

Originally Processed With FOIA(s):
2005-0336-F

FOIA Number:
2005-0336-F

FOIA MARKER

**This is not a textual record. This is used as an
administrative marker by the George Bush Presidential
Library Staff.**

Record Group/Collection: George H.W. Bush Presidential Records
Collection/Office of Origin: Science and Technology Policy, Office of (OSTP)
Series: Bromley, D. Allan, Files
Subseries: General Science Files

OA/ID Number: 62038
Folder ID Number: 62038-004

Folder Title:
Life Sciences: General [4 of 4] [1991]

Stack:

Row:

Section:

Shelf:

Position:

0

0

0

0

"CORRESPONDENCE TRACKING"

TYPE: ACTION

DOCUMENT NUMBER: 9120173

FROM: HORNER, CONSTANCE

TO: DR. BROMLEY

DATE OF
CORRESPONDENCE: 01/28/91

SUBJECT: BACKGROUND MATERIALS FOR THE THIRD MEETING OF THE
WORKING GROUP ON THE DRUG APPROVAL PROCESS.

ASSIGNED TO: Rachel Levinson

ACTION REQUIRED: AS NECESSARY

SENDER'S DUE DATE:

OSTP DUE DATE:

DATE COMPLETED:

COPIES TO: D. Allan Bromley

WHITE HOUSE TRACKING #:

CONTACT PERSON:

REMARKS:

DATE RECEIVED: 01/29/91

P- LIFE SCIENCES
FILE: HEALTH-DRUG APPROVAL

SECRET



THE DEPUTY SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

JAN 28 1991

The Honorable Allan Bromley
Director
Office of Science and Technology Policy
358 OEOb
Washington, D.C. 20506

Dear Mr. Bromley:

The third meeting of the Working Group on the Drug Approval Process will take place on Wednesday, January 30, 1991, at 2:30 P.M. in Room 474 OEOb. We will devote the meeting to a discussion of the efficacy standard (Agenda items 1 and 2).

Enclosed are background materials. These include a document summarizing the legislative history of the 1962 amendments; a synopsis of the most important court cases interpreting the efficacy standard; a summary of the arguments for and against retaining that standard; and a description of the significant revisions of its regulations that FDA has made to expedite the drug approval process. Also enclosed is a copy of the agenda.

As always I would welcome any thoughts or comments on the proposed discussion topic or other agenda items. Please call my Deputy, Ann Agnew, at 245-3400, to discuss your ideas or concerns.

Sincerely,

Constance Horner

Constance Horner
Deputy Secretary

Enclosures

DIRECTOR
OFFICE OF THE

91 JAN 29 4 9 : 22

RECEIVED

Call
377-3727
(overhead)

NOV 85 WAL

DIRECTOR

CLERK

NOV 85

PROPOSED AGENDA TOPICS FOR COUNCIL STUDY

1. Examination of FDA's Standards of Approval

In 1962 Congress required that new drugs be approved for effectiveness as well as safety. In doing so, Congress required that there must be "substantial evidence of effectiveness" prior to the approval of a new drug application (NDA). The parameters of this efficacy standard have been a source of debate since then. FDA has been criticized for applying too rigid a standard. How should the efficacy standard be interpreted and what are the ramifications for the approval of new drugs?

2. FDA's Statutory and Administrative Flexibility to Approve Drugs for Life-Threatening Diseases as Early as Possible

The Lasagna Report praises FDA for its leadership and flexibility in approving AIDS drugs rapidly. It encourages FDA to continue exercising that flexibility to further expedite reviews of new drug applications. FDA should continue to report on additional progress in this area.

The statute defines "substantial evidence" as "evidence consisting of adequate and well-controlled investigations, including clinical investigations,...on the basis of which it could fairly and responsibly be concluded...that the drug will have the effect it purports" to have. To what extent does FDA's ability to expedite drug approvals depend upon the quality of data submitted to the agency by drug manufacturers?

3. Wider Use of Advisory Committees to Assist FDA Drug Reviews

The Lasagna Report recommends strengthening the role of advisory committees. How does FDA currently use advisory committees and other outside experts throughout the approval process? Does FDA need to change current practice to include such committees and outside experts more appropriately, and, if so, how?

The Lasagna Report also recommends that sponsors be permitted to choose IRB review of INDs instead of FDA review of INDs under certain circumstances. What role do IRBs currently play in the IND approval process? Is there currently overlap between FDA staff review of INDs and IRB review of INDs? How would the elimination of FDA staff review of INDs affect the agency's workload?

4. FDA Management Resources

The Lasagna report recommends consideration of additional resources for FDA.

- a) Management Processes - How does FDA allocate its drug review resources and should they be allocated differently? Does the resource focus on drugs for life-threatening illnesses delay development of other drugs? How does FDA assure flexibility and efficiency in its review program and what is its record in doing so?
- b) Staffing - The Lasagna Report says that FDA needs additional staff and better facilities and equipment to support them. How does FDA decide what staff level is appropriate for drug reviews? Is an increase in staff called for? Are deficiencies in facilities and equipment complementary factors that adversely affect FDA's ability to hire and retain adequate drug review staff? Does FDA provide sufficient training and professional development for its staff?
- c) Review Priorities - FDA currently uses an A, B, & C classification system to assign review priorities (A = drugs of major benefit over existing therapy, B = drugs of modest benefit over existing therapy, and C = drugs of no benefit over existing therapy). Should this drug classification system that assigns review priorities be changed in any way, and if so, how?
- d) Computerization - There is general agreement that the FDA drug review process should be better automated. What are the impediments in this area, and how can that transition best be accomplished? How can government facilitate use of this technology so as to improve FDA's ability to get new drugs on the market more rapidly?
- e) User Fees - Are user fees an appropriate mechanism for reimbursing the government for drug reviews (the Administration has proposed user fees but the Congress has rejected them in this setting)? To what extent should the monies collected by such fees be an offset against, or in addition to, normal appropriations?

5. Approaches to Enhance International Harmonization of Drug Review Standards

While the policies and drug review standards of foreign countries are becoming increasingly similar to those of the U.S., important differences still exist. What are the appropriate criteria for FDA to consider in accepting foreign data in support of new drug applications? What weight, if any, should FDA give to foreign drug approvals in its own decisionmaking process? What steps, if any, can and should be taken toward the harmonization of U.S. and foreign standards for drug approvals?

6. Liability Concerns that Inhibit Sponsor Willingness to Provide Drugs Earlier in the Approval Process

What are the liability concerns of drug sponsors when new drugs are permitted on the market earlier? Is it necessary to limit such liability (e.g., through legislation) to encourage drug manufacturers to participate in drug access programs such as Treatment INDs and Parallel Track? Can further refinements be made in the recommendations of the DPC Task Force on Tort Reform to take into account concerns raised by Treatment INDs and Parallel Track?

ARGUMENTS FOR AND AGAINST THE EFFICACY STANDARD

The requirement that drugs be proven effective as well as safe for their intended use is set forth in the Federal Food, Drug, and Cosmetic Act and dates from the 1962 amendments to that law. The statute requires "substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling..." The statute defines "substantial evidence" as "evidence consisting of adequate and well-controlled investigations, including clinical investigations,...on the basis of which it could fairly and responsibly be concluded...that the drug will have the effect it purports or is represented to have...."

FDA has interpreted this statutory mandate as requiring its review of the design of clinical trials to determine whether they are "adequate" and "well-controlled" and whether the data obtained support the drug's effectiveness. The agency has also interpreted the law to require, in most cases, at least two clinical studies that demonstrate efficacy.

In the years since 1962 there has been an ongoing debate about the importance and usefulness of the efficacy requirement. The arguments have centered on the cost of new drugs, patients' access to them, and the impact of the standard on the global competitiveness of the U.S. pharmaceutical industry.

The following is a summary of the chief arguments made for and against the efficacy standard.

SUPPORT: The following arguments have been adduced to support retention of the efficacy standard:

1. The purpose of taking a drug is to ameliorate a disease or condition. A drug that is not effective is useless and may even harm some patients who take it instead of an available drug that is effective. Patients using ineffective drugs for curable conditions could develop conditions that would be more difficult and expensive to treat. Using an ineffective drug is especially dangerous when a condition which can be effectively treated with the right drug becomes life-threatening if left untreated. The cost to society in general and to government programs in particular from ineffective drug therapy would be significant.
2. Physicians rely heavily on the information derived from clinical trials determining efficacy. Lack of efficacy information will minimize physician knowledge, compounding the problem the physician already faces in choosing the appropriate drug for a given condition.

3. For many useful drugs, there is no such thing as complete safety. A drug's toxicity or safety can only be measured against its benefits. Efficacy is the measure of those benefits. Do the drug's benefits outweigh its risks, or outweigh the risk inherent in letting the disease or condition go untreated?
4. If safety alone were the standard, certain effective but highly toxic drugs would never be approved because there would be no evidence of efficacy to balance against their toxicity. (e.g., AZT).
5. Without the efficacy standard, physicians and manufacturers might have greater difficulty defending themselves in tort actions.
6. The high standards for approval in the U.S. contribute significantly to the global commercial success of American pharmaceuticals.

AGAINST: The following arguments support elimination of the efficacy standard:

1. Testing for efficacy significantly increases the cost of developing a new drug and the time required to develop it. The length and costliness of the approval process deprive patients of timely access to new drugs and put U.S. pharmaceutical companies at a competitive disadvantage internationally.
2. The efficacy standard has stifled drug innovation in the U.S. by requiring unnecessary investment of capital.
3. The efficacy standard has created a drug lag; i.e., new drugs are approved for use in other countries before they are available in the U.S., thereby preventing U.S. companies from achieving substantial market share.
4. Patients and physicians should be accorded greater freedom of choice regarding drugs, provided the drugs are "safe."
5. In cases of imminently life-threatening diseases that have no known cure, efficacy is irrelevant and the patient should be allowed to try anything the physician is willing to prescribe.

SIGNIFICANT REFORMS IN FDA DRUG REGULATIONS TO EXPEDITE APPROVAL

During the 1980's FDA took steps to expedite the review of drugs used to treat serious and life-threatening diseases that have no known cure. The agency has implemented two significant reforms and is in the process of effecting a third:

- I. TREATMENT IND: In May of 1987 FDA promulgated regulations defining a special category of Investigational New Drug known as a Treatment IND. (52 Fed. Reg. 19466 (22 May 1987).) A Treatment IND is a promising investigational new drug that the agency permits to be made available to "desperately ill patients" for treatment purposes before general marketing begins. The regulation establishes the procedures by which such drugs may be made available to certain patients even though they are not participating in clinical trials. The new procedures creating the Treatment IND category "are intended to facilitate the availability of promising new drugs to patients as early in the drug development process as possible, and to obtain additional data on the drug's safety and effectiveness." (52 Fed. Reg. at 19466.)

There are four criteria for determining whether an investigational drug should be designated as a Treatment IND:

- (1) The drug is intended to treat a serious or immediately life-threatening disease;
- (2) There is no comparable or satisfactory alternative drug or other therapy available to treat that stage of the disease in the intended patient population;
- (3) The drug is under investigation in a controlled clinical trial under an IND in effect for the trial, or all clinical trials have been completed; and
- (4) The sponsor of the controlled clinical trial is actively pursuing marketing approval of the investigational drug with due diligence.

To date there have been 19 Treatment IND's, including AZT.

- II. "SUBPART E" REGULATIONS ("BUSH INITIATIVE"): In October of 1988 the FDA issued interim regulatory procedures designed to speed the availability of new therapies to desperately ill patients. "These procedures reflect the recognition

that physicians and patients are generally willing to accept greater risks or side effects from products that treat life-threatening and severely-debilitating illnesses, than they would accept from products that treat less serious illnesses. These procedures also reflect the recognition that the benefits of the drug need to be evaluated in light of the severity of the disease being treated." (53 Fed. Reg. 41516 (21 October 1988)).

The Subpart E procedures have six key elements:

(1) Early consultation: Drug sponsors will consult with FDA early in the drug development process to review and reach agreement on the design of necessary preclinical and clinical studies.

(2) Treatment IND protocol: If Phase 2 results appear promising, FDA may ask the sponsor to submit a Treatment IND protocol to determine whether the drug can be made available for treatment use outside of clinical trials.

(3) Risk-benefit analysis: In applying the statutory standard for marketing approval, FDA will recognize the need for a medical risk-benefit judgment in determining the drug's approvability. "FDA will consider whether the benefits of the drug outweigh the known and potential risks of the drug and the need to answer remaining questions about risks and benefits of the drug, taking into consideration the severity of the disease and the absence of satisfactory alternative therapy." (53 Fed. Reg. at 41523 (21 Oct. 1988).)

(4) Phase 4 Studies: "Concurrent with marketing approval, FDA may seek agreement from the sponsor to conduct certain postmarketing (phase 4) studies to delineate additional information about the drug's risks, benefits, and optimal use." (53 Fed. Reg. at 41524 (21 October 1988).)

(5) Focused FDA Regulatory Research: At its discretion FDA may undertake regulatory research on "critical rate-limiting aspects of the preclinical, chemical/manufacturing, and clinical phases of drug development and evaluation." (53 Fed. Reg. at 41524 (21 October 1988).) FDA would undertake such research to facilitate the development of therapies to treat life-threatening or severely debilitating illnesses.

(6) Active monitoring of conduct and evaluation of clinical trials: The Commissioner and other agency officials will monitor the progress of the conduct and evaluation of clinical trials for Subpart E drugs and, if necessary, will facilitate their progress.

III. "PARALLEL TRACK" ("EXPANDED ACCESS") INITIATIVE: This term refers to a proposed policy set forth by the Public Health Service in May of 1990. (55 Fed.Reg. 20856 (21 May 1990).) Under this policy, promising new drugs would be made available through studies that: (1) lack concurrent control groups to monitor patient safety; and (2) are conducted "in parallel" with the principal controlled clinical investigations. (55 Fed. Reg. at 20857).

The parallel track proposal is limited to individuals with AIDS or HIV-related diseases. It would provide access to unapproved drugs for persons with AIDS and HIV-related diseases who lack satisfactory alternative therapy and cannot participate in controlled clinical trials. (55 Fed. Reg. at 20857).

The Parallel Track Proposal differs from the Treatment IND procedures in that expanded availability protocols under the proposed parallel track policy "might be approved for promising investigational drugs when the evidence for effectiveness is less than that generally required for a Treatment IND." (55 Fed. Reg. at 20857).

The proposed policy has not yet been finalized or implemented.

In addition to these reforms, FDA amended NDA and IND regulations, expediting the review process for all drugs.

I. NDA Rewrite, 1985

The NDA Rewrite of the new drug application ("NDA") regulations was implemented to streamline the application process for new drugs. Guidelines were written to aid sponsors in understanding data requirements, how to complete applications, and new application procedures.

II. IND Rewrite, 1987

The IND Rewrite of regulations governing drug testing had the goal of helping drug sponsors do better studies of promising new drugs. Better testing methodologies will result, in turn, in better new drug applications and more rapid FDA review. The regulations provide greater freedom for sponsors to design and implement clinical studies, a simplified application format, and the opportunity for closer cooperation between drug sponsors and FDA.

Legislative History of the 1962 Amendments to the Federal Food, Drug, and Cosmetic Act

Prior to 1962 the Federal Food, Drug, and Cosmetic Act (FFDCA) only required that a drug be proven safe before it was marketed. The 1962 amendments to the FFDCA changed the statute to require, in addition to safety, "substantial evidence" of a drug's effectiveness before it could be marketed, and the burden was placed on the sponsor to prove the drug's efficacy.

General History: The 1962 amendments grew out of extensive hearings into the ethical drug industry that were conducted from 1959 to 1962 by Senator Estes Kefauver of the Subcommittee on Antitrust and Monopoly of the Senate Committee on the Judiciary. In July of that year the Judiciary Committee reported out a drug bill, but in August President Kennedy wrote Chairman Eastland of the Judiciary Committee to urge that the Committee's bill be strengthened. President Kennedy's letter, which contained seven specific amendments, was drafted following the disclosure that numerous babies born in other countries suffered from malformations associated with use of the drug thalidomide.

The Judiciary Committee strengthened its bill to conform in general with the President's recommendations, and the Senate passed this latter bill by a unanimous vote (78 to 0) on August 23, 1962. In September the House passed a bill that closely resembled the Senate's version. The bill reported out of the conference committee was enacted on October 10, 1962, as the "Drug Amendments of 1962."

Source: Congressional Record, Oct. 3, 1962, pp. 20867--20868 (remarks of Senator Kefauver).

Effectiveness Standard: The most important change made by the 1962 amendments to the FFDCA was to add the requirement that a sponsor prove a drug effective as well as safe prior to marketing it. In addition the amendments added to the statute a definition of "substantial evidence," which remains unchanged in the current law and is defined as "evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."

In adopting "substantial evidence" as the standard for evaluating evidence of a drug's effectiveness, Congress specifically rejected a more stringent alternative, the "preponderant evidence" test. As noted by the Senate Judiciary Committee, under the preponderant evidence test,

a claim would not be accepted under the new-drug section unless it represented the preponderant view of experts qualified by training and experience in the subject that the claim was supported. The committee recognizes that in the difficult area of drug testing and evaluation there will frequently, if not usually, be a difference of responsible opinion. The committee feels that the existence of such a difference should not result in disapproval of a claim of effectiveness if it is supported by substantial evidence defined in the manner set forth (in the statute) and evaluated by the Secretary in the light of all the information available to him at the time.

The Committee then set forth the definition of "substantial evidence" quoted above, which remains unchanged in the current version of the Federal Food, Drug and Cosmetic Act, and commented further:

(A) claim could be rejected if it were found (a) that the investigations were not "adequate"; (b) that they were not "well controlled"; (c) that they had been conducted by experts not qualified to evaluate the effectiveness of the drug for which the application is made; or (d) that the conclusions drawn by such experts could not fairly and responsibly be derived from their investigations.

What the Secretary is required to do is evaluate the claims of effectiveness in the light of the information submitted to him in the new-drug application and any other information before him with respect to such drug and to decide whether there is substantial evidence, as defined (in the statute), to support the claim....

Source: Senate Report 1744, Part 2, on the Drug Industry Act of 1962, Committee on the Judiciary, 87th Congress, 2d Session (August 21, 1962), at 6.

This passage from the Senate Report is critical for interpreting the statutory standard and was cited by both the United States Supreme Court and the United States Court of Appeals for the Third Circuit in the two most important cases that discuss the meaning of "substantial evidence."

Judicial Interpretation of the Efficacy Standard

The efficacy standard has been interpreted in three significant court cases.

Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609 (1973): The Supreme Court upheld the FDA regulations that establish minimal standards for "adequate and well-controlled investigations." The agency had promulgated these regulations to implement the statutory definition of "substantial evidence." The 1962 amendments required FDA to refuse approval of any new drug application that lacks "substantial evidence" that the drug is effective for its intended use.

In reviewing the regulations, the Supreme Court found that they "express well-established principles of scientific investigation," and that "(t)he standard of 'well-controlled investigations' particularized by the regulations is a protective measure designed to ferret out those drugs for which there is no affirmative, reliable evidence of effectiveness." In affirming the regulations, the Supreme Court accepted the FDA's policy, articulated in the regulations, that "(u)ncontrolled studies or partially controlled studies are not acceptable as the sole basis for the approval of claims of effectiveness....Isolated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered."

United States v. Rutherford, 442 U.S. 544 (1979): The Supreme Court found that the statutory standards of safety and efficacy required by the Federal Food, Drug, and Cosmetic Act (FFDCA) clearly apply to drugs used to treat terminally ill patients and are not limited to drugs used in the treatment of curable diseases. The Court noted that nothing in the history of the 1938 act or the 1962 amendments implies that Congress intended to protect only persons suffering from curable diseases. On the contrary, Congress had expressed concern during the deliberations preceding the 1938 act that individuals stricken with fatal diseases such as cancer should be "shielded from fraudulent cures." The Supreme Court therefore refused to find an exemption from the statutory requirements of safety and effectiveness for drugs used to treat fatal diseases, and specifically concluded that laetrile was not exempt from the premarketing approval requirements set forth in the FFDCA.

Warner-Lambert Company v. Heckler, 787 F.2d 147 (3d Cir. 1986): In examining the efficacy standard, the court found that the reference to "experts" in the statutory definition of

"substantial evidence" does not mean that the Commissioner is bound to accept the opinion of experts offered by the drug companies that their studies are "adequate" and "well-controlled" and therefore prove the effectiveness of the drug under consideration. Rather, it is the Commissioner who must determine whether the studies themselves meet the regulatory criteria and demonstrate the drug's effectiveness. The court affirmed that the design and implementation of the studies are critical, and that the statutory standard affords the Commissioner discretion to reject the opinions of experts if all of the submitted evidence, taken as a whole, does not support their conclusion.

"CORRESPONDENCE TRACKING"

TYPE: INFORMATION

DOCUMENT NUMBER: 9120266

FROM: YOUNG, ALVIN L. (CIRRPC)

TO: DR. BROMLEY

DATE OF
CORRESPONDENCE: 01/25/91

SUBJECT: LETTER TO DR. ROESSLER

ASSIGNED TO:

ACTION REQUIRED:

SENDER'S DUE DATE:

OSTP DUE DATE:

DATE COMPLETED:

COPIES TO: D. Allan Bromley

WHITE HOUSE TRACKING #:

CONTACT PERSON:

REMARKS:

DATE RECEIVED: 01/29/91

FILE: HEALTH PHYSICS

P - Life Sciences

SECRET

9120266

COMMITTEE ON INTERAGENCY RADIATION RESEARCH
AND POLICY COORDINATION

1019 Nineteenth Street, NW, Suite 700
Washington, D.C. 20036

RECEIVED

91 JAN 29 A 9:24

January 25, 1991

OFFICE OF THE
DIRECTOR

Genevieve S. Roessler, Ph.D.
President
Health Physics Society
Route 1, Box 139H
Elysian, MN 56028

Genevieve
Dear ~~Dr. Roessler~~:

Thank you very much for your letter of 8 January 1991 in which you forwarded the report of the Health Physics Related Research Committee. We also received a note today from Dr. Bromley with the package which you sent to him. He too felt that CIRRPC was the location for this information and was thoughtful enough to forward it to me.

The Health Physics Related Research Committee report has been made available to the CIRRPC membership and is a welcome addition to the CIRRPC library. I have enclosed a copy of the CIRRPC Sixth Annual Report for your perusal.

I look forward to reviewing the Research Committee Report and continuing our excellent working relationship with the Health Physics Society.

With best regards,

Al Young
ALVIN L. YOUNG
Chairman, CIRRPC

ALY:sh

cc: D. Allan Bromley ✓

Assistant to the President for Science Technology
Enclosure: CIRRPC Sixth Annual Report

"CORRESPONDENCE TRACKING"

TYPE: INFORMATION

DOCUMENT NUMBER: 9120266

FROM: YOUNG, ALVIN L. (CIRRPC)

TO: DR. BROMLEY

DATE OF
CORRESPONDENCE: 01/25/91

SUBJECT: LETTER TO DR. ROESSLER

ASSIGNED TO:

*copy to Life Science
note "health"
reference*

ACTION REQUIRED:

SENDER'S DUE DATE:

OSTP DUE DATE:

DATE COMPLETED:

COPIES TO: D. Allan Bromley
Life Sciences

WHITE HOUSE TRACKING #:

CONTACT PERSON:

REMARKS:

DATE RECEIVED: 01/29/91

FILE: HEALTH PHYSICS

"CORRESPONDENCE TRACKING"

TYPE: ACTION

DOCUMENT NUMBER: 9120163

FROM: GOLDSTEIN, MURRAY

TO: DR. BROMLEY

DATE OF
CORRESPONDENCE: 01/24/91

SUBJECT: THE FILM "AWAKENINGS" AND ITS SCIENTIFIC PROMISE.

ASSIGNED TO: D. Allan Bromley

DAB
Do you wish to respond personally
or
ask DA/Alicia
✓ prepare a note?
Shunk
DTJ
1/30

ACTION REQUIRED: AS NECESSARY

SENDER'S DUE DATE:

OSTP DUE DATE:

02/08/91

DATE COMPLETED:

COPIES TO:

WHITE HOUSE TRACKING #:

CONTACT PERSON:

REMARKS:

DATE RECEIVED: 01/28/91

FILE: ~~BIOMEDICAL-NEUROLOGY~~
f- Life Sciences

1

1

"CORRESPONDENCE TRACKING"

TYPE: Action Item

DOCUMENT NUMBER: 9120163

FROM: GOLDSTEIN, Murray; NINDS/NIH, Bethesda, MD

TO: DAB

DATE OF
CORRESPONDENCE: 01/24/91

SUBJECT: Sorry you could not attend preview screening of
"Awakenings" and enclosing a copy of AWAKENINGS.

ASSIGNED TO: Alicia Dustira

ACTION REQUIRED: DAB Signature

SENDER'S DUE DATE: OSTP DUE DATE: 02/08/91

DATE COMPLETED: 02/20/91

COPIES TO:

WHITE HOUSE TRACKING #: CONTACT PERSON:

REMARKS:

DATE RECEIVED: 01/28/91
DATE RECEIVED DLS: 02/07/91

FILE: DLS

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20506

February 20, 1991

Dear Dr. Goldstein:

Thank you for your letter of January 24 regarding the January screening of the film "Awakenings." A member of my staff, Dr. Alicia Dustira, was able to attend and found the event to be most enjoyable.

I applaud your efforts to educate the public on the contributions that brain and behavioral science research can make during the Decade of the Brain. I also look forward to receiving the Decade of the Brain Report that your Institute has had a significant role in creating for the Federal Coordinating Council for Science, Engineering and Technology.

Sincerely,

A handwritten signature in dark ink, appearing to read "D. Allan Bromley". The signature is fluid and cursive, with the first name "D. Allan" and the last name "Bromley" clearly distinguishable.

D. Allan Bromley
Director

cc: Dr. Roger Porter

Dr. Murray Goldstein
Director
National Institute of Neurological
Disorders and Stroke
National Institutes of Health
Building 31, Room 8A52
Bethesda, Maryland 20892



9/12 01/63
DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

National Institute of Neurological
Disorders and Stroke
Bethesda, Maryland 20892
Building : 31
Room : 8A52
(301) 496- 9746

January 24, 1991

Dr. D. Allan Bromley
Assistant to the President for Science and Technology
Director, Office of Science and Technology Policy
Old Executive Office Building, Room 360
17th Street and Pennsylvania Avenue, N.W.
Washington, D.C. 20506

Dear Dr. Bromley:

I am sorry that you could not join us for our January 8 preview screening of the Columbia Pictures film "Awakenings." The evening was a complete success.

Attendees included leaders of the neuroscience community, members of voluntary health organizations, and representatives from Congress and the White House, all of whom were most impressed with the film and its scientific promise. Our guests that evening heard presentations by Senator Tom Harkin and Congressmen Silvio O. Conte and Joseph D. Early, each affirming their support for neurological research. The film was introduced by Surgeon General Antonia C. Novello. Occasions such as this screening help the public and Government focus their attention on the contributions and promise of biomedical research during the Decade of the Brain.

I am enclosing a copy of Awakenings along with a packet of background information we prepared for the event.

Sincerely yours,

Murray Goldstein, D.O., M.P.H.
Director

Enclosures

DIRECTOR
OFFICE OF THE

91 JAN 28 P12:38

RECEIVED

"CORRESPONDENCE TRACKING"

TYPE: ACTION

DOCUMENT NUMBER: 9120144

FROM: CROMWELL, JAMES H.

TO: DR. BROMLEY

DATE OF
CORRESPONDENCE: 01/18/91

SUBJECT: "THE DECADE OF THE BRAIN"

ASSIGNED TO: D. Allan Bromley

ACTION REQUIRED: AS NECESSARY

SENDER'S DUE DATE:

OSTP DUE DATE:

DATE COMPLETED:

COPIES TO: Alicia Dustira

WHITE HOUSE TRACKING #:

CONTACT PERSON:

REMARKS:

DATE RECEIVED: 01/22/91

FILE: *P- Life Sciences*
"DECADE OF THE BRAIN"



BOARD OF DIRECTORS

January 18, 1991

THOMAS M. POSEY
President
Billings, Montana

SYBLE SECKINGER
First Vice President
Serafina, New Mexico

ROBERT G. HAACK
Second Vice President
San Diego, California

DALE L. JOHNSON
Secretary
Houston, Texas

HERBERT S. REISENFELD
Treasurer
Cincinnati, Ohio

NANCY DOMENICI
New Mexico / Washington, DC

CLAIRE GRIFFIN-FRANCELL
Dunwoody, Georgia

GENEVIEVE HEARON
Austin, Texas

BRENDA W. LYLES
Houston, Texas

RONALD F. NORRIS
Newark, Delaware

CAROL REES
Ann Arbor, Michigan

TRISH VAN DEVERE SCOTT
Malibu, California

KATIE VATH
Lee's Summit, Missouri

JUNE WILD
Pewaukee, Wisconsin

LAURIE M. FLYNN
Executive Director

LYNN BORTON
Deputy Director

FREDERICK FEDELI, III
Director
Office of Government Relations

11th ANNUAL
CONVENTION
San Francisco, California
July 6 - 9, 1991

The Honorable D. Allan Bromley
Assistant to the President
For Science and Technology
Old Executive Office Building
Washington, D. C. 20506

Dear Dr. Bromley:

Fred Fedeli, Director of Government Relations,
and I respectfully request the opportunity to meet
with you briefly concerning "The Decade of the Brain".

I know that Dr. Dustira is working with you on
an article for the next issue of The Decade of the
Brain and we want to convey our gratitude on behalf
of NAMI for your efforts. Hopefully we can do this
some time next week.

With best wishes,

Sincerely,

James H. Cromwell
Research Advocate
Editor, Decade of the Brain

JHC:ac

Original of
fax of this
date, 1/18/91

NATIONAL ALLIANCE FOR THE MENTALLY ILL

2101 WILSON BOULEVARD, SUITE 302 • ARLINGTON, VA 22201
703-524-7600 • FAX 703-524-9094

"CORRESPONDENCE TRACKING"

TYPE: INFORMATION

DOCUMENT NUMBER: 9120131

FROM: KORN, DAVID

TO: DR. BROMLEY

DATE OF
CORRESPONDENCE: 01/17/91

SUBJECT: ASPECTS OF THE EMF CONTROVERSY DEALING WITH PUTATIVE
CARCINOGENICITY

ASSIGNED TO: D. Allan Bromley

ACTION REQUIRED:

SENDER'S DUE DATE:

OSTP DUE DATE:

DATE COMPLETED:

COPIES TO: Nancy Maynard
Alicia Dustira

WHITE HOUSE TRACKING #:

CONTACT PERSON:

REMARKS:

DATE RECEIVED: 01/19/91

FILE:

P- Life Sciences
CANCER/EPA DRAFT RPT



STANFORD UNIVERSITY MEDICAL CENTER

STANFORD, CALIFORNIA 94305-5302

David Korn, M.D.

Carl and Elizabeth Naumann Professor
Vice President and Dean

Stanford University School of Medicine

Room M 121
(415) 723-6436

January 17, 1991

Dr. D. Allan Bromley
Science Advisor to the President and
Director, Office of Science and Technology Policy
Old Executive Office Building, Room 360
17th and Pennsylvania Avenue, N.W.
Washington, D.C. 20506

Dear Allan:

Sometime last spring, Bob Charrow, whom I had gotten to know rather well while he was Deputy General Counsel for the Department of HHS, asked me whether I might have any interest in reviewing the data base on power frequency EMFs and expressing an opinion about the issues of putative health hazards. From my own areas of professional interest, and from the experiences I have had as Chairman of the National Cancer Advisory Board, especially with the Environmental Carcinogenesis Subcommittee of that Board, I was somewhat familiar with the EMF issues, but little did I know what a political thicket I was about to enter! I am enclosing for your interest copies of two brief pieces that I have prepared, which express my views on those aspects of the EMF controversy that deal with putative carcinogenicity. The first piece, entitled "Cancer Science and Cancer Policy" was part of a collection of essays prepared by experts that were offered last June to the EPA in a hearing that I did not attend. The second piece represents the testimony that I delivered at the more recent EPA hearing on January 14, which was concerned with a discussion of the EPA Draft Report. In preparation for the latter hearing, I spent a good deal of time reading the Draft Report in detail and looking, in addition, at some of the major source materials.

The enclosures accurately represent my views about this matter, but they really cannot begin to express the indignation I felt during the many hours I sat and listened to the presentations at the January 14 event. Most of that day was devoted to EPA staff review of the several chapters of the Draft Report, and most of the critical comment was scheduled to be delivered on January 15 and 16, during sessions that I could not attend. I was dismayed by the extraordinary efforts exhibited by many of the EPA staff commentators to strengthen an extraordinarily weak data base in an attempt to derive biological plausibility and causal inferences where none, to my mind, existed. As I stated at the hearing, I do not purport to be an epidemiologist; but I do not think one has to be an

Dr. D. Allan Bromley
January 17, 1991
Page 2.

epidemiologist to recognize how weak and "noisy" the available epidemiological data are in fact. As far as the biological data are concerned, they represent, in my view, an assortment of entirely descriptive, phenomenological observations, almost none of which has yet been reproduced, and most of which have been carried out under conditions of physical stimulation that almost defy efforts at reproducibility. Clearly, the issue of biological plausibility is important here, not only as a general consideration with respect to the interpretability of epidemiological data, but in this instance in particular, given the inherent weaknesses in those epidemiological data themselves.

I realize that you have earlier expressed your own concerns about the form and substance of these EPA studies, and it is for that reason that I thought you might be interested in reviewing the materials I have enclosed. As I indicated, I was not able to stay for the second and third days of the EPA hearing, but based on what I did endure during the first day of the event, I would suggest that the matter merits your close attention.

Sincerely,

A handwritten signature in cursive script that reads "David Korn". The signature is fluid and elegant, with a large initial "D" and a long, sweeping underline.

David Korn, M.D.

DK/sp

Enclosures

EPA Hearing on ELF (Power Frequency) EMF'S

January 14, 1991
David Korn

Introduction

I'd like to thank you for the opportunity to appear today at this meeting to offer some comments on the EPA Draft Report and the difficult question of power frequency EMF's and their putative effects on biological systems -- especially, on the issue of whether such fields may be potentially carcinogenic.

I wish to make clear that although I am the Dean of the Stanford University School of Medicine and have been serving as chair of the NCAB since March 1984, my opinions and comments are my own and do not represent the views of Stanford University, the NCI or the NCAB. Nor do they represent the views of the Health Sciences Group, which originally asked me whether I would be willing to review this matter and express an opinion on the underlying scientific and policy issues.

I know that you have received a copy of an essay I prepared last summer entitled "CA Science and CA Policy"; and although that paper was written before I had the chance to study the latest (October 1990) draft of the EPA Report, I believe now, having reviewed the EPA Draft, that the major points I attempted to make in my brief paper remain valid and continue to reflect my views.

In my paper, I attempted first to summarize some of the remarkable progress that has been made in basic biomedical research during the past two decades, which has dramatically opened and illuminated the mysterious "black

box" that represented our knowledge of the neoplastic processes prior to 1990. We have indeed been able to make enormous advances in probing the most intimate details of the genetic regulation of cell growth and differentiation, and in beginning to unravel the incredibly complicated intracellular and intercellular communications networks that accomplish cellular and tissue homeostasis. From this wealth of scientific advancement we have been able to reorganize two major types of genetic abnormalities that appear to be fundamental to the initiation and progression of neoplastic changes:

1. The abnormal activation and expression of oncogenes (or CA genes) due to one or another form of mutational change -- i.e., due to some form of injury to the DNA -- that by itself, or in concert with further derangements introduced by the activation of cellular repair processes -- results in a heritable alteration of the cell's genome. These changes, in every case studied to date, can be said to lead to the turning on of some key process in a regulatory chain of events and to the loss of the normal modulation of that process that is essential to normal cellular behavior.

2. The second form of genetic damage leads to the abnormal inactivation of genes that are normally turned on and function to suppress or restrain critical cell processes that, to date, all appear to be involved in triggering the entry of a cell into the mitotic cycle; most of these processes seem directly to be involved in the initiation of DNA synthesis. This second family of genes have been dubbed "CA Suppressor Genes" -- and progress in identifying them and elucidating their molecular bases of activity is advancing rapidly.

The unfolding of our knowledge of CA genetics has importantly clarified previously obscure processes of CA "initiation" and CA "promotion": Agents that initiate CA invariably do so by causing damage to DNA -- e.g., ionizing radiation, UV radiation, genotoxic chemicals like polyaromatic hydrocarbons; certain classes of viruses; etc. Similarly, CA promoting agents are a diverse variety of agents that lead to cellular proliferation and provide the opportunity both for the expression of the initiating genetic damage and for the accumulation and outgrowth of subsequent genetic abnormalities that seem to occur in progressive and sequential patterns. From this conceptual framework, it is clear that many promoting agents are in fact agents that cause cell and tissue injury, thereby leading to cell proliferation and repair efforts. Accordingly, with respect to such agents, as it is now becoming quite clear, issues of "toxicity" confound assessments of "carcinogenicity" and raise vexing and presently unresolved problems of "thresholds" -- a matter of substantial controversy in the present public policy arena.

I believe from all of the documents of which I am aware that there is no evidence whatsoever that 60 Hz EMF cause genetic damage; none of the cited biological experiments noted either in the OTA or in the Draft EPA Reports supports the interpretation that such EMFs are CA initiating agents; nor do they provide any support for the hypothesis that such EMFs may be CA promoting agents. To be fair, it should be acknowledged that both reports recognize the absence of evidence for CA initiation processes. But in their rather encyclopedic reviews of the potpourri of published biological data, single and

non-reproduced phenomenological observations, that have no mechanistic context of any kind that I can recognize, are from time to time interpreted with excessive generosity in attempting to reach possible relevance with known CA initiating and promotional events and to thereby infer "biological plausibility." I think these efforts are extraordinarily speculative; they badly strain credulity, and they weaken the quality of what is otherwise a commendable effort of data accumulation and evaluation.

In reviewing these materials, I continue to be troubled by the remarkable lack of specificity or reproducibility of the applied physical stimuli, and distressed by the absence of any interpretable dose-response relationships. Although the postulated "window phenomenon" is an interesting a posteriori construct to try to get around this perplexity, it really does not help much in trying to understand either a physical or a biological basis for the several modest and entirely descriptive biological effects that have been observed.

Accordingly, I believe that no biologically plausible mechanism has been articulated -- or demonstrated -- by which 60 Hz EMF might initiate or promote CA. The existence of such plausible mechanisms, based on sound biological and pathological principles, is always important in evaluating potentially injurious agents -- including potential carcinogens; and the absence of such mechanisms is of especial concern and calls for especial caution in attempting to evaluate complex epidemiological studies.

As I noted in my earlier essay, epidemiology is an important area in the biomedical sciences in that it deals with human populations in "the real world," and as such, may generate important clues for further study and development. On the other hand, however, epidemiology is fundamentally an observational science, and the topics of interest are often complex and multifactorial, thus leading to a high intrinsic susceptibility to misinterpretation, confounding, bias and frank error. I believe that the credibility of epidemiologic data depends importantly on their consistency, their coherence, their reproducibility -- and to the extent to which suggested associations and correlations conform with established biological and pathological principles of relevance to the disease state of interest. Absent such conformance, it becomes more difficult to distinguish bona fide relationships from spurious statistical associations.

The literature presents many controversial studies of this kind, some of them of many-years duration, in which disagreement and inconclusiveness remain -- e.g., caffeine (coffee) studies; studies of effects of fiber on cardiovascular or CA end-points (the recent controversy over bran); arguments about the potential costs and benefits of replacement hormone therapy in post-menopausal women -- and this, by the way, is one of the reasons that the FDA has been so extremely chary about using such data to endorse the advertising of alleged health-benefits on packaged foodstuffs.

On the basis of my review of the data assembled in the EPA Report, and in earlier reviews, I do not believe that the case for the potential carcinogenicity of 60 Hz EMF has yet been made in any kind of convincing fashion. I believe the

available data are extremely "soft" and "noisy"; that bias, confounding and chance have not been adequately ruled out; that the reported studies are highly inconsistent -- a fact, by the way, that may directly result from the lack of clear definitions of "exposure" and the remarkable absence of measurement in many of the published studies. The absence of quantitative definition; the retrospective nature of most of the studies (perhaps all of them); the relatively small numbers of cases and low statistical power; the marginally significant and low Relative Risk Ratios -- where the 95% confidence intervals in so many instances include a boundary term <1.0 -- all of these factors, to my mind, can only lead to the conclusion that no inference of 60 Hz EMF causation of CA can presently be supported.

Others in this hearing will be far more expert than I about the design and interpretation of such epidemiological studies, and in their ability specifically to address the shortcomings in the diverse group of papers that have been cited in the EPA Draft Report.

Clearly, it must be recognized that although the evidence to date does not support the conclusion of causal relationship between 60 Hz EMFs and human neoplasia, neither does that evidence permit one conclusively to rule the possibility out. The problem is scientifically intriguing -- and what is needed is additional, high-quality research. For example, in my earlier paper, I noted the large prospective study of childhood ALL that has recently been launched by the NCI and the CCSG, a study that will focus on incidence, not on mortality,

and one that proposes strong measurement components. Surely, other such studies would be most welcome.

Beyond these, however, it seems to me important that more rigorous basic research ought to be initiated as well. To my mind, there is still no plausible biological model to explain how ELF EMFs might interact with biological systems. For example, what might be a plausible mechanistic basis for a "window-phenomenon"? What, if any, mechanisms might exist that could result in energy transfer between ELF EMFs and biological systems? If purported membrane interactions might be of interest, there are powerful model systems and new technologies that could be used to design some novel experimental approaches that might ask specific questions and even provide some definitive answers. What I think we do not need, however, are more poorly designed descriptive studies, which, in the absence of plausible mechanistic hypotheses, will result in little more than additional "stamp-collecting" of dubious value.

I offer two concluding comments:

1. The EPA Draft Report should be modified to make its conclusions fit more closely the data and its own textual evaluations of that data -- which are often quite thoughtful. In its present form, it supports interpretations about a potential CA link that I believe are unwarranted and unsupported by the research to date -- or by our present framework of knowledge about CA causation.

2. One must clearly be especially cautious when evidence derived principally or solely from epidemiological studies provides the basis of proposals for important decisions in the area of health policy -- in the present instance, of cancer regulatory policy. It is certainly incumbent upon us to take appropriate steps to protect the public health and well-being; but the consequences of inappropriate or premature action based on speculation, on inadequate analysis, or on non-validated hypotheses can be enormous with respect to the expenditure of public funds and the magnitude of disruptive interposition into widespread and well-established patterns of social and economic behavior.

The potential linkage of power frequency EMF and CA has neither been demonstrated nor conclusively eliminated from possibility. More study is needed, and of a much more focussed, rigorously designed and higher scientific quality than characterizes the bulk of the work reported to date.

Cancer Science and Cancer Policy

David Korn, M.D.
Vice President and Dean
Stanford University School of Medicine

Since the enactment of the National Cancer Act and the launching of the National Cancer Program in 1972, we have made remarkable advancements in illuminating fundamental aspects of cell growth and differentiation and in beginning to unravel the complex abnormalities that lead to the spectrum of human diseases that we call "cancer." These advancements have been reflected through striking accomplishments in the fundamental biomedical sciences -- in biochemistry, molecular biology, molecular genetics, immunology, virology, and others -- which, taken together, have revealed an enormous wealth of detail about the most intricate workings of the highly interdigitated subcellular systems that function ordinarily to accomplish normal cell growth and differentiation.

Perhaps the most noteworthy of these achievements relates to the area of cancer genetics, where, during the past decade, beginning with seminal experiments with a few retroviruses known to cause malignancies in animals, it has become clear that a major underlying phenomenon in all cancer is a set of genetic abnormalities that have led to the recognition of "cancer genes" (oncogenes) and "cancer suppressor genes." Cancer genes may develop in cells through a number of different mechanisms: many cancer genes arise from alteration of normal genes essential to the life process by the phenomenon of mutation. Such mutations may be recessive and transmissible by inheritance, in which case they are present in every cell of the body, or they may arise as a result of postnatal insult caused by an agent, chemical or physical, known to

damage the genetic material, DNA. In the latter instance, the damage leads to the production of a dominant mutation and tends to be localized to particular cells and particular tissues, depending both on the nature of the inciting agent and what, if any, mechanisms the exposed individual may possess for metabolizing the inciting agent. Other mechanisms that are now recognized commonly to lead to the formation of "cancer genes" involve kinds of chromosomal damage that lead to the deletion, the rearrangement or the translocation of portions of DNA from a normal site of residence within a particular chromosome to some abnormal site where that particular piece of DNA is not normally found. As a consequence of the latter class of changes, delicate systems of genetic control, that may be thought of as switches regulating the turning on and the turning off of particular genes, become deranged; and as a consequence, specific genes may be turned on inappropriately, and often maintained in a permanent "on" state that leads to unrestrained cell multiplication.

The behavior of "cancer suppressing genes," although less completely described, can be thought of in the opposite sense: cancer suppressing genes are genes that are normally present in our cells, which function as part of master regulatory circuits to maintain in the "off" position specific genes or sets of genes that would otherwise drive the cell into inappropriate and uncontrollable multiplication.

The identification of oncogenes led naturally to a search for the abnormal products of those genes, and that search has in turn revealed the existence of an incredible array of protein molecules and structures that comprise an

elaborate communications system, within and between cells, that is essential for normal cell and tissue growth and differentiation. Some of these molecules function as "messenger elements," acting either locally, regionally or over relatively large distances; other molecules constitute links in intricate cascades of amplifying or dampening regulatory signals that are involved in stimulating or stopping cell division or in modulating cell maturation; while still other molecules are situated in or adjacent to cell membranes, where they serve as receptor elements (or transducers) for the transmissible messenger molecules. The pace of the science has been such that examples of almost every element of these complex regulatory schemes have been demonstrated as abnormal products resulting from a genetic aberration that leads to the activation of one or another cancer gene.

I emphasize these scientific principles to make the point that with this remarkable wealth of scientific clarification, many facets of the mystery of the "cancer black box" have become substantially illuminated during these past two decades. As a consequence, our understanding of many aspects of cancer causation ~~have~~^{has} become similarly more clarified, and, in particular, the established phenomena of cancer initiation and cancer promotion can now be understood far more clearly than before in terms of specific events that lead to particular changes that drive a cell into the malignant state.

In general, it is clear that "initiating agents" are invariably agents that cause permanent damage to the genetic material of a cell -- that is, to DNA. Such agents may be chemical or physical, and among the physical agents, the best established are either ionizing radiation or other forms of high energy

electromagnetic radiation (e.g., ultraviolet light) which, in every instance, can be shown to cause specific chemical or physical changes in target DNA.

"Promoting agents" seem to cause the accumulation of additional kinds of changes in DNA by a variety of routes; or they may act more directly on other discrete steps of the complex cellular regulatory system to perturb cellular homeostasis and lead to abnormalities in cell growth and cell differentiation. Numerous examples of these phenomena have now been identified both experimentally and in naturally occurring human cancers, where, for example, a progressive sequence of genetic changes can be correlated with progressive stages of cellular atypia, culminating ultimately in premalignant growths and frankly malignant cancers. The latter correlations, by the way, constitute one of the great validating triumphs of cancer genetics and represent a scientific breakthrough of fundamental importance.

Given this impressive record of scientific accomplishment, it is possible now to be far more precise and rigorous in designing protocols for studies in experimental carcinogenesis in general and in designing and interpreting epidemiological studies in particular, i.e., studies that aim to identify environmental factors and agents that may be involved in cancer causation. With the new insights into molecular mechanisms of carcinogenesis, it becomes possible to develop plausible biological hypotheses by which to explore the role of putative environmental factors in oncogenesis, both in prospective studies and in retrospective analyses. Epidemiology is, of course, an important area of the biomedical sciences in that it deals with human populations "in the real world," and as such, may generate important clues which, upon further

study and careful elaboration, may point to new directions for research or yield previously unsuspected insights about disease causation.

On the other hand epidemiology by its nature is largely a non-experimental science, that is, an observational one; and it is in the nature of epidemiological observation that the topic of interest is often highly complex and multifactorial, thus leading to a very high intrinsic susceptibility of misinterpretation or frank error. Accordingly, leading epidemiologists pursue their investigations with extraordinary care and rigor in order to minimize the probabilities of being misled by a host of factors indigenous to the structure of the study itself and to the resulting statistical manipulations of the collected data. Aside from such methodological concerns, the credibility of epidemiological data depends importantly on their consistency, their reproducibility, their coherence and the degree to which the suggested findings conform with established biological and pathological principles of relevance to the disease state under inquiry. Thus, an epidemiological study, however well designed, will not be convincing absent reasonable biological or pathological principles which can help to distinguish bona fide relationships from spurious statistical associations.

Such need for care in study design and execution, in data handling and interpretation, and in the drawing of inferences and conclusions is certainly not unique to epidemiology: indeed it is the fundamental stuff of the sound scientific method. But with respect to epidemiological studies, the need for such care is particularly compelling in light of the nature of the questions asked, the inherent limitations of study designs and the very significant probabilities of confounding, of bias or of irreproducibility. The biomedical literature is full of reports of intriguing, putatively causal relationships of factors to diseases, deduced from

carefully conducted epidemiological studies, that have simply proved to be irreproducible and ultimately, unsubstantiable.

These points must be given particularly weighty consideration when evidence derived principally or solely from epidemiological studies provides the basis of proposals for important decisions in the area of health policy in general, of cancer regulatory policy in the present instance. It is certainly incumbent upon us that we take appropriate steps to protect the public health and well being; but the consequences of inappropriate or premature action based on speculation, on non-validated hypotheses or inadequate analyses can be enormous with respect to the expenditure of public funds and the magnitude of disruptive interposition into patterns of common social and economic behavior. This admonition is particularly pertinent to the present evaluation being conducted by the EPA of the putative carcinogenicity of power frequency (50-60 Hertz) electric and magnetic fields (EMF). I offer this caution because this is an area of research that has not yet been examined sufficiently and validated by the research community and is certainly far from mature; an area that has nonetheless received wide-spread attention and is certainly capable of prompting wide-spread public concern; and an area in which an inappropriate or premature decision by the EPA could have profoundly adverse consequences for modern societies world-wide.

In forming this opinion, I have reviewed the papers of Wertheimer and Leeper, and of Savitz et al.; the background paper prepared by OTA and entitled "Biological Effects of Power Frequency Electric and Magnetic Fields"; the paper entitled "Evaluation of the Potential Carcinogenicity of

Electromagnetic Fields," prepared for the Office of Radiation Programs, EPA; and critical reviews prepared by Drs. Boutwell, Cole, and Labarthe, the latter two, respected cancer epidemiologists. I have also made additional independent inquiries of other experts.

On the basis of these readings and inquiries, I believe that the case for the potential carcinogenicity of power frequency EMFs is not convincing. The cited epidemiological studies, as Drs. Cole and Labarthe convincingly point out, are so subject to procedural and methodological challenge as to be essentially uninterpretable. Similarly, the scattered experimental studies that are cited in the OTA paper are predominantly single efforts that have not been replicated or systematically pursued to plausible or convincing conclusion. With respect to underlying pathobiological principles, it is clear that 60 Hz fields are non-ionizing and have not been shown to have any effects whatever on chromosome structure or DNA metabolism; certainly, therefore, they cannot be interpreted according to our current understandings of mutagenic or carcinogenic mechanisms. Neither is there evidence that such EMFs are capable of behaving as cancer initiators or cancer promoters. Perhaps most disturbing is the fact that there is no evidence in any of these studies of interpretable dose-response relationships, nor is it even clear that exposures can be defined or measured -- or even estimated -- with any kind of specificity or precision. Such problems of dosimetry are bad enough in the controlled laboratory environment; they totally confound efforts to attribute significant correlations, to say nothing of causal relationships, in epidemiological field studies conducted retrospectively.

In the absence of usual dose-response relationships, the concept of a "window phenomenon" has been proposed; and yet at our current state of knowledge of biology and biophysics, it is very hard to intuit the sorts of plausible biological or biochemical mechanisms might be at risk to such perturbations by "window effects." The OTA background paper, on page 67, summarizes the reviewed biological studies very well: "Current scientific understanding does not yet allow us to interpret the evidence in a single coherent framework. Even more frustrating, it does not yet allow us to draw definite conclusions about questions of possible risk or to offer clear science-based advice on strategies to minimize or avoid potential risks."

Earlier in that paper, on page 25, the text states: "Although a number of high-quality experiments have been performed in the last decade, we still do not have enough robust, replicated results to build a coherent scientific or phenomenological picture of the spectrum of effects and we are far from having a good theoretical model . . . in the field of biological effects of ELF fields, there are not yet theories to make firm hypotheses and test them. Therefore, some of the experiments described in this paper are attempts to see if there are any effects at all. Other experiments examine if there are simple hypothetical connections between experimental observations and possible health effects. We are not at the stage where experiments can be designed to test hypotheses based on a coherent framework."

In light of those appropriately conservative reflections, it is disappointing and surprising, again in the OTA background paper on page 67, to review the summary points regarding the putative relationship of ELF fields to cancer

promotion. These summary points are remarkably insubstantial and excessively speculative; for example, to reach from the exceedingly tentative suggestion that ELF fields may somehow affect cell membranes to the conclusion that these fields may cause cancer by disrupting cellular communication systems, or to try to correlate such speculation with known facts about messenger molecules and membrane-based messenger receptors is certainly unacceptable scientifically and is of dubious logic.

It is my opinion that the question of the possible roles of power frequency EMFs in human health and disease remains open, but it is certainly not one in which there is anything approaching convincing evidence in support of positive conclusions of disease causality. That is especially true with respect to the relationships of such EMFs to carcinogenicity. Speculations about these matters do abound, and further careful testing of plausible theories ought certainly to be encouraged. In this respect, I note that the National Cancer Institute is proposing, in collaboration with the Children's Cancer Study Group, a large scale collaborative investigation to determine if low frequency EMF exposure contributes to the development of acute lymphocytic leukemia (ALL), which comprises about 85% of all childhood leukemias in the United States. The proposed study will involve about 1,000 ALL cases and 1,000 matched controls, it will be prospective, it will look at incident cases and it will have a strong measurement component. This NCI-supported investigation appears to be precisely what this perplexing question requires -- sound further investigation, both epidemiological and biological, to obtain a stronger database from which to form testable hypotheses and judgments that might eventually lead to sound policy recommendations. Absent that database,

absent sound biological or pathological underlying principles, and given the fragmentary and insubstantial state of the body of evidence that has been adduced to date, I believe that the evidence of the possible carcinogenicity of EMFs is vastly insufficient to support any kind of sound decision-making with respect to new cancer regulatory policy.

**EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20506**

January 23, 1991

D.A. Henderson:

Please review the attached material and advise as to whether it would be worth Dr. Bromley's time to review it and respond, or whether Alicia or someone could respond to the letter. Perhaps you could verbally brief Dr. Bromley at some point, and have Alicia send a thank you note to Dr. Korn.

Thank you.

Ken Yale

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20506

January 31, 1991

Dear David,

Thank you for your thoughtful letter regarding the scientific evidence pertaining to EMF and risk. Your paper on "Cancer Science and Cancer Policy" clearly documents the problem. Sound policy, especially that which has far-reaching consequences, demands sound science.

I was glad to hear from you on this issue and I look forward to keeping in touch.

Sincerely yours,

A handwritten signature in dark ink, appearing to read 'D. Allan Bromley', with a stylized flourish at the end.

D. Allan Bromley
Director

Dr. David Korn
Carl and Elizabeth Naumann Professor
Vice President and Dean
Stanford University Medical Center
Stanford, California 94305-5302

"CORRESPONDENCE TRACKING"

TYPE: INFORMATION

DOCUMENT NUMBER: 9120171

FROM: FINERTY, MICHAEL P.

TO: DR. BROMLEY

DATE OF
CORRESPONDENCE: 01/15/91

SUBJECT: GERM WARFARE

ASSIGNED TO: Rachel Levinson

ACTION REQUIRED:

SENDER'S DUE DATE:

OSTP DUE DATE:

DATE COMPLETED: -----

COPIES TO:

WHITE HOUSE TRACKING #:

CONTACT PERSON:

REMARKS:

DATE RECEIVED: 01/28/91

FILE:

~~GERM-WARFARE~~

P- Life Sciences

100-100000-100000

9/20/71

Michael P. Finerty
Finerty Consulting
2970 E. 5th Street
Tucson, ARIZ 85716

Dr. Allen Bromley
Presidential Science Advisor
The White House
1600 Pennsylvania Ave.
Washington, D.C.

Dear Dr. Bromley,

Around 1350, a bunch of Genoese were defending a fort in the Lavant, when the Turkish army catapulted 4 or 5 dead bodies into the fort. Within a few days, deaths from plague erupted in the fort and the Genoese fled to Genoa carrying with them the plague bacillus and the rat fleas that spread it to the rest of Europe. Plague raged for about 300 years, killing somewhere around 50,000,000 people. It was the first instance that we can point to of the successful use of a Biological Weapon.

Plague can be controlled with Tetracycline, so that these days, it is not a threat unless one forgets how to diagnose it and how to treat it. However, Tetracycline resistance in some strains may force one to use other medicines, like Chloramphenicol and the like.

Bergey's Manual of Determinative Bacteriology, 8th Ed. Bergy Trust, Williams and Wilkins Company, Baltimore, MD 1975, was the first edition to classify the plague Bacillus, Pasturella pestis, as Yersinia pestis, neglecting the diagnostic tool, bipolar staining, which distinguishes the genus Pasturella from other bacteria. As the problem of diagnosis has not changed (bubos and bipolar staining), I recommend the World Health Organization's Manual of basic techniques for a health laboratory, (Geneva, 1980) (STILL IN PRINT) as a reliable guide to the diagnosis of Plague (Bubonic, Black, Pneumonic) in the field.

In the coming war, the most easily transmitted disease organism will probably prove to be Anthrax (Bacillus anthraxus), which does respond to penicilin. The most likely modification of this organism is the introduction of a phage or plasmid carrying the staphylococcus penicillinase gene or genes. If this is encountered, Dicloxicillin should be substituted for Penicillin V or G, Ampicillin and all other non-resistant penicillins. Anthrax can be diagnosed by the chains of bacilli and spores in the blood, first identified by Robert Koch.

Dr. Bromley, p.2

We can probably expect that enemy bullets, fragmentation devices, and missiles will be coated with Clostridium sp. (organisms of tetanus, gas gangrene and others) to disable as many of the ground troops as possible from even minor wounds. Again, porting in a Staphylococcus penicillinase gene would render most penicillins useless; however, Dicolxicillin to the rescue.

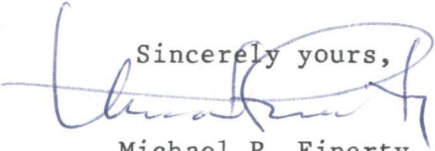
Army troops are usually vaccinated for Plague during boot camp. Anthrax also lends itself to Jennerian prophylaxis as demonstrated by Pasteur in France in the 1880's and 1890's. Institute Pasteur, Paris, can probably give you complete details the moment you ask them.

Another possibility is the use of Botulin poisoning from the organism Clostridium botulinum. Vaccination against both the organism and the toxin work and have been used by researchers in Food Science in the USA for years. It is estimated that one pound of the toxin would be enough to do in the entire population of the USA.

If you have read any of the Koran in translation, you know that the Arabs believe in the "Great Catastrophe," a baptism of fire of some kind. This belief may render all attempts at reconciliation useless, as believing arabs think that dying for Allah during this period of history is a sure ticket to heaven. They have both precedent and success in using biological weapons in the past. They may try it again this time.

The best of luck to you and the President in the coming conflict.

Sincerely yours,


Michael P. Finerty

Phone H (602) 795-0464

"CORRESPONDENCE TRACKING"

TYPE: INFORMATION

DOCUMENT NUMBER: 9120063

FROM: DAVID PACKARD

TO: DR. BROMLEY

DATE OF
CORRESPONDENCE: 01/04/91

SUBJECT: LETTER FROM BOB GLASER ON CONTRIBUTIONS OF
UNIVERSITIES & THEIR RESEARCH LABORATORIES IN
BIOLOGY & BIOLOGICAL SCIENCE

ASSIGNED TO: Rachel Levinson

*Document sent
Comment please*

ACTION REQUIRED:

SENDER'S DUE DATE:

OSTP DUE DATE:

DATE COMPLETED: -----

COPIES TO: D. Allan Bromley
Thomas Welch

WHITE HOUSE TRACKING #:

CONTACT PERSON:

REMARKS:

DATE RECEIVED: 01/08/91

P- Life Sciences *Biology*
FILE: BIOLOGY & BIOLOGICAL SCI

[REDACTED]

[REDACTED]

"CORRESPONDENCE TRACKING"

TYPE: INFORMATION

DOCUMENT NUMBER: 9120063

FROM: DAVID PACKARD

TO: DR. BROMLEY

DATE OF
CORRESPONDENCE: 01/04/91

SUBJECT: LETTER FROM BOB GLASER ON CONTRIBUTIONS OF
UNIVERSITIES & THEIR RESEARCH LABORATORIES IN
BIOLOGY & BIOLOGICAL SCIENCE

ASSIGNED TO:

ACTION REQUIRED:

SENDER'S DUE DATE:

OSTP DUE DATE:

DATE COMPLETED:

COPIES TO: D. Allan Bromley
Dr. Phillips
Thomas Ratchford
Dr. Wong

Rachel Levinson

WHITE HOUSE TRACKING #:

CONTACT PERSON:

REMARKS:

Life Sciences —

DATE RECEIVED: 01/08/91

FILE: BIOLOGY & BIOLOGICAL SCI

DAVID PACKARD
26580 TAAFFE ROAD
LOS ALTOS HILLS, CALIFORNIA 94022

91-21063

January 4, 1991

Dr. D. Allan Bromley
Exec. Office of the President
Office of Science & Technology Policy
Old Executive Office Building
Washington, D.C. 20506

Dear Allan:

Here is a letter from Bob Glaser on the contribution of universities and their research laboratories in biology and biological science.

I fully support his view that "there is no way we can sustain this rate of progress" without major federal support.

Sincerely,



David Packard

DP/gd

Enclosure

cc: Members of PCAST

LUCILLE P. MARKEY CHARITABLE TRUST

MIAMI, FLORIDA



525 MIDDLEFIELD ROAD, SUITE 130
MENLO PARK, CALIFORNIA 94025
(415) 323-6700

ROBERT J. GLASER, M.D.
TRUSTEE AND
DIRECTOR FOR MEDICAL SCIENCE

November 28, 1990

Mr. David Packard
26580 Taaffe Road
Los Altos Hills, California 94022

Dear Dave:

When you and I were talking at the last HP Board meeting, you suggested it might be helpful if I provided you with some examples of research, which originated in universities or research institutes, and which ultimately had enormous impact upon society as a whole. There are a great many examples one could cite, and you obviously are familiar with many of them. I know you don't want a long dissertation, but I am attaching herewith some examples that might prove useful.

The progress in biology and biological science has been incredible, as it has been in chemistry, physics, and engineering. At the time I started my research career late in the 1940s, the research enterprise, at least in medicine, was pretty limited, and by today's standards also rather primitive. A very significant difference then was that instrumentation was simple and quite inexpensive, and the cost of doing research relatively small. In the ensuing years, the impact of technology has greatly raised the cost of many forms of research; I remember when I was a student, the great cardiologist, Sir Thomas Lewis, who died in 1945, was lauded for his ability to do great experiments "with a test tube, a tin can and a piece of string". That was an exaggeration but nonetheless, the equipment Sir Thomas used in his day would not get one very far today.

Since the Markey Trust began only seven years ago, I have had occasion to spend a good bit of time in some of the leading biomedical research laboratories across the country, and in every instance, it has been apparent that funding for essential equipment and specialized facilities such as tissue culture

NOV 29 1990

Mr. David Packard
November 28, 1990
Page two

laboratories and sequencing instruments is often inadequate. Without state of the art equipment, even the brightest scientists are at a real disadvantage. If we are to continue to make progress, we need to try to do the best we can to support the brightest young people and to provide scientists with the necessary laboratories and equipment to exploit the incredible opportunities that exist today. Although private donors and foundations can have a role in the continuing advance of science, without major federal support through the NIH, the NSF, and other agencies, there is no way we can sustain the rate of progress that would be desirable.

Like many others, I hope the body on which you are serving will be able to make the case for greater investment by the federal government in the support of science. In the long run, the people of our nation and its economy cannot help but benefit from an enhanced effort.

I hope the foregoing and the attachment will be of some value.

Very sincerely yours,



Robert J. Glaser, M.D.

Attachment

The following are example of major advances in medicine based on work originally done in univeristy and research institute laboratories:

Diagnostic and therapeutic X-ray

Penicillin and streptomycin

Insulin for diabetes

Vitamin B12 (cyanocobalamin) for pernicious anemia

Microvascular surgery and cardiac bypass surgery

Pulmonary function studies

Transmembrane potential differences

Ionic factors in cardiac contraction

Heparin and dicoumarol for anticoagulation

Cardiac catheterization

Blood transfusion

Cathode ray oscilloscope

Measurement of blood gases

Tissue staining

Poliomyelitis

Respiratory distress syndrome in infants

Vasoconstrictor agents

DNA as the genetic material

Many forms of chemotherapy

Transplantation

Joint replacement (hips and knees)

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20506

January 31, 1991

MEMORANDUM FOR ALLAN BROMLEY

FROM:

D.A. HENDERSON

SUBJECT:

COMMENTS ON BOB GLASER LETTER TO DAVID
PACKARD

Bob Glaser is a highly respected internist, until fairly recently President of the Kaiser Foundation. He speaks with authority.

The exponentially growing need for instrumentation is very real. At the same time, corporate support is scarce and not infrequently given as discounts rather than gifts; foundation support may not be nil but I have difficulty identifying the last piece we received against a \$100 million/year restricted funds budget; and private contributions are close to nil outside of clinical laboratories. NIH, NSF or scarce "general funds" were the principal sources of support and such is the case, I believe, for other academic health centers and research universities. Any Request for Proposal (RFP) for instrumentation grants inevitably brought a tidal wave of requests.

There is increasing (and sensible) reliance on shared-instrumentation facilities--in my experience, uncommon 10-15 years ago but now standard in most biomedical laboratories. They do not solve the problem but they ameliorate the pain.

THE WHITE HOUSE

WASHINGTON

February 21, 1991

Dear Dr. Glaser:

Dave Packard has passed on to me your letter of November 28.

I would certainly agree with you that the need for modern instrumentation in university research is growing exponentially. At the same time, corporate support is scarce and not infrequently given as discounts rather than gifts. Foundation support is relatively small and those with whom I have discussed the question make a point that as the individual item cost of modern instrumentation increases, it becomes increasingly difficult to find a foundation willing to provide the matching that is frequently required in Federal programs. It is also true that outside of clinical laboratories, private contributions are rather rare and generally small. All that being the case, NSF and NIH are the principal Federal sources of funding together with the general funds available within the universities themselves.

This is a problem that will obviously get worse and one that requires additional attention as well as additional mechanisms. In the area of mechanisms, it has become much more standard now than it was even five years ago for researchers in a given university to share in the use of expensive facilities. In the supply area, you perhaps will have noted in the FY'92 budget that President Bush sent forward to the Congress on February 4 of this year, there is a special new program within the National Science Foundation of \$50 million targeted to the provision of modern research instrumentation to universities on a 50-50 matching basis. I recognize that this will not be of direct help to many people in the life sciences and would hope that it would be possible to establish similar programs within NIH in subsequent years.

As we both recognize, this instrumentation question is only part of a much larger matter concerning the state of university and college infrastructure in this country. For more than a decade the management of these institutions have tended to protect their people as their most valuable resource and in consequence have deferred maintenance and modernization, as well as investment, in new capital equipment for both research and teaching. The latest report from the National Science Foundation has estimated that the overall need is some \$12 billion with \$4 billion of that total being allocated to modernization and renovation of existing structures to bring them up to modern research standards.

We were unable in the 1992 budget cycle to respond to this need at the Federal level with the exception of a \$25 million bricks and mortar program within the Department of Agriculture, but you are probably aware that there is a very active group in the Congress led by Senator Terry Sanford and Representative George Brown who are crafting legislation to address this infrastructure problem.

My thanks for your very helpful letter and with all best wishes,

Sincerely yours,

A handwritten signature in dark ink, appearing to read "D. Allan Bromley", written in a cursive style.

D. Allan Bromley
Assistant to the President
for
Science and Technology

Dr. Robert J. Glaser
Lucille P. Markey Charitable Trust
525 Middlefield Road, Suite 130
Menlow Park, California 94025

DAVID PACKARD
26580 TAAFFE ROAD
LOS ALTOS HILLS, CALIFORNIA 94022

January 4, 1991

Dr. D. Allan Bromley
Exec. Office of the President
Office of Science & Technology Policy
~~Old Executive Office Building~~
Washington, D.C. 20506

Dear Allan:

Here is a letter from Bob Glaser on the contribution of universities and their research laboratories in biology and biological science.

I fully support his view that "there is no way we can sustain this rate of progress" without major federal support.

Sincerely,


David Packard

DP/gd

Enclosure

cc: Members of PCAST



OFFICE OF THE
ASSISTANT DIRECTOR
FOR BIOLOGICAL, BEHAVIORAL,
AND SOCIAL SCIENCES

NATIONAL SCIENCE FOUNDATION
1800 G STREET N.W. • WASHINGTON, D.C. 20550

RECEIVED

January 31, 1991
51 JAN 31 P 4: 48

OFFICE OF THE
DIRECTOR

Office of the Assistant to the President
for Science and Technology

The attached is background information for Dr. Bromley meeting with Dr. Frederick Bernthal, Acting Director, NSF; Dr. John White, Acting Deputy Director, NSF; and Dr. Mary E. Clutter, Assistant Director, BBS/NSF; on Friday, February 1, 2:00 p.m.

Peggy Weber
Secretary to the
Assistant Director, BBS

Presidential Young Investigators

Background

- o Program established in FY 1984 with the objectives of 1) keeping "the best and the brightest" young faculty involved with teaching and research and, 2) promoting a partnership among universities, government and industry.
- o PYI awards are based on **nominations** by department chairs or deans; merit review by special panels based on nomination letter, letters of reference, and nominee statements of research interests and CVs.
- o Typically 200 awards have been made annually, with 100 to ENG (original focus based on perceived "brain drain" from academia to industry) and the remainder spread across disciplines (Directorates) based on perceived need.
- o PYI awards provide five years of support of up to \$100K/yr. NSF provides the first \$25K and matches other contributions. Thus, NSF pays a maximum of \$62.5K/yr for each award.
- o Many accomplishments accrue to the PYI Program to date. Over 1200 young faculty have been put on a "fast track" because of the PYI opportunity.

What is coverage total.

Quantitatively what does this mean?

Issues

- o The success rate varies across disciplines leading to the perception that "success" for PYIs is higher than for regular proposals. In some programs as much as 20% of the annual budget is invested in PYI's.
- o The PYI review is seen as a "beauty contest" (comparison of CVs, attend the "right" schools, study under the "right" person, etc.) because no proposal is required.
- o Although the possibility of matching funds was a motivation to PYIs to seek such support, success has been mixed. For example, an industrial match leading to collaborative research has not been fully realized.
- o No differences between PYI and non-PYI groups with respect to **perceptions** of innovation in their research; too little focus on the impact of the PYI on educational activity as a basis for and requirement of the PYI award.
- o PYI awards do not satisfy the need for research initiation awards across all disciplines.

Sounds too high.

What does this mean

- o *Not really Presidential*
- o *Not exclusive enough - There are too many*
- o *Husband & wife team winners? How many?*

Possible Solutions

- o A more highly selective approach; reduce number of awards from 200 to approximately 100. Such a reduction would stress the honorific value of the PYI award.
- o Change criteria to emphasize early achievements as a faculty member and further potential for innovation in both teaching and research. This would add substance to the review and reduce the concern that the PYI is a "beauty contest."
- o Increase the base award size from \$25K/yr to \$40K/yr for 5 years and retain the matching opportunity. Assist the PYIs in possible industrial contacts by preparing and distributing a brochure highlighting interests and accomplishments of PYI awardees.
- o Selection as a PYI is an honorific award based on the potential of the nominee, not on a particular competing research project. Therefore, research initiation awards are not a suitable substitute. A separate agency-wide research initiation program should be considered.

Mary

NATIONAL SCIENCE FOUNDATION

1800 G STREET, N.W.
WASHINGTON, D.C. 20550

Directorate for Education and
Human Resources

MEMORANDUM

DATE : January 17, 1991
TO : Damar Hawkins, Executive Assistant, OSTP
FROM : Director, Division of Research Career Development, EHR
SUBJECT: Presidential Young Investigator Awards Program

Following up our telephone conversation earlier this week, I am forwarding a collection of background information about the Presidential Young Investigators program. This information includes:

1. The most recent program announcement (guidelines for nomination and nomination materials)
2. A brief history of the program
3. A fact sheet
4. A copy of the memo signed by the President approving the 1990 awards

Our schedule calls for NSF to forward to OSTP an alphabetic list of the names of proposed 1991 awardees in early February. Our target date for the announcement of awards is mid- to late- March.

We appreciate the cooperation that you are giving us in this matter.

Terence L. Porter
Terence L. Porter

Attachments

*Any limit on the number
of PVI at any given institution?*

THE PRESIDENTIAL YOUNG INVESTIGATOR AWARDS PROGRAM

History and Background

In 1982, Dr. George Keyworth, Head of the Office of Science and Technology Policy, proposed a national program intended to increase the attractiveness of academic careers in engineering and computer science. Acceptance of his idea resulted in the inclusion of the Presidential Young Investigator Awards Program in President Reagan's budget request for the National Science Foundation in December, 1982.

Another objective, in addition to that of enhancing academic careers, was encouragement of the private sector to participate with the federal government in supporting academic research and teaching. The PYI program strongly emphasizes the idea that industry's self interest is best served by ensuring the continuing production by this nation's academic institutions of new ideas and highly-trained professional scientists and engineers.

The program has undergone changes; for example, in addition to engineering and computer science it now includes the other fields of specialization supported by NSF. An original limitation to Ph.D. granting institutions has been removed -- faculty members from predominantly undergraduate institutions are now eligible for nomination.

Description of Award

The award, which extends over five years, is part fellowship, part prize and part research grant. It provides an annual base award from NSF of \$25,000, plus dollar-for-dollar matching of funds from industry and other selected sources which meet specified guidelines. The maximum which will be matched each year is \$37,500. Therefore, a PYI can obtain a maximum of \$100,000 each year during the five years of the award. The awardee's institution also must contribute by guaranteeing the academic-year salary and agreeing to a maximum of ten percent of NSF funds to defray administrative costs in lieu of indirect costs.

The PYI has considerable latitude in the research pursued and is free to transfer the award to a different institution approved by NSF. The relative freedom to engage in "risky research" is considered to be one of the benefits of the PYI award.

Operation of the Program

The nominations are received by the Foundation's Division of Research Career Development which is responsible for coordination and management of the program. The nominations are submitted to the Research Directorates who are responsible for selecting the awardees, providing the funds and administering the awards.

House "risky" money to the death!

Eligibility Criteria

1. The nominee must be a U.S. citizen or permanent resident as of the closing date for submission of nominations.
2. The nominee must have a Ph.D. degree, or equivalent, awarded, or to be awarded after a specified date which will change each year. For example, the Ph.D. degree for 1991 candidates must have been awarded after December 31, 1984.
3. The nominee must have begun a tenure-track position after a specified date which will change each year. For example, the tenure-track position for 1991 candidates must have begun after April 30, 1987.
4. The nominee must be conducting research in a field supported by the NSF.
5. The nominee must be nominated by the department chairperson or analogous official at a U.S. institution that awards a baccalaureate or higher degree in a field supported by NSF.

Nomination Materials

1. Cover Sheet providing basic information about the nominee and the nominator.
2. Nominator's Narrative Statement limited to one page describing the nominee's demonstrated ability and qualifications as a researcher and teacher, future potential, and how the award will enhance the institution in its research and teaching mission.
3. Nominee's Research and Teaching Qualifications limited to one page summarizing research and teaching accomplishments and how the award will enhance the nominee's development as an academic leader.
4. Nominee's Research Plan limited to one page describing research interests and plans during the period of the award.
5. Support and Commitments: Signature of the nominee declaring intention to undertake or continue an academic career if award is received; nominator's acceptance of responsibility to provide support and to assist in obtaining matchable funds; endorsement and signature by a representative of the institution who is authorized to commit the institution to the terms of the award.
6. Reference letters on NSF supplied forms from three individuals from institutions other than that of the nominee.
7. Supplementary Nominee Information about gender, ethnic/racial status and handicap as part of its Privacy Act Records System.

*Should not be included here
at all!*

8. Personal Data Form sent directly to the Office of Science and Technology Policy to facilitate White House clearance in the event of an award.

Results

To date there have been 1256 awards of which 168 have been made to women; the overall success rate has been 12.9%. As of Fall 1990 the NSF has contributed over \$220 million, and the private sector and other eligible donors have contributed about \$120 million. The overall contributions of matchable funds represent about 80% of the maximum.

The PYI program has identified a group of individuals who represent the Nation's outstanding young scientists and engineers. The momentum and the freedom to be creative this award has given these selected individuals has strengthened one of the Nation's most valuable resources, one which by definition is one of its scarcest.

THE FUTURE

One of the priorities which this nation must address is expansion of the reservoir of science and engineering talent from which individuals such as PYI's are drawn. Therefore, careers in science and engineering must be encouraged at the very earliest age among women and minorities who now represent but a very small percentage of those nominated for PYI awards.

*Should be purely merit-based
as a Presidential award. Other programs
may be needed to address other
problems.*

Presidential Young Investigators

Initiated: FY 1984

Competitions to date:

	1984	1985	1986	1987	1988	1989	1990	Total
Nominees	1549	1089	886	1122	1806	1657	1591	9700
Awards	200	200	100	200	148	197	211	1256
%Success	12.9	18.4	11.3	17.8	8.2	11.9	13.3	12.9

Eligibility: First tenure-track position within 3 1/2 years.
Ph. D. within 5 3/4 years.

Annual Funding: \$25,000 base NSF grant plus up to an additional
(up to 5 years) \$37,500 on a dollar-for-dollar matching basis to
support raised from private industry or non-
profit Foundations.

1990, 1991 Participation Data: (1991 awards to be announced in March)

	1990		1991	
	Nominations	Awards	Nominations	Awards
Total	1591	211	1605	N/A
BBS	374	26	399	N/A
CISE	206	34	232	N/A
ENG	537	85	533	N/A
GEO	60	6	69	N/A
MPS	398	60	372	N/A
Females	222	42	255	N/A
Minorities	58	9	49	N/A
Perm. Res.	319	43	278	N/A
PUI Inst.	193	7	192	N/A
Disabled	N/A	N/A	8	N/A

Institutional Distribution: The first 1256 PYI awardees represented 124 institutions distributed among 40 states and the District of Columbia.

Matching Funds Success: As of Fall 1990, the matching funds success rate of awardees through the 1989-1990 academic year is approximately 80% of the maximum possible. This represents approximately \$120 million of contributed funds from the private and non-profit sector over six years.

Program Review: The Foundation recently completed an internal review of the future of the PYI program, including its terms and conditions, and the internal management mechanism. The resulting recommendations are now before the senior officials of NSF.

THE PRESIDENT HAS SEEN

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF SCIENCE AND TECHNOLOGY POLICY
WASHINGTON, D.C. 20508

April 11, 1990

ACTION MEMORANDUM FOR THE PRESIDENT

FROM: D. ALLAN BROMLEY *Alan*
SUBJECT: 1990 PRESIDENTIAL YOUNG INVESTIGATOR AWARDS

I. ACTION-FORCING EVENT: The FY 1990 Presidential Young Investigator Awards.

II. BACKGROUND: In 1982, Dr. Jay Keyworth, Director of the Office of Science and Technology Policy and Science Advisor to President Reagan proposed a national program intended to increase the attractiveness of academic careers to graduating professors in engineering and computer science. The Presidential Young Investigator Awards Program was first proposed in President Reagan's FY 1983 budget request for the National Science Foundation. The first Presidential Young Investigator Awards were announced by Dr. Jay Keyworth in 1983.

The award, which extends over five years, is part fellowship, part prize, and part research grant. It provides an annual base award from NSF of \$25,000, plus dollar-for-dollar matching of funds from industry and selected sources which meet specified guidelines. The Presidential Young Investigator awardee can obtain a maximum of \$100,000 each year during the five years of the award. The awardees institution also must contribute by guaranteeing the academic year salary and agreeing to use a maximum of ten percent of federal funds to defray administrative costs. To date there have been 1045 awards given.

III. RECOMMENDATION: Formal approval of the attached list of FY 1990 Presidential Young Investigator Awardees.

IV. DECISION: Approval Signature: *Al B*

Date 4-30-90

☒ approve

☐ approve as amended

☐ reject

Attachments:

- A - List of proposed awardees
- B - Background and Description paper of award
- C - Award statistics