its findings and conclusions.

b) The manner in which studies are reviewed is uneven. Some studies are clearly less substantial than others, yet they often receive equal or greater attention. Discussion of findings includes too much unwarranted speculation about causal interpretation. Often such speculation appears unbalanced, giving emphasis to positive findings while de-emphasizing negative ones.

c) The critical importance of exposure assessment does not receive sufficient attention, particularly in relation to surrogate measures and to potential misclassification.

d) In evaluating individual studies, and then reaching conclusions for the field as a whole, the report fails to focus coherently on the major epidemiologic issues that ultimately shape any assessment of risk. In addition to exposure assessment, these issues particularly involve ability to discern exposure-response relationships, to make precise measurements of risk levels, and to evaluate the potential influence of confounding variables. The report greatly needs to address these particular issues in an organized and critical manner.

3.4.2 Recommendations

a) Chapter 3 should be extensively re-worked.

Major consideration should be given to full published studies or studies in which manuscripts have received peer review and are in press. Data presented in abstract form, as letters to journals, or as case series anecdotes should be clearly labeled as such. Where other data deserve review (such as the recent work by Peters et al.), their pre-publication nature should be recognized.

The Subcommittee suggests focusing detailed discussion of findings on the several studies of greatest importance and, in those instances, perhaps not exceeding three or four pages each. Other studies (abstracts, letters, etc.) could be summarized more briefly. An appendix might be used if it seems necessary to include extensive detail.

b) Coverage of the literature should be extended through 1990, and beyond as available, especially with respect to the study by Peters et al. The 1989 Coleman et al. study (Brit J. Cancer) deserves fuller consideration, as does information suggesting a role for traffic density as a confounding factor.

c) A succinct summary table displaying only key findings (Note: There is a "summary table" on pp. 3-127 to 3-131 of the EPA's October 1990 document.) and limitations in major studies may help to focus the assessment and might become a nucleus for formal meta-analysis of data. It may also be useful to construct graphs that display odds ratios and confidence intervals for various population/exposure comparisons in major studies.

d) It may be useful to compare data across studies in relation to cancer site, e.g., risks observed for childhood cancers as a whole as opposed to leukemia or central nervous system tumors in particular.

e) Throughout the report, special care should be taken to avoid gratuitous speculation or surmise which may favor either negative or positive interpretations of data beyond the actual limits of those data. The conservative intent of the report can only benefit by evenhanded caution and careful precision in its wording.

3.4.3 Exposure Assessment

A separate, expanded section should be developed addressing issues of exposure assessment. Such a section should particularly discuss the value and limitations of exposure surrogates, gradients, and models in relation to epidemiologic investigations.

a) Exposure Surrogates. The use of surrogates for exposures, particularly for past unmeasured exposures, is not uncommon in occupational epidemiologic studies. The use of wire codes in community studies, as done in the Wertheimer, Savitz, and Peters studies, is appropriate and defensible. The use of surrogates may very well result in less misclassification than occurs when inherently variable spot present-day measurements are used to represent unmeasured average exposures that occurred in past years.

b) Exposure Gradients. A gradient in exposures of study subjects is necessary in environmental or occupational epidemiologic studies. The choice of cut-points in dichotomous or multistage exposure classifications may influence the results of statistical analyses. This matter may deserve some summary comment relative to reported studies.

c) Exposure Models. Use of exposure models may be superior to the direct use of exposure measurements for current exposures. Exposure models based on available historic information that can be validated by use of current measurement data are particularly useful for studies dealing with past unmeasured exposures. Wire code surrogate data have been indexed to magnetic field levels in a relatively unsophisticated approach to modeling. Progress is being made in this area (M. R. Flynn et al., "Validation of expert judgment in assessing occupational exposure to magnetic fields in the utility industry," Appl. Occup. Environ. Hyg. 6: 141-145, 1990). Exposure modeling has been addressed in the course of the Peters study and one hopes this will be discussed in the forthcoming publication of the work.

3.4.4 Criteria for Assessing Significance of Data

The revised report should summarize the epidemiologic and statistical principles that govern the report's assessment of epidemiologic data. Such a section should include both methodologic aspects and interpretive considerations and should apply those principles to the overall evaluation of epidemiologic evidence in this field.

Important methodologic topics useful for assessing individual studies include how a study measures exposure (extent of exposure misclassification), how subjects are selected to insure comparability, how potential confounding variables are addressed, choice of statistical measures, and considerations of study size and power. Criteria for interpretation of results in the field as a whole include consistency among different studies, strength of association, degree of evidence for exposure-response relationships, and potential clinical specificity.

Also important for assessment of epidemiologic data is consideration of the biological plausibility of epidemiologic findings in relation to findings from other research disciplines. Although the Subcommittee did not directly address this larger issue in detail, the Subcommittee does recognize the critical importance of such issues in reaching a valid assessment of possible cause-effect relationships between nonionizing-radiation exposures and human cancer. Such considerations will ultimately need to balance the strengths and weaknesses of epidemiologic findings in relation to the strengths and weaknesses of evidence in allied disciplines (experiments in animal toxicology, in cellular and molecular systems, and in the physics of nonionizing radiation).

3.5 Comments on Chapters 4 and 5

3.5.1 Overview

Both chapters mix review and evaluation in an inappropriate manner. Studies should first be summarized objectively. They should then be evaluated in a discussion that covers both strong points and weak points.

Biological and potential health effects from ELF exposure now constitute an active area of research. The report should be updated to include data that have become available since the release of the present draft.

ELF and RF data should be presented and discussed in completely separate sections of the report, with comment and conclusions provided separately for each frequency range. However, where both ELF and RF are present (e.g., ELF-modulated RF; ELF transmission lines carrying or picking up RF), such data should be presented and discussed under both headings.

The summary tables included in the chapters were helpful. Such tables should be expanded and updated to reflect recent research findings.

From the information presented in Chapters 4 and 5, it is clear that hypothetical constructs relating observed biological effects to possible health effects (specifically, increased

cancer risk) can be delineated. However, there are insufficient data on many of the critical steps in the linkage to infer causality on the basis of animal or cellular data.

3.5.2 Comments on Chapter 4

This chapter deals with biological effects observed in animals exposed to electric and magnetic fields in the ELF range and to RF fields assumed to be nonthermal.

Taken as a whole, animal data reviewed and discussed in this chapter, together with data from more recent animal experiments, strongly suggest (and in some instances can be said to demonstrate) that ELF magnetic and electric fields are capable of eliciting biological effects.

The distinction between biological effects and health effects is an important one. It is especially relevant in the context of the question of possible health effects from electric and magnetic field exposure. The report must be precise in distinguishing between these two concepts and carefully guard against the tacit assumption that the observation of one (biological effects) automatically implies that the other (health effects) exists.

In response to the specific charge to the Subcommittee to comment on the value of animal data in interpreting human epidemiologic studies, the Subcommittee believes that the animal data provided are not easily applied to the interpretation of results from human epidemiologic studies for the following reasons:

a) There are few data from different laboratories that demonstrate consistent biological effects using the same experimental protocols. However, newly published information is emerging that will address this shortcoming.

b) There have been no lifetime animal studies in which carcinogenesis was specifically investigated as a consequence of magnetic-field or electric-field exposure.

c) With few exceptions, animal studies were not directed at testing of a specific model or hypothesis relevant to possible mechanisms of electric and magnetic field effects in biological systems.

d) There is insufficient evidence of linear or monotonically increasing exposure response from the animal studies reviewed, and where response is linked

to exposure (or dose), the effects appear to be "all or none" above some threshold.

e) Field intensities used in the experiments reviewed vary widely and are often above those commonly encountered by humans.

3.5.3 Comments on Chapter 5:

The title of Chapter 5 should be changed. The studies reviewed and cited should not be presented as "supporting evidence for carcinogenicity." The report, in fact, reviews data that are relevant to and consistent with the hypothesis that electric and magnetic fields may increase cancer risk. A positive lifetime carcinogenicity study would constitute supporting evidence. Such a study has not yet been done. In fact, this chapter deals with potential mechanisms of interaction of electromagnetic fields with biological systems. The revised report should make it clear that these cellular effects can only establish relationships and mechanisms of interaction.

In view of the testimony to the Subcommittee regarding the theoretical (mainly thermodynamic) constraints on biological effects of low-frequency low-intensity fields, Chapter 5 should include a discussion of the underlying assumptions regarding size, structure, and conductive and dielectric properties of the biological systems (cells, organs, or whole animals) under consideration. The lumped transmission line model for signal detection in collections of cells as presented to the Subcommittee in testimony by Dr. Arthur Pilla, for example, may serve as such a set of assumptions. These should be contrasted with the assumptions used by Dr. Robert Adair in his recent Physical Review paper (A43: 1039-1048, 1991).

EPA should consider deleting discussion of data on electric and magnetic field exposure of plant cells, but adding the voluminous results available in connection with electric and magnetic field stimulated bone repair.

Not mentioned in this document is the lack of effects reproducible among laboratories, and lack of agreement or understanding of what constitutes exposure or dose. Until there is progress in these two areas it will remain impossible to summarize the results of this field in a manner that will approach "a consensus viewpoint."

A carefully worded statement regarding the difficulty of some of the assay techniques should be included in this chapter. Training in one aspect of biological assays may not qualify one to conduct an assay on another system. Many laboratories have reported failure to replicate a result when in fact the laboratory lacked the necessary expertise to conduct the assay

appropriately. Conversely, a laboratory may report positive results because it lacks the necessary expertise to carry out reliable experiments.

A number of studies are presented dealing with DNA/field interaction. No effects were found on breakage of strands or repair of damaged strands. There is no evidence that genetic mutations are induced by ELF electromagnetic fields. However, effects of ELF magnetic fields on gene transcription and translation have been reported.

EPA should carefully review epigenetic factors in cancer risk. Such factors include possible effects on transcription/translation, hormonal effects, and effects on the immune system.

Fairly small fields have been reported to alter the flux of calcium ions across cell membranes. Although some of the in vitro calcium efflux data are open to concern about experimental design and physiological interpretations, these effects appears to be characterized by "windows" in frequency and intensity. Although lower in amplitude, this alteration in calcium ion flux appeared in the same direction as changes caused by known cancer promoters. An important consequence of altered calcium flux would be a change in production of parathyroid hormone and ornithine-decarboxylase.

Melatonin is a hormone with important regulatory functions. A number of experiments have shown correlation between breast cancer and decreased melatonin production. Exposure of rats to a variety of low-strength electric and magnetic fields has been shown to decrease melatonin levels in blood and pineal gland.

The melatonin data are an important reason for recognizing the existence of biological effects due to electric and magnetic fields. It is not clear, however, that melatonin changes lead to health effects. Although the phenomena are well described in the report, they should not be presented as "supporting evidence of carcinogeniqity." More recent data on breast cancer and prostate cancer in males should be included in the melatonin discussion, because increased risk for these specific cancers was hypothesized on the basis of the melatonin findings.

References that are missing include the Gabriel et al. paper and the Meltz references that were supplied to the Subcommittee by Dr. Martin L. Meltz. This chapter (or the mechanism chapter) should include mention of the work of Dr. James C. Weaver and Dr. R. Dean Astumian. The work of C. A. L. Bassett and others on pulsed electromagnetic field (PEMF) treatment of bone is also pertinent (see, for example, C. T. Brighton and S. R. Pollack, Eds., Electromagnetism in Medicine and Biology, 1991).

In summary, the Subcommittee believes the following:

a) The EPA's interpretation of the human and animal evidence of carcinogenicity is not supported by data available in the literature.

b) Biological effects and health effects must be clearly distinguished, and although there may now be hypothetical constructs for linking observed biological effects to cancer risk, there is insufficient basis from animal and cellular data for postulating human cancer risk from exposure to ELF electric and magnetic fields.

c) In part because of insufficient data, EPA has not properly evaluated the ways in which proposed biological mechanisms of electric and magnetic fields may affect interpretation of human data. However, the melatonin findings as they relate to male breast and prostate cancer, and other work on DNA transcription leading to enhanced growth, may constitute findings from which biological mechanisms to assist in interpretation of human data may eventually be developed.

d) The title for Chapter 5 is misleading and should be changed; although the topics discussed in Chapter 5 are relevant to the issue, the underlying assumption of the existence of increased risk is disturbing.

e) The data presented in Chapter 5 do not constitute supportive evidence for carcinogenic effects of electric and magnetic fields in humans and animals.

4.0 ADDITIONAL COMMENTS ON THE SCIENCE

The Subcommittee's mandate was to review the EPA report and answer specific questions in relation to it. In view of the opportunity that the Subcommittee had during its deliberations to hear testimony and discussions regarding the issue of any risk associated with ELF, in the brief sections that follow, the Subcommittee gives a summary of its collective response to what it has identified as substantive questions. Until these questions have been answered, no opinion can be advanced on the possibility of a relationship between ELF and human disease.

The Subcommittee of 17 individuals represented expertise in twelve disciplinary areas: biostatistics, engineering, epidemiology, experimental biology, exposure assessment, medicine, neuro-endocrinology, physics, physiological psychology, radiation oncology and carcinogenesis, risk analysis and toxicology. The breadth of opinion and diversity of view within the Subcommittee would likely be replicated by any other group with a correspondingly wide spectrum of expertise.

The Subcommittee feels it important to express its viewpoint on three underlying scientific issues, concerning (a) epidemiology, (b) biological effects, and (c) carcinogenicity. These issues are critical for the understanding of scientific issues in research regarding electric and magnetic fields and must be addressed in any future EPA discussion of the potential carcinogenicity of electric and magnetic fields.

a) The Subcommittee has concluded that the epidemiological evidence is suggestive of an association between surrogate measurements of magnetic-field exposure and certain cancer outcomes. In such studies, the existence of confounders is always a possibility, but since no common confounder has yet been identified, the existing evidence cannot be dismissed. In the absence of much better exposure information and an understanding of which exposures are significant, no precise exposure-response relationship has yet been adduced. This lack, together with limited understanding of possible biological mechanisms, prevents the inference of cancer causality from these associations at this time.

b) The Subcommittee accepts that effects on biological systems have been shown to occur at moderate field intensities. (An example of such effects is the well-documented work on phosphenes.) However, the evidence for effects at very low field strengths is not so widely accepted. Even if effects on living systems at lower fields do occur, the assumptions leading to estimations of physical constraints for effects on

isolated small spherical cells without ferromagnetic structures may not be applicable to larger cells or cell systems such as neurons or neuronal networks. Many intervening steps must be clarified before the biological phenomena so far shown can be taken as direct evidence of health impairment or carcinogenesis in the human.

c) The EPA document does not present a holistic model of carcinogenesis within which the strength of existing evidence concerning the carcinogenic properties of electric and magnetic fields can be assessed. The revised document should do so. Low-frequency electric and magnetic fields do not carry enough energy to cause mutations directly. The Subcommittee recognizes that the incidence of cancer might well be affected by an agent that does not produce mutations. The known influence of factors such as hormonal imbalance and nutrition on cancer promotion is an example of epigenetic effect.

5.0 Policy Recommendations

The Subcommittee also wishes to express two specific policy recommendations that in its view follow inescapably from the scientific recommendations.

POLICY RECOMMENDATION #1: The Subcommittee is unanimous in its belief that the question of electric and magnetic field effects on biological systems is important and exceptionally challenging, and that the Subcommittee's advice to the EPA should be that the report should be rewritten by EPA, and then re-reviewed by the Science Advisory Board.

POLICY RECOMMENDATION #2: EPA should complete its efforts with regard to RF electromagnetic fields (including microwaves) and issue exposure guidelines independent of present issues pertaining to lower frequencies. The current EPA report inadvertently leads even the careful reader to conclude that the potential carcinogenicity of electric and magnetic fields of ELF (i.e., powerline) frequencies is the only--or at least the principal--subject of concern with regard to nonionizing fields. Such a conclusion would reinforce the skewed and somewhat sensationalized picture presented to the public in recent years by the news media and government agencies responding to this publicity. The report should therefore declare explicitly that the attention given to nonionizing electric and magnetic fields derives in the first place from long-standing concern over the hazards of RF (including microwave) radiation. EPA has expended substantial resources on the study of such radiation over a period dating back to the EPA's inception, and EPA should complete its efforts directed toward the issuance of RF exposure guidelines. RF fields present long-known and well-understood hazards such as temperature elevation in tissue and heat stress resulting from acute exposuresagainst which users and the general public must be warned and protected. Any published exposure guideline should specifically identify the hazards from RF exposure.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OCT 12 1990

OFFICE OF
RESEARCH AND DEVELOPMENT

MEMORANDUM

SUBJECT: Science Advisory Board Review of the EPA Document on the Carcinogenicity of Electromagnetic Fields

FROM: William H. Farland, Ph.D.
Director
Office of Health and Environmental Assessment
Office of Research and Development (RD-689)

Ken Sexton, Sc.D.
Director
Office of Health Research
Office of Research and Development (RD-683)

Richard Guimond
Director
Office of Radiation Programs
Office of Air and Radiation (ANR-458)

TO: Kathleen Conway, DFO, Radiation Advisory Committee
Science Advisory Board (A-101F)

We are hereby requesting Science Advisory Board (SAB) review of two draft EPA documents. The first, "Evaluation of the Potential Carcinogenicity of Electromagnetic Fields", was prepared by the Office of Health and Environmental Assessment at the request of the Office of Radiation Programs (ORP). The second document, "Human Exposure to Electromagnetic Fields: A National Research Agenda" was prepared by the Office of Health Research at the request of the Administrator as a companion to the first document. Both documents were prepared and revieved by scientists in the ORP and the Office of Research and Development (ORD). Both documents will be available to the SAB in early November.

The first document is scheduled for release to the public in early November as an external review draft. The Agency is planning for a 60-day public comment period and a concurrent Science Advisory Board review. An earlier draft has already been

reviewed by a panel of experts outside the Agency and the external review draft includes revisions made in response to their comments. The document reviews the available evidence relating to the potential carcinogenicity of electromagnetic fields between 3 Hz and 30 GHz. This evidence includes epidemiological studies, chronic lifetime animal tests and laboratory studies of biological phenomena related to carcinogenesis.

The Agency seeks the advice of the Board on the accuracy and completeness of the entire document and on the question of whether the interpretation of the available information reflects current scientific opinion. In addition, we would like the Board to address the following specific issues:

1. Is the interpretation of the human and animal evidence of carcinogenicity supported by the available information?

2. Does the animal or biological effects information provide a basis for postulating that there is a human hazard from exposure to extremely low frequency fields or either modulated or unmodulated radiofrequency radiation?

3. Has the agency properly evaluated the way in which the findings on biological effects and field-tissue interaction mechanisms affect the interpretation of the human studies?

4. Is the choice of topics in chapter 5 appropriate and is the interpretation of the biological effects literature as it relates to carcinogenesis supported by the available information?

5. Is the Agency's carcinogen classification system applicable to electromagnetic fields?

6. Does the information cited in the document support the conclusion that there is not enough information to designate specific values of magnetic field strength as being hazardous to human health?

The second document will be reviewed by appropriate Federal Agencies and other non-federal interested organizations during October and will also be available for SAB review in early November. The purpose of the National Research Agenda on EMF is to identify the major research needed to: 1) accurately assess the human health effects from exposure to EMF and 2) identify and recommend appropriate exposure guidelines and control technology to protect human health. The document describes a national view of the necessary research in the areas of exposure assessment, biological effects, and control technology, without regard to who

or which organization might do the research. We are requesting the SAB to address the following issues in their review of the document:

1) Does the document identify the major research needs for EMF? Specifically are any identified needs inappropriate and are all the needs identified?

2) Is the level of detail sufficient to set priorities among the research needs?

3) Do any research needs stand out as higher priority issues for assessing human health risks?

APPENDIX B: Detailed Technical Comments

Comments of the individual group members on Chapter 4 follow:

The described animal studies focus exclusively on RF exposures and thus bear little relevance to ELF fields produced by transmission lines and household electricity. The mechanisms of tissue effects from 1000 Mhz exposure may not relate to mechanisms at 60 Hz. Therefore, as pointed out previously, RF and ELF field effects should be handled separately in this section of the report.

The specific presentation of experiments in this chapter introduces problems. For example, reanalysis of the Guy et al. data from 1985 to reach conclusions other than those presented by the authors is inappropriate in this type of report. Scaling to normalize absorption rate is questionable. Some RF studies may be excessively thermal. The relevance of all studies should be discussed in regard to the spectrum of exposure frequencies.

The cited studies appear to have little relevance to ELF fields as produced by transmission lines and household electricity. For example, there is no evidence that the interaction mechanisms involved at 1000 MHz are in any way similar to those at 60 Hz. Since the interaction is most likely to depend critically on frequency, scaling to normalize absorption rate is certainly inappropriate. Moreover, the grouping of glandular organs implied in the presentation is highly unorthodox. No conclusions for ELF can be derived from these experiments.

The microwave chapter should give the conclusion as originally stated in the 1985 report by Guy et al., which combined all malignant tumors and reported a significant difference between exposed and controls, but this difference disappeared when benign tumors were included. The Guy report concludes that the observed differences are not of biological significance.

Much attention is given to the fact that the exposure conditions in the Guy study were "...calibrated to simulate human exposure at the upper limit allowed by the ANSI standards" scaled from the weight of a small child exposed to 450 MHz (a standard radar). These calculations apparently do not take into account that resonance for animals in the circularly polarized waveguide used by Guy differs from estimates on resonance taken in an anechoic chamber or a multimode cavity.

The use of the post hoc analysis of the Guy data in this document must be seriously questioned. Such an analysis should at the very least be submitted for publication before it can add any benefit to the document. Such re-analysis of data is quite common in literature. If Kunz believes in this re-analysis, he should submit it for publication with all the appropriate co-authors. If the study had been intended as a cancer study or if it were ELF one might think that it was important enough to the overall theme of the report to waive the peer review requirement. Since the original Guy study meets neither of those two criteria, there is no reason to include such a re-analysis in the present document.

The report states that the Sprague Dawley rat was chosen to mimic heterogenous variety of human population. But the Guy study used all males and Sprague Dawleys are an albino strain. Creel has suggested many unusual attributes of albinos. The paper by Creel on albino rats as experimental animals should therefore be cited and discussed.

If the Guy post hoc analysis is included in Chapter 4, it should be given much less attention and the statistical questionability of the results should be focused. Four significant differences can be found in the post hoc analysis of the Guy data. The fact that the exposed group lived longer than the control was not significant; nor was the analysis of the cause of death. With regard to the tumor incidence, the post hoc analysis showed significant differences using a one-tailed Fisher's exact test for benign pheochromocytoma of the adrenal medulla ($p < 0.023$), malignant tumors at all sites ($p < 0.0012$), carcinomas at all cites ($p < 0.018$), and glandular carcinoma for combined glands ($p < 0.018$). The EPA report makes no mention of how many statistical tests were done on these data. It would seem that multiple independent tests on all the possible effects would have yielded a suspected significance that might even exceed the four reported.

The Prausnitz and Susskind study was excessively thermal. It is unclear how an exposure of 0.1 mW/cm^2 over 4.5 minutes could induce a 3.3 degree C temperature increase, for example. This study has been criticized and these other criticisms should be included in this report. The most important to include are probably Roberts and Michaelson (Health Physics 44: 430-433. 1982) and Kirk (Life span and carcinogenesis, in J. Elder and D. Cahill, Eds., Biological Effects of Radiofrequency Radiation. EPA-600/8-83-026F, 1984). The criticisms focus on the fact that the colony of mice had an infection of pneumonitis during the study and that the leucosis reported may not have been leucosis. The authors note that the exposed animals lived longer than the controls (an observation also made by others) and suggest that the mild heating enabled exposed animals to thwart the virus with which the colony was infected. There is also a question of how

many multiple comparisons were made to arrive at the very few statistical significant effects reported.

The Szmigielski et al. (1982) study must be criticized for the lack of pertinent information. The only effects were on promotion of skin cancer. Heating the skin could have been the mechanism. This section should make it clearer that this is not a robust study or conclusion. There was no control of heating.

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