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Cancer Panels: [President's Cancer Panel-Historic Background Information] [1]

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PRESIDENT'S CANCER PANEL

National Cancer Program ◆ National Cancer Institute

Executive Secretary
Maureen O. Wilson, Ph.D.
Assistant Director
National Cancer Institute
31 Center Drive
Room 4A48-2473
Bethesda, Maryland 20892-2473
Phone: 301-496-1148/FAX: 301-402-1508
E-mail: PRESCAN@nih.gov
WEB Site: http://deainfo.nci.nih.gov/advisory/pcp/pcp.htm

March 19, 1998

Mr. Jerry Mande
Office of Science and Technology
New Executive Office Building - Room 436
17th Street & Pennsylvania Avenue, N.W.
Washington, D.C. 20502

Dear Jerry:

As requested, I am enclosing an abbreviated summary of the President's Cancer Panel activities from the Panel's inception in 1971 to date. We have provided reference to specific legislation where it impacted the activities of the Panel and have also provided copies of all the available written reports as appendices to the narrative.

Please feel free to contact me at 301-496-1148, if you have any questions.

Sincerely,

Maureen O. Wilson, Ph.D.
Executive Secretary

Enclosures

The President's Cancer Panel

An Overview:

1971 to 1998

Prepared for the Office of the Vice President

March 18, 1998

Maureen O. Wilson, Ph.D.
Executive Secretary
President's Cancer Panel

National Cancer Instiute
31 Center Drive
Building 31, Room 4A48, MSC-2473
Bethesda, Maryland 20814-2473

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Background

The President's Cancer Panel (PCP) was created under the authorities of the National Cancer Act in 1971 (P.L. 92-218) and has continued under subsequent reauthorizations.[1] The effect of the Act was to enlarge the authorities of the National Cancer Institute (NCI) to advance the national effort against cancer by conducting and supporting research on the cause, diagnosis, prevention, and treatment of cancer. Under Title VI, Part A of the Public Health Service Act (42 U.S. Code 281 *et seq.*), these authorities include research relating to rehabilitation from cancer and continuing care and support of cancer patients. Collectively, the program of research efforts is referred to as the National Cancer Program--it is the Panel's duty to monitor the development and execution of the activities of the Program and report annually to the President on its efficacy.[2] Under Section 407 of the Act, the Panel is further charged to identify any delays and blockages in the rapid execution of the Program and bring them immediately to the attention of the President.

The PCP consists of three persons appointed by the President whose expertise and background provide them with the qualifications necessary to appraise the Program. By law, two members are appointed from among the ranks of distinguished physicians and scientists. Although the third member of the Panel may be, and has been, a scientist or physician, a prominent representative of consumer interests in cancer research has generally held this appointment.[3] It was originally suggested in the House Appropriations language that this individual be "skilled in the field of management." [4]

The Chair of the Panel is appointed by the President to a one-year term. Businessman Benno Schmidt, of J. H. Whitney, Co., was the initial Chair of the Panel. He was followed by Nobel Prize winner, Joshua Lederberg, Ph.D., and then by philanthropist and Chairman of Occidental Petroleum Corporation, Armand Hammer, M.D. Harold Freeman, M.D., of Harlem Hospital

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[1]P.L. 93-352: The National Cancer Act Amendments, 1974.
P.L. 95-83: The Biomedical Research Extension Act, 1977.
P.L. 95-622: The Community Mental Health Centers Act, 1978.
P.L. 96-538: The Health Programs Extension Act, 1980.
P.L. 99-158: The Health Research Extension Act, 1985.
P.L. 100-607: The Health Omnibus Extension Act, 1988.
P.L. 103-43: The National Institutes of Health Revitalization Act, 1993.

[2]Charter, President's Cancer Panel, May 29, 1996: Attachment A.

[3]Membership Listing of President's Cancer Panel 1972-1998: Attachment B.

[4]House Report 92-659, 1971.

Center has been the Chair since 1991. The other Panel appointments are currently held by Paul Calabresi, M.D., and Frances Visco, J.D.[5]

In order to accomplish its responsibilities under the law and to meet the demands of assessing a national research program undergoing rapid expansion, the Panel, under Benno Schmidt, held monthly meetings with the leadership of NCI in Bethesda, Maryland. These meetings reviewed the strategic plans, goals, and achievements of the National Cancer Program, and identified delays and barriers in the rapid execution of the Program, as seen by NCI.

The National Cancer Act also is the statutory basis for the By-Pass Budget, an NCI professional needs assessment of the requirements to support new and continuing initiatives submitted by the Director, NCI, to the President for transmittal to Congress. Initially, the Panel also served the function of "by-passing" NIH and the Department of Health and Human Service (DHHS, formerly the Department of Health Education and Welfare). After each monthly meeting with NCI staff, Benno Schmidt met personally with the Director of the Office of Science and Technology Policy (OSTP) the White House, to discuss the needs and goals of the NCI and its role in the Program.

Reauthorization legislation in 1977[6] reduced the mandated number of annual Panel meetings from twelve to four. In addition, the Panel was directed to make available to the President of the Senate and to the Speaker of the House, "The Annual Report of the Chairman to the President." Under Secretary Califano, direct communication between the NCI and the White House was redirected through the Department (i.e., the personal meetings between Benno Schmidt and OSTP were replaced with meetings with DHHS staff). More recently, written communication from the Panel has been directed to the President and to the Special Assistant to the President for Health Policy, with copies provided to the Director, NIH, the Secretary, DHHS, and Congressional staff. The By-Pass Budget continues to be submitted annually by the Director of the NCI to the President for transmittal to Congress after allowing reasonable opportunity for review (but without change) by the Director, NIH, and the Secretary, DHHS.

Panel Activities

The early years of the PCP, between 1972 and 1978, were marked by a pattern of intense and personal communication with the NCI and the OSTP about specific needs of the NCI supported intramural and extramural research program. Benno Schmidt continually championed the need

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[5]Current Panel roster and biographical sketches: Attachment C.

[6]Community Mental Health Centers Act, P.L. 95-622, Section 408(3).

to expand basic research knowledge and the need to achieve a balance between competing basic and applied research interests during this period of extraordinary financial expansion.[7]

In 1981, Armand Hammer was appointed Chairman of the Panel and departed from previous Panel protocol which relied heavily on assessing the status of National Cancer Program from Bethesda, Maryland. In 1982, he took the Panel to various cancer centers around the Nation to "examine regional conditions and issues regarding the role of the centers in their geographic regions in reaching the goal of reducing cancer mortality." This practice has been perpetuated under Harold Freeman, M.D. although the issues explored under his leadership have been broader.[8]

Beginning in 1981, the Panel: reported on the extension of cancer therapy into the community through the Community Clinical Oncology Program established to support clinical research under the leadership of community physicians; remarked on the NCI intent to pursue and intensify its research efforts in the areas of nutrition and chemoprevention; noted the disparity in incidence and survival rates between Blacks and other minority groups when compared to Whites; and identified the steps taken by the NCI to pinpoint environmental and host factor differences that could account for differences in cancer risk. The Panel also reported on the establishment of the Physician's Data Query (PDQ) system to provide extensive information about cancer treatment to patients and physicians; and identified the development of hybridoma technology (monoclonal antibodies) and recombinant DNA technology as important tools to create new cancer treatments and decrease overall laboratory costs in probing basic cellular processes.

In 1982 and 1983, the Panel solicited the input of the research community to identify critical issues in peer review and grant award procedures at NCI. Among these were reduced funding levels available in all programs of biomedical research; the need for long-term, stable funding for core support, specific research projects, and adequate support for more risky feasibility research and collaborative projects; the need for improved composition of study sections and modified scoring systems to reduce unfair prejudice voting in study sections; and the need for a defined appeal process. In direct response to the Panel's recommendations, revised procedures were created for the NIH peer review system and the NCI established the Outstanding Investigator Grant (OIG) that afforded greater support for high risk research. Notably, the first OIG award was made to Drs. Michael Bishop and Harold Varmus who received the Nobel Prize for their work in 1989.

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[7]The NCI budget expanded from $288 million in 1971 to $815 million in 1977. A brief history of the National Cancer Program for this period may be found at : Schmidt, Benno C., (1977). "*Five Years into the National Cancer Program,*" JNCI: 59 (2 Suppl.): p. 687. Attachment D.

[8]A full listing of President's Cancer Panel meetings beginning in 1981 is provided in Attachment E.

In 1986, the Panel looked not only at innovations in research in its regional meetings, but began its review of the progress made against cancer since the enactment of the National Cancer Act. The Panel looked at specific research progress against disease by identifying new basic discoveries and their potential as tools to elucidate disease mechanisms, numbers of new drug treatments, new treatment and chemopreventative trials, and their availability nationwide. The Panel, noting improvement in relative survival rates in certain cancers and a decrease in mortality for those under the age of 55, was quick to point out the increasing difference in incidence as well as survival rates between Blacks and Whites in this country. In the Chairman's Report, Dr. Hammer pointed out to the President that the amount of funding afforded to cancer research was less than one percent of the cost of medical care in this Nation, and that the National Cancer Program could benefit from a two-to-three fold increase in that level.

The Panel's site-by-site review of the research institutions contributing to the National Cancer Program created an appreciation of the resources available to people through this Program, but also highlighted its limitations. For example, a national collaborative chemoprevention program was created to exploit anti-carcinogenesis agents, and NCI set aside funds for a multi-institutional national effort to allow prominent scientists to freely collaborate in AIDS drug discovery and development. Biological therapy was added to the armament of surgery, radiation, and chemotherapy, as weapons against cancer and AIDS. However, a barrier to achieving program goals was identified in the financial need for construction funding to modernize regional facilities to conduct research and administer care using more complex and sensitive tools. Furthermore, a critical need and weakness of the National Cancer Program reported to the President in 1987 was a shortage of funds for research manpower development. Although NCI examined the funding to proposals in these areas in specially constituted study sections, a relatively flat appropriations line limited response made to these concerns. At personal cost, Dr. Hammer joined with the American Cancer Society to commission an independent survey of the construction needs of the facilities supporting the National Cancer Program research effort[9]. Also in 1987, Dr. Hammer initiated a STOP CANCER campaign in which he challenged the Federal Government to match approximately $500 million which the campaign intended to raise privately.

In 1987, the Panel examined innovations in treatment in the areas of melanoma, lung cancer, breast cancer, colorectal cancer and focused on the role of oncogenes in the disease process. The Panel highlighted both the progress and the potential of biological therapies, including growth factors and newly discovered suppressor genes for the treatment of cancer and AIDS; the need for further intensive research on lung cancer; the need for effective therapies against drug resistant cancers; and pointed to advances in recombinant DNA and related technology funded by the Federal government which created the underpinnings of a new biotechnology industry. The Panel identified smoking as responsible for 30 percent of deaths due to cancer; dietary and nutrition practices as responsible for an additional 35 percent of deaths due to cancer; called for

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[9]These needs and Dr. Hammer's personally commissioned study are noted in the 1985 Appropriations Report language, Senate Report 98-544.

the use of effective screening practices for breast and cervical cancer to reduce mortality due to cancer; and called for widespread use of state-of-the-art treatments for cancer as essential in the reduction of deaths due to cancer. Also in 1987, the Panel pronounced the framework for the National Cancer Program network of research and treatment facilities envisioned in 1984 to be complete. At that time, the network consisted of 60 cancer centers; 50 community clinical oncology program centers; 18 multi-institutional cooperative clinical trial groups; the Surveillance, Epidemiology and End Results program to measure progress through the examination of incidence, survival and mortality statistics; the Cancer Information Service to respond to questions from patients and practitioners; and the Physician's Data Query (PDQ) system to disseminate the latest in information about clinical trial options. However, the Panel pointed immediately to a continued need to expand this network, to support clinical trials, and sustain critical basic research efforts to maintain the momentum in progress against cancer.

Through 1988, the Panel continued reviewing the regional importance of the basic, consortium, and clinical cancer centers; the relationships of these centers with their parent academic institutions; the role of the centers in promoting health and delivering care; and their impact on regional health care policy and delivery. The role of the centers in local voluntary efforts to control and prevent cancer expanded greatly under the National Cancer Act. Seen as a primary vehicle of the National Cancer Program drive to prevent and eliminate cancer, the centers offered a panoply of innovative cancer research supported by Federal funding--they provided a link between basic science and clinical applications. Together with the Community Clinical Oncology Program awardees, the clinical trials network of national cooperative groups and other NCI funded research efforts, this infrastructure highlighted the diversity of cancer as a disease and the regional problems faced in mounting a coordinated national effort against cancer.
In 1988, the Panel reported to the President that the budget for clinical trials had effectively not increased in five years and that this was limiting progress against cancer. It also accepted a charge from the Presidential Task Force on Regulatory Relief to examine the process by which investigational drugs are granted marketing approval by the Food and Drug Administration (FDA). In response to this charge, the Panel established a committee under the direction of Louis Lasagna, M.D., to review the current procedures for the approval of new drugs for Cancer and AIDS. This study, frequently referred to as the "Lasagna Report," was completed in 1990 and provided specific recommendations regarding the process of drug review, its oversight, and the need for cooperative and collaborative relationships between the FDA, NCI and the National Institute of Allergy and Infectious Diseases, drug sponsors, and advocacy groups.[10] It also offered well thought out alternatives for endpoints and clearance processes needed to expedite important drug approval. Many of the recommendations made by the committee were implemented and led to faster availability of new drugs for the treatment of cancer and AIDS.[11]

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[10]See Attachment F: The Final Report of the National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS.

[11]For reports of the Chairman, President's Cancer Panel, to the President, 1981-1989, see Attachments G-M.

During 1991, after the death of Dr. Hammer, Dr. Harold Freeman, as Chair of the Panel, called for the Panel to expand its consideration of issues beyond research efforts supported by the NCI "as consistent with the intent of the National Cancer Act." On the premise that poverty is associated with diminished access to health care, greater participation in risk promoting lifestyles, and a higher likelihood of substandard living conditions which contribute to late diagnosis and higher death rates due to cancer among poor Americans, he led the Panel in an ongoing exploration of the impact of poverty and cancer. The Panel, under his leadership, has consistently called for the extension of the benefits of cancer research to all Americans through the elimination of economic and cultural barriers to obtaining access to cancer care--in the areas of prevention and early detection, as well as treatment. According to Dr. Freeman, these are barriers that neither NCI nor research alone can overcome--areas that need the full weight of the Federal government and the full participation of all sectors of the American public to address.

In 1991, at the request of Vice President Quayle, the Panel created the President's Cancer Panel Special Commission on Breast Cancer to review issues surrounding breast cancer. Its report, submitted in 1994, focused on two areas--continued research and progress against breast cancer and universal access to all beneficial discoveries--and offered eight specific recommendations towards those ends.[12]

From 1991 through 1995, Dr. Freeman led the Panel in a continued examination of the needs of the underserved in this Nation, through meetings on poverty and cancer, cancer and the family, cancer statistics and chronic cancer health care disaster areas, and cancer and culture. In addition, the Panel examined progress against prostate cancer, lung cancer, leukemia and AIDS.[13]

In response to a mandate in the 1993 appropriations report language[14], the Panel joined with the National Cancer Advisory Board in an examination of the National Cancer Program. The Panel invited testimony from outspoken critics of the National Cancer Program to evaluate the meaning of current statistics on cancer incidence and mortality with regard to the progress against cancer made by the National Cancer Program. This and other meetings of the Panel provided key input to "Cancer at a Crossroads: A Report to Congress for the Nation," prepared by the Subcommittee of the National Cancer Advisory Board to Evaluate the National Cancer Program.[15]

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[12]See attachment N: "Breast Cancer : A National Strategy-A Report to the Nation."

[13]Attachments O-Q.

[14]S.R. 102-397 p. 24.

[15]Report of the Chairman, 1992-1994 (Attachment P), and "Cancer at a Crossroads, " Attachment R.

Throughout this period, the Panel consistently reiterated the need to provide increased funding to the NCI to accelerate the translation of discoveries related to cancer prevention, detection and treatment, as well as associated support services, rapidly into application in the community. Dr. Freeman called for speedy identification of obstacles to access these discoveries and for the delineation and coordination of the roles of NCI and all participants in the National Cancer Program. In addition he spoke to the need to establish a cooperative public-private effort to educate all Americans with regard to health care options and how to access those options.

In 1994, the Dr. Freeman convened an ad hoc meeting of the Panel to examine the adequacy of the Federal Trade Commission (FTC) Test for determining tar, nicotine, and carbon monoxide content of domestic cigarettes in response to a request issued by Representative Henry Waxman, Chairman of the Subcommittee on Health and the Environment. In the conclusions from this meeting, the Panel stressed that switching to a cigarette with low tar and nicotine content was a poor substitute for quitting. The Panel went on to emphasize that how an individual smokes was as important as what that individual smoked, indicating that smoking behavior may be adjusted to compensate for lower nicotine levels by increasing the number of cigarettes smoked or the volume of smoke inhaled. The Panel advised that current labeling of cigarette packages based on the FTC test was misleading and that better labeling was needed to provide adequate consumer information.[16]

In his 1995 report to the President, Dr. Freeman addressed a basic need within the National Cancer Program to educate consumers, to empower them with adequate knowledge about cancer to allow them to make conscious decisions to avoid cancer causing behaviors and choose health promoting activities. This, he stated, is the responsibility of all Federal, state, and local organization that have responsibility for health related activities. To facilitate this decision making process, the Panel called for strengthened data collection in a manner that was standardized, coordinated, and subjected to rigorous quality control and confidentiality procedures. In addition, the Panel called for the education of all healthcare professionals to maximize their access and use of this knowledge, and for the development of a health promoting curriculum for children starting in the elementary grades. In calling for wider access to cancer research data, the Panel also refocused attention on the impact of technologic developments, including genetic testing, on the health care and personal rights of the individual. The Panel called for enhanced public-private support for participation in clinical trials with equal sharing of expenses by all participants, including managed care providers, and for development of incentives to encourage young researchers to choose a clinical research path.[17]

Its prior examination of the obstacles to progress against cancer lead the Panel to explore the impact of the evolving health care system on the war on cancer. The Panel, in its 1996 recommendations to the President, concluded that the uninsured and underinsured are

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[16]Attachment S.

[17]See Attachment Q.

increasingly at risk in our current health care system. A disproportionate number of these individuals are elderly, disadvantaged, or identified as minorities already at risk and with the fewest proponents to promote their health care interests. The Panel went on to recommend that participation in clinical research should be incorporated into the standard of care for cancer through access to peer-reviewed clinical cancer detection, treatment, and prevention trials. Such standard care should be provided under all forms of managed care and indemnity insurance. Furthermore, the cost of clinical research and training must be paid to assure that the U.S. will retain a preeminent place in medical research and the delivery of care, regardless of the structure and financing of our health care system. Additionally, a well delineated processes of appeal must be made a part of all health care plans. Such a process must be simplified, standardized and fully disclosed to consumers. Consumers at all levels must be educated to promote and understand the value of participation in, and support for, clinical research. Without such an understanding, the public is unlikely to demand that such services be covered in U.S. health care plans.[18]

Most recently, the Panel explored the concerns of those it has identified to be most at risk in our evolving health care system--those designated as special populations, minorities, the poor, the elderly, the uninsured, and the underinsured. In a year-long series of meetings the Panel considered these concerns by reviewing how racial classifications impact the gathering and application of cancer statistics, how such information is applied in older-aged individuals, and what their concerns are in the National Cancer Program. The first 1997 report from the Chair to the President focused on the meaning of race in science and boldly stated that ". . . race as used in the United States is a social and political construct derived from this Nation's history, it has no basis in science or anthropology." The Panel went on, however, to recognize that "racism, rooted in the erroneous concept of biological racial superiority, has powerful societal effects and continues to influence science."[19] This review has caused individuals within and outside the NCI to reconsider the meaning of cancer statistics and to begin to consider how to better draw meaningful scientific conclusions regarding populations, without sacrificing the need to redress social inequalities in the country. Additional reports on 1997 Panel activities are in progress with special emphasis on America's older citizens and concerns of these and other populations with regard to the U.S. health care system. Realizing that all Americans have a right to expect and receive quality care, the Panel will examine the quality of cancer care in the country during 1998.

Conceived initially as a vehicle to bring concerns of the National Cancer Institute and the National Cancer Program directly to the President, the Panel now serves largely as an ombudsman for the National Cancer Program. The Panel explores issues it defines to be of broad reaching impact to the Program and conveys its findings and recommendations to the President.

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[18]Attachment T.

[19]Attachment U.

Attachment A

Charter of the President's Cancer Panel

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

CHARTER

PRESIDENT'S CANCER PANEL

Purpose

The National Cancer Act of 1971 (Public Law 92-218), the Health Research Extension Act of 1985 (Public Law 99-158), and the National Institutes of Health Revitalization Act of 1993 (Public Law 103-43) enlarged the authorities of the National Cancer Institute (NCI) and the National Institutes of Health (NIH), in order to advance the national effort against cancer by conducting and supporting research with respect to the cause, diagnosis, prevention and treatment of cancer, rehabilitation from cancer, and the continuing care of cancer patients and also the families of cancer patients under Title IV, Part A, Public Health Service Act (42 U.S. Code 281 et seq). The statutory responsibility of the President's Cancer Panel (Panel) is to appraise the National Cancer Program (Program).

Authority

42 U.S. Code 285a-4; Section 415 of the Public Health Service Act, as amended. This Panel is governed by the provisions of Public Law 92-463, as amended (5 U.S. Code Appendix 2), which set forth standards for the formation and use of advisory committees.

Function

The Panel shall monitor the development and execution of the activities of the National Cancer Program, and shall report directly to the President. Any delays or blockages in rapid execution of the Program shall immediately be brought to the attention of the President.

Structure

The President's Cancer Panel shall consist of three persons appointed by the President, who by virtue of their training, experience, and background are exceptionally qualified to appraise the National Cancer Program. At least two of the members of the Panel shall be distinguished scientists or physicians. Members shall be appointed for three-year terms. Any member appointed to fill a vacancy occurring prior to the expiration of the term for which that member's predecessor was appointed

shall be appointed only for the remainder of that term. A member may serve until the member's successor has taken office. If a vacancy occurs on the Panel, the President shall make an appointment to fill the vacancy not later than 90 days after the date the vacancy occurred. The President shall designate one of the members to serve as the Chair for a term of one year. The Chair may serve until a successor has been appointed.

Management and support services shall be provided by the Office of the Assistant Director, National Cancer Institute.

Meetings

Meetings shall be held not less than four times a year, at the call of the Chair with the advance approval of a Government official who shall approve the agenda.

A Government official shall be present at all meetings. Meetings shall be open to the public except as determined otherwise by the Secretary; notice of all meetings shall be given to the public.

A transcript shall be kept of the proceedings of each meeting of the Panel, and the Chair shall make the transcript available to the public.

Compensation

Members who are not officers or employees of the United States shall receive for each day they are engaged in the performance of the duties of the Panel compensation at rates not to exceed the daily equivalent of the annual rate in effect for Executive Level IV of the General Schedule, including travel time; and all members, while so serving away from their homes or regular places of business, may be allowed travel expenses, including per diem in lieu of subsistence, as authorized by Title 5 U.S. Code Section 5703, as amended, for persons in the Government service employed intermittently.

Annual Cost Estimate

Estimated annual cost for operating the Panel, including compensation and travel expenses for members, but excluding staff support, is $213,831. Estimate of annual person-years of staff support required is .6, at an estimated annual cost of $47,575.

Reports

The Panel shall submit to the President periodic progress reports on the National Cancer Program and shall submit to the President, the Secretary of Health and Human Services (Secretary), and the Congress an annual evaluation of the efficacy of the Program and suggestions for improvements, and shall submit any other reports as the President shall direct.

In addition, an annual report shall be prepared not later than December 31 for submission to the Secretary through the Assistant Secretary for Health and the Director, National Institutes of Health, which shall contain, as a minimum, the Panel's functions, a list of members and their business addresses, the dates and places of meetings, and a summary of the Panel's activities and recommendations during the year. A copy of the report shall be provided to the Department Committee Management Officer.

Duration

Continuing (unless renewed by appropriate action prior to its expiration, the charter for the President's Cancer Panel will expire May 31, 1998).

APPROVED:

MAY 29 1996
Date

Director, NIH

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

NOTICE OF RECHARTERING

OF THE PRESIDENT'S CANCER PANEL

This Panel was established by statute and has functions which are of a continuing nature so that its duration is not governed by Section 14(a) of the Federal Advisory Committee Act but is otherwise provided by law. The Panel is hereby rechartered in accordance with Section 14(b)(2) of said Act.

MAY 29 1996

Date

Director, NIH

Attachment B

Membership Listing
of
The President's Cancer Panel

1972 - 1998

The President's Cancer Panel
Past and Present

Name of Member	Date of Service	State
Robert Good, M.D.	02-17-72 to 02-20-73	New York
Ray D. Owen, Ph.D., D.S.C.	08-17-73 to 02-20-76	California
R. Lee Clark, M.D.	02-17-72 to 02-20-77	Texas
Benno C. Schmidt*	02-17-72 to 02-20-78	New York
Paul A. Marks, M.D.	08-11-76 to 02-20-79	New York
Elizabeth C. Miller, Ph.D.	09-13-77 to 02-20-80	Wisconsin
Joshua Lederberg, Ph.D.*	12-05-79 to 10-04-81	New York
Bernard Fisher, M.D.	12-05-79 to 02-20-82	Pennsylvania
Harold Amos, Ph.D.	07-03-80 to 02-20-83	Massachusetts
John A. Montgomery, Ph.D.	03-22-83 to 02-28-89	Alabama
Armand Hammer, M.D.*	10-05-81 to 01-04-91	Washington, D.C.
William P. Longmire, Jr., M.D.	06-12-82 to 02-20-91	California
Gaza J. Jako, M.D.	04-08-91 to 02-20-92	Massachusetts
Nancy G. Brinker	04-09-91 to 02-20-93	Texas
Harold P. Freeman, M.D.*	08-09-91 to 02-20-00	New York
Henry C. Pitot, M.D., Ph.D.	05-08-92 to 02-20-95	Wisconsin
Frances M. Visco, Esq.	05-14-93 to 05-14-99	Pennsylvania
Paul Calabresi	05-01-95 to 02-20-99	New Hampshire

*Chair

Attachment C

Current Panel Roster and Biographical Sketches

PRESIDENT'S CANCER PANEL

National Cancer Program ◆ National Cancer Institute

Chairman
Harold P. Freeman, M.D.
Harlem Hospital Center

Frances M. Visco, J.D.
National Breast Cancer Coalition

Paul Calabresi, M.D.
Brown University
Rhode Island Hospital

Executive Secretary
Maureen O. Wilson, Ph.D.
Assistant Director
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E-mail: PRESCAN@nih.gov
WEB Site: http://deainfo.nci.nih.gov/advisory/pcp/pcp.htm

President's Cancer Panel

Harold P. Freeman, M.D.
Director of Surgery
Harlem Hospital Center
Room 11-104
506 Lennox Avenue
New York, New York 10037

Chairman, President's Cancer Panel
Appointment April 15, 1991 to February 20, 2000

Frances M. Visco, Esq.
President
National Breast Cancer Coalition
200 South Broad Street
8th Floor
Philadelphia, Pennslyvania 19102

Member President's Cancer Panel
Appointment May 14, 1993 to May 14, 1999

Paul Calabresi, M.D.
Professor & Chairman, Emeritus
Department of Medicine
Brown University - Aldrich 138
Rhode Island Hospital
593 Eddy Street
Providence, Rhode Island 02902

Member President's Cancer Panel
Appointment May 1, 1995 to February 20, 1999

Maureen O. Wilson, Ph.D.
Assistant Director
National Cancer Institute
31 Center Drive, Room 4A48
Bethesda, Maryland 20892-2473 (Meetings Untitled)

Executive Secretary
President's Cancer Panel

BIOGRAPHICAL SKETCH

Harold P. Freeman, M.D. Director, Department of Surgery, Harlem Hospital Center, New York City; and Professor of Clinical Surgery, Columbia University College of Physicians and Surgeons, New York City. Dr. Freeman was born in Washington, D.C. and graduated from the Catholic University of America where he received the Harris Award for "Outstanding Scholar, Gentleman, and Athlete." He later received an award for Outstanding Alumnus in the Medical Arts at Catholic University, and more recently was inducted into the Athlete's Hall of Fame of the University. He graduated from Howard University Medical School, Washington, D.C. and completed internship and residency in General Surgery at Howard University Hospital where he received the Daniel Hale Williams Award for Outstanding Achievements as Chief Resident. Subsequently he was Senior Resident in Cancer Surgery for three years at Memorial Sloan-Kettering Cancer Center, New York City.

Dr. Freeman is a Diplomate of the American Board of Surgery and a Fellow of the American College of Surgeons. Dr. Freeman served as a member of the Executive Committee of the Board of Governors of the American College of Surgeons. Dr Freeman served on the Executive Council of the Society of Surgical Oncology. He has served as Chairman of the Surgical Section of the National Medical Association and on numerous occasions has been a consultant to the National Cancer Institute, including six years as a member of the NCI Breast Cancer Task Force. Currently he is the Chairman of the Eastern Region of the Black Leadership Initiative on Cancer (a National Cancer Institute program). He has been Medical Director of the Breast Examination Center of Harlem, a program of Memorial Sloan-Kettering Cancer Center, since 1979. In addition, Dr. Freeman is Chairman of the New York State Commission for a Healthy New York and Chairman of the New York State Breast Cancer Treatment Quality Advisory Panel. In 1992 Dr. Freeman was appointed to the Ethics Committee of the Board of Regents of the American College of Surgeons. He is a Fellow of the American Surgical Association.

Dr. Freeman was elected to membership in the Institute of Medicine of the National Academy of Sciences in 1997.

Dr. Freeman has received Honorary Doctor of Science Degrees from Albany Medical College, Niagara University, Adelphi University, and the Catholic University of America.

Dr. Freeman served as National President of the American Cancer Society, 1988-1989.

Dr. Freeman is the chief architect of the American Cancer Society's initiative on cancer in the poor and is a leading authority on the interrelationships between race, poverty and cancer. Related to this, the "Harold P. Freeman Award" was established by the American Cancer Society in 1990. This award may be given annually in ACS divisions throughout America to individuals who have made outstanding contributions in the fight against cancer in the poor.

Dr. Freeman is Chairman of the President's Cancer Panel. He was appointed to this position for three year terms first by President Bush in 1991 and subsequently by President Clinton in 1994 and 1997. Dr. Freeman has lectured extensively throughout the United States as well as in Europe, Africa, South America, China and the Middle East on numerous subjects related to cancer prevention and treatment.

FRANCES M. VISCO is the first President of the National Breast Cancer Coalition (NBCC), (elected in April, 1992) and a member of its Board of Directors. Formed in May 1991, NBCC is a grassroots advocacy organization of more than 300 organizational and thousands of individual members. Until March, 1995, Ms. Visco was a partner in a large Philadelphia law firm. Her practice was concentrated in the area of commercial and multi-district litigation. She resigned her practice to work solely on NBCC activities. Ms. Visco is an honors graduate of St. Joseph's University and of Villanova Law School where she was an editor of The Villanova Law Review and a chair of the Women's Law Caucus. She is a graduate of the 1991-92 leadership class of Leadership, Inc.

On May 14, 1993, President Clinton appointed Ms. Visco as one of three members of the President's Cancer Panel. She was a member of the President's Cancer Panel 1992 Special Commission on Breast Cancer until its dissolution in February, 1994. Ms. Visco also sits on the Department of Defense Breast Cancer Research Program Integration Panel, which oversees the Department of the Army peer-reviewed research program, and co-chairs the National Action Plan on Breast Cancer. She has also been appointed to the National Cancer Policy Board.

Ms. Visco is a member of the Board of Directors of the Linda Creed Breast Cancer Foundation, an organization founded in memory of Philadelphia songwriter Linda Creed. Until recently, she was also a member of the Board of Women's Way, the nation's oldest and largest women's funding federation. She also sits on the consumer advisory board of the Temple University Comprehensive Breast Center, the Legislative Affairs Committee of the American Cancer Society, Philadelphia Division, the legislative committees of the Greater Philadelphia Chamber of Commerce; the Advisory Committee to the Women's Center for Health Promotion at Thomas Jefferson University Hospital and the hospital's Advisory Council to the undergraduate and graduate nursing programs, and the Advisory Committee for the Revlon/UCLA Women's Health Program.

Ms. Visco has appeared frequently on national television discussing women's health issues and has testified before various Congressional committees and panels. She has lectured throughout the country on the politics of breast cancer and other women's health advocacy issues. Because of her active role in breast cancer advocacy, Ms. Visco was honored in January, 1993 on ABC's World News Tonight with Peter Jennings as "Person of the Week." In May of 1994, Ms. Visco was honored as the first woman recipient of the Judge Learned Hand Award by the Philadelphia Chapter of the American Jewish Committee. At the November 30, 1994 National Women's Law Center Awards Dinner, Ms. Visco was honored for her work in women's health. In March, 1995, she received *Mirabella* Magazine's first Powerhouse Award. In May, 1996, Ms. Visco received an Honorary Doctor of Humane Letters Degree from the University of Connecticut, and in September, 1996, she received an Honorary Doctor of Public Service Degree from Cedar Crest College. Ms. Visco was honored as one of *Glamour* Magazine's Women Of The Year in December, 1996.

Ms. Visco is a breast cancer survivor. She resides in Philadelphia, Pennsylvania and is married and the mother of a ten year old son.

PAUL CALABRESI, M.D.

Paul Calabresi, M.D. was appointed Director of Brown-Tufts Cancer Center in November 1997 after the New England Medical Center/Lifespan merger. Dr. Calabresi is currently Professor of Medicine and Chairman Emeritus of the Department of Medicine at Brown University School of Medicine and Director of the Division of Clinical Pharmacology at Rhode Island Hospital. He is a Clinical Professor of Medicine at Tufts University, and an appointment as Professor of Medicine at Tufts University is in process.

Dr. Calabresi is a graduate of Yale College and Yale University School of Medicine. He was a Resident on the Harvard Medical Services at Boston City Hospital. Prior to his appointment at Rhode Island Hospital, Dr. Calabresi established the Division of Medical Oncology and served as Director of the Clinical Pharmacology Research Center at Yale University (1965-1967), Physician-in-Chief and Chair of Medicine at the Roger Williams Hospital in Providence (1968-1991), Chief of Medicine at the Women and Infants' Hospital in Providence (1974-1980), and Chair of Medicine at Brown University (1974-1993). Dr. Calabresi is a Fellow of the Institute of Medicine of the National Academy of Sciences and a Master of the American College of Physicians.

As a senior national oncology authority he is currently a member of the President's Cancer Panel and has been the Chairman of the National Cancer Advisory Board and a member of the Advisory Council to the Director of the NIH. He has served on nearly two dozen prominent committees and study sections of the National Cancer Institute and has been awarded the Oscar B. Hunter Memorial Award in Therapeutics from the American Society of Clinical Pharmacology and Therapeutics.

Dr. Calabresi is an internationally-recognized authority on the pharmacology of anticancer agents. He is an Associate Editor for the journal *Cancer* and has been a member of the Editorial Board of *The New England Journal of Medicine*. He has authored or edited more than 200 manuscripts and books on the pharmacology of antineoplastic agents and the management of cancer.

Attachment D

Schmidt, Benno, C. (1977). *"Five Years into the National Cancer Program,"* JNCI: 59 (2 Suppl.): p. 687.

Five Years Into the National Cancer Program: Retrospective Perspectives—the National Cancer Act of 1971

Benno C. Schmidt[1]

It is over 5 years since the passage of the National Cancer Act of 1971. This Anniversary Issue provides an appropriate occasion to assess our progress and to consider the opportunities for making the Federal support of cancer research more effective. With a fourfold increase in the budget, the National Cancer Institute (NCI) has been able to support during the past 5 years the most extensive program in biomedical research ever undertaken anywhere. There has been during this period an enormous extension of our science base and our knowledge as a result of the vast amount of excellent fundamental basic research that has been supported. But this extension of our knowledge only underlines how vast are the areas of ignorance which remain. Just as the past 5 years have brought a greatly enlarged science base, they have also brought important improvements in the clinic in dealing with cancer, but here again our progress only serves to emphasize how far we have to go.

While the National Cancer Program has had the strong support of the Congress, the Administration, the public, and a large segment of the scientific community, criticisms are still coming in from many quarters. This is to be expected in a program of this size and complexity, and these criticisms need careful listening to and even more careful sorting out.

I would like to deal here with several of the important questions that continue to arise and to see if we can, to some extent at least, separate myth and misconceptions from valid criticisms.

The two most important and persistent questions about the cancer program deal with opposite sides of the same issue. On the one hand, it is said that there is not a sufficient recognition in the cancer program of the importance of fundamental basic research. On the other hand, it is said that we are spending too much on fundamental basic research and not enough on applied and clinical research oriented toward a more immediate payoff. These questions go to the essence of whether the cancer program has the proper balance, and they deserve serious and continuing consideration. Other criticisms of the program include the following:

- Those in charge of the program are under the mistaken impression that techniques of business management can be used to unravel the profound mystery of biology.
- An attempt is being made to target research that cannot be targeted.
- We have become shackled by our own efforts at planning in areas where planning is impossible.
- Our insistence on targeting has resulted in an enhanced use of contracts at the expense of grants, and contracts mean less effective research.
- Our preoccupation with centers is causing us to fund second-rate research at places called centers, whereas first-rate research applications go begging in our traditionally excellent educational institutions.
- Control, demonstration, and service expenditures are siphoning off the funds that should be used for research.
- There is a lack of appreciation of the necessity for training the manpower needed to provide for the continuity of excellence that good research demands.
- Environmental carcinogenesis is receiving too little emphasis.
- The cancer program is raising false hopes and false expectations that will result in disillusionment and ultimate abandonment of the program to the detriment of all science.

These are the most frequently voiced complaints. There are others, but the ones I have mentioned provide more than a full agenda for this report.

First, is the cancer program supporting enough basic research? To put the answer to that question in context, let us take a brief look at a bit of history. In 1970, when the Senate of the United States appointed a Senate panel to make recommendations for cancer research, biomedical research in general and cancer research in particular were on the back burner. The budget of the NCI was $180 million. In 1971, as a result of the discussions that the Senate panel stimulated in the Congress, the NCI budget was increased to $228 million. In 1972, the first year after the passage of the National Cancer Act, the budget was $378 million. In 1973, it was $432 million; in 1974, $589 million; in 1975, $691 million; in 1976, $762 million; and this year's budget is $815 million. As a result of these increases, we have been able to give this country programs in both basic biomedical research and clinically oriented research in cancer that are unprecedented, both in their scope and their excellence. While the other institutes of the National Institutes of Health (NIH) have not had increases comparable to those given the NCI, the total NIH budget for biomedical research is $2.5 billion in 1977 compared to $1 billion, 143 million in 1970.

In 1976, 52% of the NCI budget, or $396 million, was

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where surgery, radiation, or both are used to eliminate the primary tumor. In addition, it has now become apparent that tumors are antigenic, and immunotherapy therefore will almost certainly become an important tool in treatment, particularly in the postoperative periods when low volumes of tumor exist.

It is possible then that, even with our existing tools, we may be able to improve significantly the survival of patients today. In those cases where tumors are resectable, there has been a tremendous increase in the past 3 or 4 years in the emphasis on the use of chemotherapy and immunotherapy postoperatively to treat patients with detectable or nondetectable micrometastases. Early results with these techniques are encouraging, and it now appears likely that cure rates will be materially increased for such common tumors as breast and colon cancer over those achieved in the past by surgery alone.

These recent developments represent a drastic alteration in the way medicine is practiced in this country. Utilization of these advances in cancer treatment often requires the melding of the talents of several specialties (the surgeon or radiation therapist, the medical or pediatric oncologist, and the researcher), and such a joint effort has not been and is not today common medical practice. It must become more common in cancer therapy, so long as our basic knowledge is at present levels, and this is an area where I hope we can look to the comprehensive cancer centers to lead the way. In fact, some of the most significant advances in cancer treatment occur not as a direct product of sponsored research but as normal or unusual progress in a good center where surgeons, medical oncologists, and researchers are working together every day in the handling of cancer patients. This unsponsored but natural fallout is one of the greatest values to be derived from support through research, construction, and training grants of this center-type environment.

Under the Cancer Control Program, the NCI is mandated by the Congress to extend clinical research to demonstration programs in areas where beneficial technologies exist but where their acceptance and utilization are not widespread. This is an area that troubles a great many scientists because they are concerned that the entry of the NCI into the service area, even to this extent, will ultimately result in the diminishing of NCI's resources for research. Fortunately, the Congress has to date been willing to budget the control activities separately, and I see no indication of a change in this policy. So long as this is true, the NCI should be able usefully to expend the control dollars without diminishing its research capability.

In fiscal year 1976, control expenditures were $54 million; this year they are budgeted at $60 million. The more important control programs include breast cancer detection, cervical screening, programs for screening persons with hazardous occupational or chemical exposure, rehabilitation programs following cancer surgery, programs to enable comprehensive centers to extend cooperation to other hospitals in their areas, demonstration networks for breast cancer and head and neck cancer, community-organized programs in cancer control, and radiologic physics centers to assist hospitals throughout their areas properly to plan and program their radiation therapy.

As for the charge that the cancer program is overly targeted, I wish I could make clear once and for all the fact that those who manage the national cancer effort are not obsessed with the idea of targeting. Some applied research can and should be targeted because the science base exists, and in those cases, with the advice of the best scientists available, a targeted effort is made. However, we are as aware as anyone anywhere of the limitations of targeted research, and we are not attempting to target the basic research that will give us the understanding of the origins and nature of cancer. Similarly, with respect to the issue of contracts versus grants, we have been substantially diminishing the percentage of contract support and increasing grant support in the area of basic science, and we intend to continue to do so. One of the problems of communications has been that our budgets often lump all contracts together, and this figure is sometimes taken by members of the scientific community to represent contract research. In fact, over half the contract expenditures are for necessary supplies and service that can be obtained only through the contract mechanism. The contract mechanism is used for the support of basic research today principally in areas where it was in use before the passage of the National Cancer Act, primarily cancer virology, and in these limited areas its use with strengthened peer review has been continued in order not to impede strong ongoing programs. However, the present management of the NCI has been deemphasizing the contract mechanism in the support of basic research and will continue to do so.

This brings me to the National Cancer Plan, which has been the subject of so much criticism from so many scientists. When Dr. James Watson was reported recently as having said at the Massachusetts Institute of Technology that the National Cancer Program was a "sham," he was, in fact, talking about the National Cancer Plan. He made this somewhat clearer in a letter of apology to the NCI Director than he did in his speech, but there is no question that he was talking about the plan and not the program. I suspect that, if we took a vote, most scientists would be happier if there were no cancer plan—if there had never been a plan. It seems to imply to a lot of people that somebody in a position of authority thinks that the problems of cancer can be dealt with in the same manner as the problems of building an atom bomb or landing a space craft on the moon. I assure you there is no such thought. The plan is not designed to tell us how to run the program. The plan was an attempt by the scientific community, by those responsible for doing the science, to indicate those areas which, at the present time, seem to offer the greatest promise. Like most plans, its principal value may well be in the communications that take place during the planning process. It is also a useful vehicle for the assessment of the program on a continuing basis and the presentation of the program to the Office of Management Budget (OMB) and the Congress. However, it does not put the program in any sort of straitjacket nor does it put blinders on those who are administering the program. The program is, in fact, what goes on at several hundred educational and research institutions plus the intramural work at the NCI. This is determined almost entirely by the best peer review available in the scientific community. So, in the last analysis, scientific initiative and peer review, not the plan, determine the cancer program.

spent on basic research. This compares with less than $100 million in 1970. Throughout the past 5 years, the National Cancer Program has consistently devoted about half the substantial budget increases to the support of basic research. Moreover, a large portion of that is investigator-initiated, peer-reviewed, grant-supported, basic research. For example, of the $396 million devoted to basic research in 1976, $152 million represents traditional research grants, $58 million represents the basic research portion of program project grants, $30 million represents support of basic research in the excellent intramural program on the NIH campus, $30 million is for construction and fellowship grants in support of basic research, and $79 million represents research contracts in areas, such as virology, that were already being supported by the contract mechanism prior to the passage of the National Cancer Act of 1971 and which, with strengthened peer review, we have continued to support by contract rather than disrupt good ongoing programs. These amounts are spent in support of fundamental research to expand our knowledge at the most basic levels. So when my friend, Dr. Arthur Kornberg, says, "We don't know enough about biology to do a proper job in spending huge amounts of money successfully on cancer," it seems to me that the fact is disregarded that a substantial amount of the money provided for cancer research goes to the support of excellent basic biologic research in the very areas of ignorance to which Kornberg refers.

During a recent hearing of the Senate Health Subcommittee, I was asked whether we should be supporting so much basic research under the cancer program. The question was, "Can we afford so much basic research or should we devote our funds to activities where the probable payoff is more immediate and more apparent?" My answer is that we cannot afford *not* to support basic research. Without it, there will be no payoffs. Basic research is the lifeline of medicine. It is essential to provide the science base upon which to build improved technologies for prevention, diagnosis, and treatment of cancer. What we need at the end of the line, and simply must have if cancer is to be eliminated from the roster of major human diseases, is an understanding of the underlying processes of cancer at a far more profound and sophisticated level than we possess today. For we are, in truth, profoundly ignorant about the real nature of cancer. We do not really understand what happens. We cannot fully explain the processes, although there are now attractive clues all over the place. Viruses may be centrally involved (in some cancers at least they probably are), and therefore virology is an important part of the effort. The basic processes of cell differentiation, membrane structure, and physiology are surely involved, and we are moving in those areas. Carcinogenesis, cellular genetics, molecular biology, immunologic recognition systems, the regulators of growth and differentiation, perhaps even influences of the nervous system—all of these represent fields for inquiry, and none of us can really predict at this stage of our ignorance where the most crucial bits of information now lie hidden away from us. We are confronted by one of the most complex mysteries in all of nature. There are no books to follow for instruction. Committees cannot provide the questions we need, much less the answers. We must explore every lead that looks like a good lead, watching for suggestions. For work of this kind we are totally dependent on the flexibility of human imagination, above all the imagination of our youngest and brightest investigators.

We are looking for new ground, but we have come far enough along in the biologic revolution to know, for an absolute certainty, that the problem of cancer is an approachable and solvable biologic problem, even though none of us can predict when or at what cost. This is the reason that expenditures for basic research under the cancer program since 1972 have totaled well over $1 billion, and a large fraction of this is investigator-initiated, peer-reviewed, grant-supported, basic research being done under increasingly rigorous standards of peer review for excellence.

We *must* continue the support of fundamental basic research, and no one should assume that good basic research cannot be supported by a categorical institute. Whether this basic research involves research directed at disease mechanisms, categorical in the sense that investigators will be driven by their own interest in the puzzle of one disease or another, or whether it is noncategorical, pure, undifferentiated biomedical research of the kind that has taken us deep into the biologic revolution, we must encourage and support this type of research. It is the excellence of the research that matters, not whether it is supported by the NCI or the National Institute of General Medical Sciences. Some scientists assume that, if basic research is supported by the NCI, it is somehow targeted or directed. That is not so.

One thing that worries me is the developing notion that there is good basic biomedical research that is relevant and there is good basic biomedical research that is not relevant and that scientists or administrators should be able to tell the difference in advance. The individual questions are much too small. It is the total of the science base that becomes relevant, and any building block that elucidates cell structure or mechanisms is relevant, although it may not seem so when described separately in advance. We must not allow this notion or any other to erode our support of the best basic science.

Simultaneously with the expansion of our knowledge through the support of fundamental research, we must also make the best effort of which we are capable today in the areas of prevention, diagnosis, and treatment of cancer. This means the support of applied research where an adequate science base exists and the support of clinical research for the development, application, and trial of the best technologies of which we are capable. In 1976, $241 million was obligated under the National Cancer Program for treatment research, of which $68.5 million was spent for the direct support of research in clinical treatment. While we have not had spectacular breakthroughs in cancer comparable to the antibiotics in infectious diseases or the polio vaccine, there is no question that the cancer patient has a better chance of surviving today in the hands of good cancer doctors than has been true at any time in the past. Not only are we doing better all the time with acute lymphocytic leukemia, osteogenic sarcoma, a number of other tumors in children, Hodgkin's disease, and other lymphomas, but a new era has begun in the use of combination therapy for the treatment of the more common tumors. Postoperative or postradiation chemotherapy appears to be effective in a large number of cases to avoid metastasis and recurrence

cancer program and in biomedical research generally that we bring a portion of our brightest young people into these programs, and fellowships and training grants have proved to be the most effective and most economical ways of doing that. These are among the best dollars we spend in terms of value received.

Fortunately, one way or another the NCI has been able to keep its training programs going at about the same dollar level as existed before the OMB action. However, the training programs of other parts of the NIH, particularly the predoctoral programs of the National Institute of General Medical Sciences, have been adversely affected, and that ultimately affects the cancer program as surely as if these programs were in the NCI.

One of the worst aspects of the training picture during the past few years under both the Weinberger Program and the National Research Training Act has been the on again-off again uncertainty that comes with defining new programs, producing new regulations, not having funds in certain periods, having funds in other periods, and putting the whole research establishment in the hurry-up-and-wait, now-you-have-it-now-you-don't posture. However, we are substantially supporting training, and I hope we can get a uniform understanding and a uniform program that can go on year after year without the turbulence that has characterized the past several years. This has been distressing, I know, from the standpoint of the institutions, and it has made for less efficient expenditure of the Federal dollars in this field.

In recent months the public interest in chemical carcinogenesis has enormously increased. This interest has now manifested itself legislatively in the Toxic Substances Act. In urging the NCI to devote more of its resources to environmental carcinogens, some have greatly oversimplified the problem. It has been suggested that, since the general assumption is that at least 80% of all cancer is environmental in origin and since environmental carcinogens can be identified by toxicologic testing, we could eliminate 80% of the cancer by determining and eliminating those elements in our environment that are causing the cancer. Unfortunately, the problem is not that simple. We have been able to identify and peg a number of chemical carcinogens, but undoubtedly many have not yet been identified, and the scientific methods available to us today for identification of carcinogens are not adequate to identify quickly and clearly the carcinogens in our environment.

The best method for identifying carcinogens today is through animal bioassays. These tests take 3 years, require 600 laboratory animals, cost $150,000, and often are not conclusive. Nevertheless, the NCI has been doing such testing for a number of years, and this work was greatly intensified after the passage of the National Cancer Act. At present, NCI commences the testing in its animal standard bioassay program of 60-70 carefully selected substances each year. This means that approximately 200 substances are under the standard bioassay test at any given time. The NCI is also involved in special studies of approximately 50-60 compounds per year. One of our biggest needs today is an in vitro test that would enable us to screen rapidly and inexpensively for environmental carcinogens. The NCI has supported research in this area for many years, and intensively since 1972. We have several in vitro tests that look promising, and some, such as the Ames' test, are good enough today to be useful in preliminary screening. However, the number of false-positives and false-negatives is sufficient to make animal testing essential as a backup procedure.

The NCI will continue to support research to improve these rapid and inexpensive in vitro tests and to use them to the fullest extent possible in the selection of chemicals for animal screening. We want the best programs in chemical carcinogenesis that are possible to provide and, if we are able to define the most effective approach, we will do our best to obtain funds sufficient to conduct whatever programs the public interest requires.

In 1976 the NCI spent $120 million on environmental carcinogenesis. This included the animal bioassay program, epidemiologic and field studies, program on smoking and health, and a small portion of the control monies that were spent on environmental carcinogenesis, primarily occupational exposure to carcinogenic substances.

Grants in the field of carcinogenesis included support of research in the identification and discovery of environmental carcinogens, in the mechanisms of action of chemical carcinogens including cocarcinogens (particularly viruses and chemical carcinogens), and the development of in vitro tests for rapid and inexpensive screening. The NCI also supports epidemiologic work designed to explore cancer incidence and to relate this to environmental factors where possible.

Extensive cooperation exists today between the NCI and the Environmental Protection Agency, the Food and Drug Administration, the National Institute of Occupational Safety and Health, and other agencies with responsibility for some part of the environmental carcinogenesis problem. This cooperation is being tightened up and better formalized under the Toxic Substances Act, so that the role of each agency will be well defined and parts of the problem will not fall in the crack. The total Federal effort must be effectively coordinated. A National Clearinghouse on Environmental Cancer has been set up by the NCI to serve as an information center and an early warning network for scientists, industry, Federal agencies, and others concerned with environmental carcinogenesis.

One discouraging aspect of the environmental carcinogenesis picture is our experience with cigarettes. There is absolutely no question that cigarettes are carcinogenic and that the epidemic increase in primary lung cancer is due to cigarette smoking. Apart from the cases of lung cancer caused by occupational carcinogens such as asbestos, uranium, and others, virtually all primary lung cancer occurs in long-term, habitual smokers. It is also reasonably certain that some portion of cancers of the bladder, esophagus, pancreas, and head and neck are also due to smoking. Therefore, it is clear that a large portion of the environmentally induced cancers are associated with cigarette smoking. Yet we are not able by law, education, or any other way to eliminate this carcinogen from the environment. We have not been able so far even to reduce total use. Our only hope is that lower tar and nicotine content will make some contribution to the reduced carcinogenicity of this environmental hazard.

Those of you who are engaged in this work at your own universities know that the plan is not determining what science you do or how you do it. I have never believed that worries about the plan were particularly well founded. Of course, there is a large element of unplanned, untargeted, undirected, investigator-initiated science required in this undertaking, but no one thinks differently and there is nothing in the plan to cause them to think differently. The program is designed to provide an open system with fair peer review and an environment optimal for discovery. We need brilliance, hard work, serendipity, and a large measure of good luck. I hope we are doing nothing to block ourselves off from any of these.

Another frequently heard charge, and one also recently repeated by Watson at the Massachusetts Institute of Technology, is that our centers' support represents the support of inferior research and thus deprives institutions of greater excellence of that support. This allegation does not withstand examination. In supporting the 19 comprehensive centers that have thus far been recognized, we are not only helping to bring better clinical care to a greater number of our citizens, but also supporting some of the best research institutions that exist in this country.

At the time the National Cancer Act was passed, three institutions in the nation were recognized as having comprehensive cancer centers. They were:

Memorial Sloan-Kettering Cancer Center, New York, New York
M. D. Anderson Hospital and Tumor Institute, Houston, Texas
Roswell Park Memorial Institute, Buffalo, New York

Since the passage of the National Cancer Act, 16 additional institutions have been recognized as having comprehensive cancer centers. They are:

Sidney Farber Comprehensive Cancer Center, Boston, Massachusetts
Yale University Comprehensive Cancer Center, New Haven, Connecticut
The Fox Chase Cancer Center, Philadelphia, Pennsylvania
The Johns Hopkins Oncology Center, Baltimore, Maryland
Georgetown University-Howard University Comprehensive Cancer Center, Washington, D.C.
Duke University Comprehensive Cancer Center, Durham, North Carolina
Comprehensive Cancer Center of the State of Florida, Miami, Florida
University of Alabama Comprehensive Cancer Center, Birmingham, Alabama
Illinois Cancer Council, Chicago, Illinois
University of Wisconsin Cancer Center, Madison, Wisconsin
Mayo Comprehensive Cancer Center, Rochester, Minnesota
Colorado Regional Cancer Center, Denver, Colorado
University of Southern California/Los Angeles County Comprehensive Cancer Center, Los Angeles, California
Fred Hutchinson Cancer Research Center, Seattle, Washington
Ohio State University Cancer Research Center, Columbus, Ohio
University of California, Los Angeles Cancer Center, Los Angeles, California

No one would question the fact that the research done at these great institutions, both fundamental and clinically oriented, compares favorably with the best biomedical research done anywhere. Certainly these institutions are also in the forefront of those that provide the best clinical care in cancer. The advances that take place at these institutions will greatly enhance the success of our efforts against cancer—both in the understanding of the disease and in the treatment of it during our period of incomplete understanding. We can be enormously proud of our achievement in extending so successfully the number and geographic distribution of these outstanding comprehensive cancer centers. The belittling of the effectiveness and accomplishments of these great institutions reflects a sad lack of understanding of the total picture in cancer research and treatment today.

By historic happenstance, the term "centers program" at the NCI has come to refer to all institutions that receive "core grants," "program project grants," or both. Therefore, we support under our centers program research not only at the great institutions which I have mentioned as having comprehensive cancer centers but also at many other institutions that have been called specialized centers because they receive core or program project grants. These institutions include Stanford University, the University of California, the University of Indiana, Harvard University, the Massachusetts Institute of Technology, the University of Minnesota, the Albert Einstein College of Medicine, the Mount Sinai Hospital, and some 50 other fine institutions too numerous to mention, but including, ironically, Cold Spring Harbor Laboratory, where Watson's support has gone from $435,000 in 1970 to $1,962,665 in 1976 under the NCI centers program. So I say to Watson and those like him who question the excellence of the research supported under the centers program that peer review is alive and well in the centers program just as it is in other programs of the NCI.

There *is* a legitimate worry about the comprehensive cancer centers that relates to future funding in the event of the recognition of too many such centers. Comprehensive cancer centers must compete on the merits of all other institutions for the cancer research dollar. Therefore, if too many centers are recognized and we have centers that cannot compete on merit, we will then be in a position of having recognized centers that we are unable to support. The fear is that, under such circumstances, political pressures would be brought to bear that would force the support of the comprehensive centers at the expense of other institutions capable of better cancer research. The answer to this perceived future problem is strictly to limit the recognition of the comprehensive centers and to recognize them only at institutions that have established academic, clinical, and scientific leadership and that are clearly capable of competing on merit.

The most serious mistake we have made in the support of our biomedical research during the period that I have been actively associated with this enterprise was the discontinuance by OMB of the biomedical fellowship and training programs. It is absolutely essential to our success in the

Will we do better if the causative properties of other entrenched substances in our culture are established? We are not going to eliminate the bulk of the environmentally induced cancers by eliminating the substances that cause 5 or 10% of the disease. However, we must pursue the identification of these substances and the determination of how they work, for that is a part of the knowledge we must have in order to make progress against this disease. We must do our best to keep new carcinogens from entering our environment and to get rid of as many as possible that are with us. This will not be an easy task, but the NCI will intensify its effort to carry adequately its portion of this mission.

I would like to say a few words about the biomedical research budget, because there is no question that the combined problems of inflation and recession and the economic difficulties that confront us have created great pressure for the reduction of Federal expenditures on biomedical research. This is one of the few areas that can be reduced, and therefore it is a prime target. However, it is my opinion and has been my advice to the President and to the Congress that it would be a serious mistake to cut these programs in such a way as to lose the momentum that has been established. We must continue our Federal support.

We have had in the United States in the past 25 years a revolution in basic biomedical science. This had been largely due to the Federal commitment to basic biomedical research implemented through that remarkable institution of the Federal Government, the NIH, and its extraordinary partnership with the medical schools, universities, teaching hospitals, and research institutions of this nation. This mix of public support and private sector initiative has made our biomedical research effort the envy of the world. It should be a national priority of the highest order to maintain the momentum of this program. It may well be our nation's most valuable contribution to human civilization during this period in our history.

Unfortunately, in a free enterprise system, basic biomedical research cannot be carried forward on the scale that is required without Federal support. Profit incentives are not there to support adequate basic research in this area, and philanthropic institutions, while providing the bulk of the facilities and personnel needed for this enterprise, must have Government help to stimulate and to sustain their activities at the level that the public interest requires.

The cost of medical care is such an enormous and increasing expense for our people and, therefore, for the Government, that we cannot afford to starve the research efforts that will provide us the knowledge we need to avoid the crushing burdens of medical care. If it were not for the results of past biomedical research, we would still be saddled today with the horrendous costs and burdens of tuberculosis, polio, and all of the infectious diseases which, through the products of research, have been virtually eliminated. We must continue our research until cancer, heart disease, stroke, arthritis, multiple sclerosis, diabetes, and other diseases that agonize our people and fill our hospitals have been added, or largely added, to that list.

If any well-run business were spending $130 billion per year on medical care, it would be spending at least 5% of that amount on research to reduce those costs. While we cannot go to that level under today's circumstances, sound business judgement requires that we not cut back on the present effort.

Finally, the Federal expenditures in biomedical research are leverage dollars. Hundreds of millions of dollars of institutional facilities built by our universities and other philanthropic institutions and thousands of people whose salaries are paid by these institutions are mobilized in the cause of biomedical research by the relatively few Federal dollars that are spent in stimulating this activity. However, stop the flow of Federal dollars under today's circumstances and these essential activities will grind virtually to a standstill. This we must not do.

For the past 2 years, the cancer budget has been level in constant dollars. This has put the program this year under serious pressure. By virtually eliminating construction dollars, we will be able to get by without too serious damage to the program. However, if we do not get a reasonable increase for 1978, there will be a loss of momentum which we cannot afford.

The scientific and medical community and all of us connected with the program must continue to explain at every opportunity to the American people and to the Congress that the cancer program is a vast undertaking that will require long-term support and great patience. We are still far away from being able to put either a date or a price tag on the ultimate conquest of cancer. We are making progress in our understanding of this disease, and there is no question that the benefits of our research are increasingly available to the American people in the form of better treatment as time goes by. But it is a long road that will require patience and constancy on the part of the Congress, the Administration, and the public. In fact, at this stage of our progress, it is true in a very real sense that ". . . the goal is the course we travel together, and the end is only the beginning."

Our mission remains:
"To sail beyond the sunset, and the baths of all
the western stars . . .
"To strive, to seek, to find, and not to yield."
—Alfred Tennyson
from *Ulysses*

Attachment E

President's Cancer Panel Meetings

PRESIDENT'S CANCER PANEL MEETINGS
1981 - 1998

(Meetings Untitled)

October 27, 1981	National Institutes of Health, Bethesda, MD
December 3, 1981	International Club, Washington, DC
March 29, 1982	Harvard School of Public Health, Boston, MA
June 22, 1982	UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA
September 14, 1982	Westin Hotel, Seattle, WA
November 8, 1982	National Institutes of Health, Bethesda, MD
March 4, 1983	University of Texas System Cancer Center, Houston, TX
April 18, 1983	Northwestern University Medical School, Chicago, IL
October 12, 1983	Memorial Sloan Kettering Cancer Center, New York, NY
December 1, 1983	National Institutes of Health, Bethesda, MD

Involvement of Cancer Centers in the National Cancer Program and Efforts to Achieve National Goals

March 9, 1984	Southern Regional Institute, Birmingham, AL
April 9, 1984	University of Southern California, Los Angeles, CA
September 7, 1984	San Francisco Airport Hilton, San Francisco, CA
October 1, 1984	Fred Hutchinson Cancer Research Center, Seattle, WA
November 9, 1984	University of Hawaii at Manoa, Honolulu, HI
February 25, 1985	**Cancer Centers and the National Cancer Program** The Wistar Institute, Philadelphia, PA

(Meetings Untitled)

April 22, 1985	Johns Hopkins Hospital and Oncology Center, Baltimore, MD
June 3, 1985	Memorial Sloan-Kettering Cancer Center, New York, NY
January 30, 1986	Beverly Wilshire Hotel, Los Angeles, CA
April 11, 1986	**The Molecular Characterization of Childhood Cancers and It's Application to Innovative Approaches to Cancer Therapy** St. Jude Children's Research Hospital, Memphis, TN

Innovations in Cancer Treatment

September 30, 198	Dana-Farber Cancer Institute, Boston, MA
December 15, 1986	University of Chicago Cancer Research Center, Chicago, IL
March 16, 1987	UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA
October 23, 1987	University of Pittsburgh School of Medicine, Pittsburgh, PA
November 20, 1987	**(Meeting Untitled)** National Institutes of Health, Bethesda, MD

Innovations in Cancer Treatment

March 1, 1988	Columbia University Comprehensive Cancer Center, New York, NY
May 17, 1988	University of Wisconsin Clinical Science Center, Madison, WI

September 19, 1988	**Innovations in Cancer Treatment and Prevention** University of Arizona College of Medicine, Tucson, AZ
November 7, 1988	**(Meeting Untitled)** National Institutes of Health, Bethesda, MD
March 6, 1988	**Cancer Diagnosis, Treatment and Prevention in Minority Populations** Howard University, Washington, DC
April 26, 1989	**Cancer Control in Minority Populations** Meharry Medical College, Nashville, TN
October 13, 1989	**Biomedical Training and Technology Transfer** Stanford University, Stanford, CA (Palo Alto)
December 11, 1989	**Advances in Cancer and AIDS Therapies** National Institutes of Health, Bethesda, MD
April 5, 1990	**Cancer Causation and Prevention: From Basic Research to Community Action** Columbia University Comprehensive Cancer Center, New York, NY
October 22, 1990	**Cancer Communication and Information Transfer** Brown University, Roger Williams General Hospital, Providence, RI
November 16, 1990	**Human Gene Therapy** National Institutes of Health, Bethesda, MD
December 7, 1990	**Fundamental Research on Cancer: Issues and Progress** University of California, San Francisco, CA
July 9, 1991	**Cancer and Poverty** National Institutes of Health, Bethesda, MD
September 20, 1991	**Training and Science** Morehouse School of Medicine, Atlanta, GA
December 9, 1991	**Breast Cancer Research: Progress and New Perspectives** M.D. Anderson Cancer Center, Houston, TX
February 21, 1992	**Cancer Research and Technology Transfer in the 1990's: Old Tools, New Tools** School of Medicine University of California, San Francisco, CA
June 8, 1992	**Cancer in Minority Populations: Opportunities and Obstacles** American Health Foundation, New York, NY
October 5, 1992	**The Role of Voluntary Organizations in the National Cancer Program** National Institutes of Health, Bethesda, MD
November 13, 1992	**Prostate Cancer** National Institutes of Health, Bethesda, MD
April 1, 1993	**Breast Cancer Specialized Program of Research Excellence (SPORE) at the University of California, San Francisco and the Relationship with Area Breast Cancer Patient Organizations** University of California, San Francisco, CA

July 30, 1993	**Cancer and the Family** Preceding American Cancer Society Meeting, La Jolla, CA
September 22, 1993	**Evaluating the National Cancer Program: An Ongoing Process** National Institutes of Health, Bethesda, MD
November 15, 1993	**Cancer Statistics and Related Issues** La Guardia Hotel, New York
January 30, 1994	**The Role of Government Agencies in the National Cancer Program** National Institutes of Health, Bethesda, MD
April 7-8, 1994	**Avoidable Causes of Cancer** National Institutes of Health, Bethesda, MD
October 5, 1994	**Lung Cancer: Clinical, Societal and Governmental Challenges** Holiday Inn, McLean, VA
November 30, 1994	**Cancer and Cultures of America** San Francisco Hilton and Towers, San Francisco, CA
March 28, 1995	**The Human Genome Project** National Institutes of Health, Bethesda, MD
June 6, 1995	**AIDS Neoplasms** National Institutes of Health, Bethesda, MD
July 20, 1995	**Progress in Leukemia** Inter-Continental Hotel, Chicago, IL
September 15, 1995	**The Information Superhighway: What Does it Mean for Cancer?** University of Maryland, Baltimore, MD
	Fighting the War on Cancer in an Evolving Health Care System
July 30, 1996	*Where Are We Today -- Existing Problems For Cutting-Edge Clinical Research in Today's Environment* Fred Hutchinson Cancer Center, Seattle, WA
September 24, 1996	*Issues Of Access In Today's Health Care System* San Antonio Convention Center, San Antonio, TX
October 25, 1996	*Translational Research--The Interface With Insurance Reimbursement: A Northeast Perspective* Brown University School of Medicine, Rhode Island Hospital, Providence, RI
November 22, 1996	*Coping Strategies For Maintaining Outreach, Information Dissemination, Teaching, Recruitment And Care in Today's Health Care Environment* Duke Comprehensive Cancer Center, Durham, NC
	Concerns of Special Populations in the National Cancer Program
April 9, 1997	*The Meaning of Race in Science — Considerations for Cancer Research* Herbert Irving Cancer Center, Columbia University, New York, NY

July 31, 1997	*Cancer and the Aging Population* University of Michigan Comprehensive Cancer Center, Ann Arbor, MI
September 29, 1997	*The Real Impact in the Reduction in Cancer Mortality* National Institutes of Health, Bethesda, MD
November 21, 1997	*Responsiveness of the Health Care System to the Needs of Special Populations* H. Lee Moffitt Cancer Center, Tampa, Fl

Quality of Cancer Care/Quality of Life

April 23, 1998	*Defining Quality of Cancer Care* UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA
June 2, 1998	*Quality of Life and Survivorship* Yale University School of Medicine, New Haven, CT
October 6, 1998	*Decision Making Based on Quality of Care* Roswell Park Memorial Institute, Buffalo, NY
November 17, 1998	**Issues in Environmental Carcinogenesis** University of Arizona Comprehensive Cancer Center, Tucson, AZ

Attachment F

Final Report of the National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS

National Committee To Review Current Procedures For Approval Of New Drugs For Cancer And AIDS

President's Cancer Panel | National Cancer Program | National Cancer Institute

Executive Secretary:
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August 15, 1990

FINAL REPORT

OF THE

NATIONAL COMMITTEE

TO REVIEW CURRENT PROCEDURES

FOR APPROVAL OF

NEW DRUGS FOR CANCER AND AIDS

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EXECUTIVE SUMMARY

On the basis of its review of current procedures for approval of new drugs for cancer and AIDS, the committee makes the following findings, conclusions, and recommendations.

I. A Permanent Policy and Oversight Committee. A permanent Policy and Oversight Committee, appointed by and reporting to the Secretary of Health and Human Services, should be established to monitor the Food and Drug Administration's (FDA) needs and performance with regard to the regulation of drugs and biologics for human use.

II. The Need for More and Better Drugs for Cancer and AIDS. A national policy should be adopted to foster the developement of new drugs for AIDS and cancer in order to meet the needs for all patients who suffer from these diseases. The remarkable advances in drug development and in molecular and tumor biology will inevitably make available candidate molecules for the treatment of these ailments.

III. Expediting Approval of Important New Drugs. The FDA should continue to exercise its statutory and administrative flexibility to approve AIDS and cancer drugs for marketing at the earliest possible point in their development.

IV. The FDA Standard for Effectiveness of New Drugs. FDA should pay particular attention to the statutory definition of "substantial evidence" of effectiveness, which reflects the intent of Congress that new drugs be approved for marketing on the basis of the scientific judgment of qualified experts that sufficient clinical data exist to demonstrate therapeutic benefit.

V. Surrogate Endpoints in Clinical Trials. Progress has been made by FDA in approving drugs on the basis of surrogate endpoints in clinical trials but additional work and consultation is needed to reach further agreement in this area.

VI. Community-Based Clinical Trials. Community-based trials that permit widespread access to investigational drugs without sacrificing statistical analysis of drug effectiveness should be developed and encouraged.

VII. The Relationship Between FDA and Drug Sponsors. Drug sponsors bear the burden of submitting plans for investigational new drugs (INDs), conducting clinical trials, and preparing new drug applications (NDAs) in an efficient and competent manner in order to help expedite the approval of important new drugs. More open discussion between FDA and drug sponsors, and involvement of advisory committees where appropriate, is needed to avoid misunderstanding about FDA guidance on clinical trials. The relationship between FDA and drug sponsors must be informal, highly interactive and foster a spirit of mutual cooperation, if drug development and approval are to proceed expeditiously.

VIII. Patient Advocacy Groups. FDA is commended for its responsiveness to the needs of patient advocacy groups and should continue its efforts in this area.

IX. FDA Advisory Committees. A fundamental restructuring of the FDA advisory committee system is needed, under which all advisory committees would have their own independent staff located in the Office of the FDA Commissioner, would be responsible for their own agenda, and would more closely monitor the progress of the new drug approval system.

X. FDA, NCI, and NIAID Cooperation. The joint efforts of FDA, NCI, and NIAID in solving clinical endpoint and other drug development and approval problems are commended and should be continued.

XI. Cross Membership in NCI, NIAID, and FDA Advisory Committees. To foster close relationships between the government agencies involved with AIDS and cancer drugs, the National Cancer Institute, the National Institute of Allergy and Infectious Diseases, and FDA should each have a permanent representative sitting as a voting member of the appropriate advisory committees in the other agencies.

XII. IRB Review of Phase I Clinical Studies. To promote increased study of potential drug treatments in humans, sponsors should have the right to select, as an option, submitting an IND for a phase I clinical study for review by an institutional review board (IRB) rather than by FDA.

XIII. IRB Review of Phase I and II Noncommercial Clinical Research Studies. To reduce FDA burdens, phase I and phase II noncommercial clinical research aimed at finding new uses for marketed drugs should also be handled through review by an IRB in lieu of FDA review.

XIV. Reduction of FDA Clinical Holds. FDA should reduce both formal and informal clinical holds on INDs to the minimum needed to assure human safety.

XV. The Treatment IND. FDA is commended for codifying the treatment IND in published regulations, which should be implemented in a more flexible way to permit the use of treatment INDs earlier in the drug development process where alternative therapies are unavailable.

XVI. The Expanded Access (Parallel Track) IND. Where there is assurance that adequate clinical trials are in progress and will not be compromised, patients should have the right to obtain investigational drugs under expanded access INDs.

XVII. Outside Review of NDAs. To reduce the burden on FDA, sponsors should have the option of paying FDA for outside review of NDAs by qualified experts who have no conflict of interest.

XVIII. Supplemental NDAs for Technical Changes. Supplemental NDAs for manufacturing and other technical modifications to an approved NDA should automatically become effective 180 days after submission unless FDA specifically rejects the application for particular safety reasons.

XIX. Insurance Coverage for Investigational Drugs and Ancillary Costs. The cost of investigational drugs, and marketed drugs prescribed for unlabeled indications, as well as all ancillary medical care, should be covered by Medicare, Medicaid, and private insurance, if the use has been approved by expert government agencies, in authoritative medical compendia, or by a committee established by the Secretary of Health and Human Services to deal with this matter.

XX. FDA Resources. FDA resources must be provided at a level commensurate with the importance of the new drug approval functions for which the agency is responsible.

PREFACE

In June 1988, George Bush, then Vice President of the United States and Chairman of the Presidential Task Force on Regulatory Relief, wrote Armand Hammer, M.D., Chairman of the President's Cancer Panel, requesting that the Panel

> "undertake a systematic study of drug regulation as it affects progress in developing and making available therapies for cancer and for AIDS, and make recommendations for improvements. This study could include an examination of a number of issues regarding statutory, regulatory and administrative requirements and suggest changes that, while preserving protection for patients, would accelerate the conduct of clinical trials, improve access for cancer patients to promising new treatments, and facilitate the transfer of new therapies to medical practice."

Dr. Hammer responded to the Vice President in June 1988, agreeing to undertake the requested study.

The President's Cancer Panel determined to undertake this study through a National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS. Louis Lasagna, M.D., agreed to serve as Chairman in October 1988, eight other members of the committee were selected and agreed to serve in November 1988, and the charter for the committee was published in 53 Fed. Reg. 46942 (November 21, 1988). Beginning in January 1989 and extending through April 1990, the committee held 10 hearings at which government agencies, patient advocacy groups, representatives of the pharmaceutical industry, professional so-

cieties, and other interested organizations and individuals presented their views on all aspects of the wide variety of subjects encompassed within the committee's charge. The committee then prepared this report, which represents a distillation and critical evaluation of the testimony and materials presented.

INTRODUCTION

Life-threatening illnesses for which inadequate therapies exist deserve urgent attention by society. Cancer and AIDS qualify eminently for this designation. Patients suffering from these diseases cannot afford the luxury of waiting for drug development and regulation to move as slowly as they usually do toward ultimate regulatory approval and marketing. For cancer and AIDS patients, time is running out, and they are understandably impatient with delays in obtaining the pharmacotherapy which represents their only hope.

Because the new technology available for solving some of these therapeutic problems is at the cutting edge of modern science, flexibility is required to make the process as efficient as possible, with a willingness to change protocols, dosage, and dosage regimens promptly as data accumulate from early clinical experience. Regulatory personnel in the Food and Drug Administration (FDA) must adapt to these new needs, and take a positive attitude toward such innovation. For cancer and AIDS patients, phase I studies are no longer only dose-ranging and safety evaluations; evidence of therapeutic benefit is increasingly sought at these earliest levels of human investigation.

New technology also represents for these patients, who are often refractory to all available therapy, the best standard of care and their one hope of achieving significant benefit. Drugs for life-threatening diseases that are shown to be effective through such clinical trials reduce the number of premature deaths, restore years of productive life, enhance the quality of life, shorten hospital confinements, and speed recovery.

These are significant societal benefits. These facts explain why medical care costs associated with such research deserve to be covered by Medicare, Medicaid, and private insurers, since in this case research and treatment are inextricably linked.

FINDINGS, CONCLUSIONS, AND RECOMMENDATIONS

I. A Permanent Policy and Oversight Committee. The Food and Drug Administration (FDA) needs a permanent standing Policy and Oversight Committee, as a continuation and expansion of the National Committee to Review Current Procedures for Approval of New Drugs for Cancer and AIDS, to monitor the agency's needs and performance with regard to regulation of drugs and biologics for humans. Its members should be knowledgeable national leaders selected by the Secretary of Health and Human Services from candidates nominated by the Institute of Medicine. The Policy and Oversight Committee should meet regularly and report to the Secretary of Health and Human Services.

II. The Need for More and Better Drugs for Cancer and AIDS. Because of differences in the response of individual patients to AIDS and cancer drugs, a wide variety of therapeutic agents is needed. It is the experience of the clinician members of the committee that, rather than a homogeneous population of AIDS or cancer patients, there are numerous subpopulations, each of which has its own characteristics, limitations, and needs with respect to drug therapy. It is therefore essential that we adopt a national policy of fostering a multiplicity of drugs for AIDS and Cancer, in an attempt to meet the needs of all of the subgroups that comprise the people who suffer from these diseases.

III. Expediting Approval of Important New Drugs. FDA has the legal authority to approve, and in fact has approved, new drugs on the basis of one scientifically valid study, and on the basis of phase I and phase II clinical studies without the need for a phase III clinical study. The committee agrees with FDA that, particularly in the area of drugs for AIDS and cancer, this statutory and administrative flexibility should increasingly be used to approve drugs for marketing at the earliest possible point in their development, and commends the agency for its leadership in early approval of important new AIDS drugs. By relying more heavily on the opinion of the qualified experts who serve on the agency advisory committees, FDA should approve new drugs for cancer as well as AIDS earlier than has been true in the past.

IV. The FDA Standard for Effectiveness of New Drugs. Because of its special relevance to issues faced today in developing new drugs for cancer and AIDs, the FDA needs to pay particular attention to the congressional intent in requiring substantial evidence of effectiveness prior to approval of a new drug application (NDA), as described in the Senate Report on the Drug Amendments of 1962:

> "The term 'substantial evidence' is used to require that therapeutic claims for new drugs be supported by reliable pharmacological and clinical studies. When a drug has been adequately tested by qualified experts and has been found to have the effect claimed for it, this claim should be permitted even though there may be preponderant evidence to the contrary based upon equally reliable studies. There may also be a situation in which a new drug has been studied and its effectiveness established only to the satisfaction of a few investigators qualified to use it. There may be many physicians who would deny the effectiveness simply on the basis of a disbelief growing out of their past experience with

> other drugs or with the diseases involved. Again, the studies may show that the drug will help a substantial percentage of the patients in a given disease condition but will not be effective in other cases. What the committee intends is to permit the claim for this new drug to be made to the medical profession with a proper explanation of the basis on which it rests. In such a delicate area of medicine, the committee wants to make sure that safe new drugs become available for use by the medical profession so long as they are supported as to effectiveness by a responsible body of opinion and scientific fact."

By applying these principles, patients suffering from AIDS and cancer will have available to them new drugs for the treatment of their disease at the earliest stage at which there is responsible scientific evidence to justify marketing.

The committee recognizes that, by making new drugs available for marketing at this early stage, when there is substantial evidence but not yet definitive evidence of effectiveness, there is an attendant greater risk of serious adverse reactions that have not yet been discovered. Cancer and AIDS patients have made it clear to the committee, however, that in light of the seriousness of the diseases involved, they are willing to accept this greater risk. Earlier approval of new drugs will mean that the patient will bear greater responsibility, along with the physician, for understanding and accepting the risks involved.

V. Surrogate Endpoints in Clinical Trials. We applaud the willingness of FDA to be flexible with regard to appropriate treatment endpoints in clinical trials and believe that the contract between FDA and the Infectious Diseases Society of America to review endpoint dis-

agreements in the field of antibiotics may provide a prototype for similar future arrangements in other disease areas. The committee sees need, however, for three additional developments:

1) Research by industry, academia, and the National Institutes of Health (NIH) -- specifically the National Cancer Institute (NCI) and the National Institute of Allergy and Infectious Diseases (NIAID) -- is needed on the correlative data on surrogate and ultimate endpoints required to justify the use of such surrogates.

2) FDA, NCI, and NIAID, perhaps with the advice of appropriate advisory committees, should continue their work to reach agreement on general principles on surrogate endpoints and to respond to specific needs regarding surrogate endpoints as they arise with regard to a new drug for AIDS or for cancer or a given cancer type.

3) More attention needs to be given to the use of subjective and objective quality of life assessments that can serve per se as a basis for regulatory approval of new drugs.

Phase III cancer studies often address comparative activity of a marketed drug and an investigational drug. This makes possible randomized clinical trials in which an active control is used and therefore no placebo group is required. Since effectiveness but not superiority is required for NDA approval, equality between the two drugs demonstrates sufficient effectiveness for marketing approval. Effectiveness, not comparative efficacy, should be the basis for approval or disapproval of a drug. Since phase II studies determine efficacy and phase III studies comparative efficacy, such phase III studies should not be required during the pre-NDA period.

Since survival differences for many slow-growing tumors such as ovary, breast, colon, and other common tumors may take years to demonstrate, survival is in general an impractical and unethical endpoint for cancer drugs. Of the anticancer agents currently on the market, very few have been shown independently to affect survival. Most of these agents are capable of producing tumor regression in certain diseases. When such agents are used in combination for selected tumors, a major improvement in survival and cure has occurred. It is only after initial NDA approval of the drug as a single entity that its full potential is realized, because physicians are then free to use it in combination with other drugs in accordance with their best clinical judgment. While still under investigation, such combination uses occur only infrequently and with little opportunity for full clinical exploration. For all of these reasons, large phase III studies have been, and should continue to be, conducted in the postapproval setting.

Drugs that produce, in phase II studies, a significant rate of tumor regression (in excess of 20-30 percent) should be approved. This approach is supported by FDA statistics which indicate that over 90 percent of agents found to be active on the basis of phase II studies were confirmed to be active in follow-up phase III studies. Thus phase III studies, which represent a major effort and delay, have not contributed significantly to NDA approval prospects. Historically, it is in the period after regulatory approval that the ultimate utility of anticancer drugs (either alone or in combination) is delineated.

The development of AIDS drugs could be facilitated by approving drugs that are shown to have an unequivocal beneficial effect on an accepted surrogate marker (e.g., CD_4 cells) as well as improvement in the quality of life

(e.g., improved functioning, weight gain, decreased incidence of opportunistic infections) in controlled clinical trials. Proof of prolongation of life need not be a requisite for FDA approval.

VI. Community-Based Clinical Trials. We urge that groups that advocate or conduct early clinical investigation with drug candidates for AIDS and cancer do so through mechanisms that will generate useful data for clinical, scientific, and regulatory purposes. AIDS and cancer patients have the most to gain from sound scientific research, and the most to lose from inadequate and poorly-conducted trials that fail to provide meaningful data on drug effectiveness. We endorse the development of community-based trials that permit widespread access to investigational drugs without sacrificing statistical analysis of drug effectiveness and thus that can lead to early regulatory approval.

VII. The Relationship Between FDA and Drug Sponsors. Sponsors of new drugs have a responsibility to expedite regulatory approval by planning, executing, and analyzing clinical trials and by preparing NDAs in an efficient and competent manner. FDA properly points out that poorly planned and executed clinical trials, and inadequately prepared NDAs, can be a major factor in delaying the approval of important new drugs.

FDA is criticized if it fails to provide helpful guidance to drug sponsors, resulting in clinical trials that are inadequate to justify approval of the drug, or if it gives too much guidance, and thus is seen as "micromanaging" clinical trials that are properly the responsibility of the sponsor and the investigators. The committee recognizes that there is no perfect solution to this dilemma. FDA reviewers must be sensitive to the fact that even routine suggestions can be interpreted as rigid commands, and spon-

sors and investigators must recognize that FDA advice is intended to be helpful but that they bear full responsibility for the clinical trial that is to be undertaken. More open discussion, and involvement of advisory committees where appropriate, should lead to greater mutual respect and trust.

If the drug development and approval process is to proceed expeditiously, it is essential that there be free and open communication between FDA and drug sponsors at all times. The relationship between FDA reviewers and drugs sponsors must be informal, highly interactive, and foster a spirit of mutual cooperation. An atmosphere of arms-length formality will slow down the process, raise artificial barriers to drug development and approval, and seriously harm the public health. The development and approval of AIDS and cancer drugs depends upon helpful cooperation, not adversarial isolation. Communications should most frequently be by telephone, fax, and computer, to provide current information, quick responses to important questions, and a feeling of genuine partnership. The artificial barriers that have been erected through years of criticism on the part of both the regulators and the regulated have created a serious threat to rapid development and approval of new drugs, and can no longer be tolerated.

VIII. Patient Advocacy Groups. We commend FDA for its recent efforts to be responsive to the needs of patient advocacy groups. The growing importance of such groups advocating more rapid therapeutic trials and access to proposed remedies for AIDS and cancer represents both an opportunity and a threat. The opportunity resides in the ability of such groups to force government, academia, industry, and FDA to increase the pace of drug development and approval. The threat resides in the possibility that too easy access to investigational drugs will lead to delays in recruitment of subjects for

clinical trials and thus delay ultimate FDA approval and marketing. FDA is properly charged with the responsibility for reconciling these different challenges by enhancing the opportunity for expedited drug approval and reducing the threat of impediments to clinical investigation, and we recommend that FDA continue its efforts in this area.

IX. FDA Advisory Committees. FDA's technical advisory committee system for human prescription drugs is not consistently performing the functions needed by the public. We recommend a fundamental restructuring of this system. The committees should have their own independent staff and should be appointed by, and report directly to, the Office of the FDA Commissioner. Recommendations for membership should be actively sought from professional societies, the Institute of Medicine, the pharmaceutical industry, and the general public, as well as from FDA, and not solely by announcements in the Federal Register, but also by active solicitation of nominations.

The tasks of these committees could include discussion of issues brought up by FDA, industry, the public, or committee members themselves. The committees should meet more frequently than they do at present, at fixed intervals, and manage their own agenda. They should be involved at an early stage in the history of the evaluation of a drug in humans, at least to the extent of being available for advice. The committees should also monitor the progress of investigational new drugs (INDs) (including any formal or informal "clinical holds" by FDA) and new drug applications (NDAs), provide oversight for the priority ranking of drugs (and the need for change in ranking over time), serve as arbiters in disputes between sponsors and FDA, routinely vote on recommendations regarding approval for cancer and AIDS drugs, and conduct oversight on the implementation by FDA of committee recommendations. Uniform

procedures should be in place for all such committees, including the adequate briefing of new members with regard to relevant statutes, regulations, and the process of drug development.

X. FDA, NCI, and NIAID Cooperation. We commend FDA, NCI, and NIAID for their efforts to solve clinical endpoint and other drug development and approval problems by holding regularly scheduled meetings of appropriate staff, and strongly urge a continuation of this practice.

XI. Cross Membership in NCI, NIAID, and FDA Advisory Committee. As an element in fostering close relationships and mutual understanding between the government agencies involved in the development and approval of new drugs for AIDS and cancer, the committee recommends that NCI, NIAID, and FDA each have a permanent representative sitting as a voting member of the appropriate advisory committee in the other agencies. Thus, an FDA employee would sit on the NCI and NIAID committees to inform them about the regulatory process, and NCI and NIAID employees would sit on appropriate FDA committees to inform them about critical drug development and clinical needs. A spirit of mutual cooperation will lead to greater understanding and improvements in drug development and regulatory approval.

XII. IRB Review of Phase I Clinical Studies. The public would benefit if more potential drug treatments reached human study. The cost, complexity, and paperwork burdens of phase I clinical studies need to be reduced. Sponsors should have the right, as a voluntary alternative to the current system of submitting an IND to FDA, to obtain the approval of an institutional review board (IRB) specifically constituted to provide the technical expertise

(in such disciplines as pharmacology and toxicology) required to review the IND for safety consideration. Criteria for the appropriate expertise for members of such an IRB need to be delineated.

XIII. IRB Review of Phase I and II Noncommercial Clinical Research Studies. The many INDs for phase I or II studies filed with the agency by noncommercial academic investigators studying a possible new use for marketed drugs now consume a significant amount of FDA time and could also be handled, as a voluntary alternative, by IRB review without involving FDA. FDA has exempted some, but not all, academic research on marketed drugs, and should expand this exemption.

XIV. Reduction of FDA Clinical Holds. The committee is concerned about the large number of INDs currently experiencing either formal or informal "clinical holds" for reasons that have little to do with safety concerns. Formal clinical holds range from 10 to 15 percent of all INDs, and informal holds run higher. This practice inhibits clinical research and hinders drug development, and should be reduced to the minimum needed to assure human safety.

XV. The Treatment IND. The committee commends FDA for codifying the treatment IND in published regulations. The committee agrees with FDA that the regulations codifying this concept represent appropriate scientific and regulatory standards. Patient advocacy groups have complained, however, that the regulations are being interpreted too conservatively by FDA. They argue that, under the wording and intent of the regulations, a treatment IND should be permitted earlier in the drug development process. Consistent with their overall philosophy, they state that desperately ill patients are prepared to accept the greater risks inherent in treatment INDs that are approved at such

an early stage, and argue that a treatment IND should not be reserved for use as a "bridge" to NDA approval after the drug has already been shown to be safe and effective. With one exception, treatment INDs have been approved by FDA relatively late in the drug development process.

The committee agrees that, with the exception of dideoxyinosine (ddI), FDA has thus far implemented the new treatment IND process in a conservative manner. The committee recommends that FDA be more flexible, and permit the use of treatment INDs earlier in the process where alternative therapies are unavailable. Although this will clearly present greater risks to patients, because some of the drugs may eventually be found either to be ineffective or to present an unacceptable benefit/risk ratio, patients with life-threatening diseases who have no alternative therapy are entitled to make this choice.

XVI. The Expanded Access (Parallel Track) IND. Because of continuing frustration with the conservative implementation of the treatment IND concept, patient advocacy groups have pushed for additional mechanisms to permit early access to investigational drugs for life-threatening diseases where no acceptable alternative exists. Expanded access (the "parallel track") permits the use of an investigational drug as early as the end of phase I for all patients who cannot be accommodated in a clinical trial or a treatment IND, and for whom no alternative treatment exists. Thus, there is even less evidence of safety and effectiveness for a drug made available through an expanded access IND than there is for a drug that is approved for use in a treatment IND.

The committee recognizes the serious potential for abuse of this system. Expanded access should be permitted only where there is assurance that adequate clinical trials are in progress and will not be compromised. Once this assurance exists, however, the committee supports the rights of patients to

obtain investigational drugs under these circumstances. Faced with the consequences of a lack of therapy for AIDS and cancer, an expanded mechanism for early access to investigational drugs is morally, ethically, and scientifically justified.

XVII. Outside Review of NDAs. Congress has placed many new responsibilities on FDA in the last decade, while the number of employees in the agency has decreased. Because in the short term no quick solution is apparent to these inadequate resources, we believe that ways to decrease the burdens on FDA should be identified. One possibility is to expand on a concept long in place within the agency, i.e., paying outside experts to review sections of an NDA. With properly selected outside experts, this has worked well, and has allowed review to proceed more expeditiously. It the principle works for sections of an NDA, it should apply to an entire NDA. Sponsors should have, as a voluntary alternative to the present system, the option of paying the FDA for outside review by qualified experts who have no conflict of interest, perhaps most easily supplied through an external contractor, with the expectation that review would be both competent and timely. Critique from such outside review would be forwarded to FDA for additional scrutiny and judgment, but not for total re-review, which would defeat the purpose of this mechanism.

XVIII. Supplemental NDAs for Technical Changes. Most supplemental NDAs relate to changes in manufacturing and other technical modifications to an approved NDA. These consume a great deal of FDA resources to no great social purpose. The handling of changes in manufacturing and other technical supplemental NDAs should be expedited by imposing a mandatory 180 day review period for final approval unless the application is rejected for particular

safety reasons. If FDA does not respond within 180 days with a detailed and specific reason why the change would result in a safety hazard, the supplemental NDA should be considered approved.

XIX. Insurance Coverage for Investigational Drugs and Ancillary Costs. Insurance coverage of investigational drugs, and of marketed drugs prescribed for unlabeled indications, should rely primarily on their approval by expert government agencies for therapeutic use (such as the NCI approval of Group C cancer drugs and the FDA approval of drugs under treatment INDs) or their status in authoritative medical compendia (such as the three that were intended for use under the Medicare Catastrophic Coverage Act of 1988). Usage approved by such expert authority is more valid as a basis for reimbursement than FDA approval of an NDA, since NDA approval may not as yet have been sought by the specific manufacturer, and in fact for some drugs or uses might never be sought. Coverage should be identical under Medicare, Medicaid, and private insurance, whether they are paid for directly or under a prospective payment system, and should not vary from region to region or carrier to carrier.

Coverage should be automatic once the usage is approved in one of the compendia. Individual carriers should have no discretion with respect to such matters. This policy should apply equally to inpatient services, outpatient drugs administered by a physician, and self-administered prescription drugs if that benefit becomes effective. For indications or drugs that are approved by experts but have not yet found their way into authoritative compendia, an independent advisory committee may be needed to authorize reimbursement of unapproved drugs or unapproved uses.

The touchstone of drug coverage should be the medical judgment of the attending physician. We are here consonant with the decision in Weaver v. Reagan, 886 F.2d 194 (8th Cir. 1989), that Missouri Medicaid could not lawfully deny coverage of AZT to AIDS patients because, even though the drug was still investigational and not yet approved by FDA, nonetheless it was determined to be medically necessary by the attending physician:

> "The Medicaid statute and regulatory scheme create a presumption in favor of the medical judgment of the attending physician in determining the medical necessity of treatment. In denying coverage of AZT to the plaintiff class, the defendants have done nothing to overcome that presumption except to rely on the FDA approval process in a manner expressly rejected by the FDA. In the face of widespread recognition by the medical community and the scientific and medical literature that AZT is the only available treatment for most persons with AIDS, we find that Missouri Medicaid's approach to its coverage of the drug AZT is unreasonable and inconsistent with the objectives of the Medicaid Act."

Accordingly, the court ordered Missouri Medicaid to pay for the use of AZT by any AIDS patients "whose physicians have certified that AZT is medically necessary treatment."

Coverage for the hospital, physician, and other medical care costs for patients involved in cancer and AIDS clinical trials should take cognizance of the fact that peer-reviewed, scientifically sound trials provide state-of-the art treatment for patients desperately needing such treatment but for whom currently available drugs are ineffective. For such patients, scientifically

meritorious investigational drug therapy is the best available treatment and together with ancillary medical care should be covered by all health insurance agencies.

XX FDA Resources. FDA resources, building facilities, and data processing capability are grossly inadequate for the important responsibilities for approval of new drugs delegated to FDA, and deserve prompt attention by Congress. The incredibly cramped quarters at Rockville and their deficiencies for storing, handling and analyzing data have been well described in a recent GAO report on the agency's request for more resources. Even with an appropriately increased budget, it is difficult to see where new employees would be placed. For specific analysis of FDA resource needs we defer to the Advisory Committee on the Food and Drug Administration, recently appointed by Secretary Sullivan, which will be examining this issue in detail.

Attachment G

Report of the Chairman to the President,

October 1981 - October 1982

October 1981-October 1982

President's Cancer Panel

Report of the Chairman

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health

NIH Publication No. 83-2609
April 1983

President's Cancer Panel

National Cancer Program National Cancer Institute

February 21, 1983

The Honorable George Keyworth
Director
Office of Science and Technology Policy
The White House
Washington, D.C.

Dear Jay:

As Chairman of the President's Cancer Panel, it is my responsibility to report to the President on the state of the National Cancer Program. Accordingly, I have prepared the attached report covering the period since I became Chairman. I think it is a record of achievement and progress.

Aside from my Panel work, I have been very involved in other activities in the cancer field. In January of 1982 I sponsored the first Armand Hammer Conference on Hybridoma and Monoclonal Antibodies and Cancer at The Salk Institute in La Jolla, California, which was attended by leading scientists from over 20 different countries. Dr. DeVita, Director of the National Cancer Institute, attended this conference and later told me it was on the cutting edge of research in the field. It was so well received that I sponsored another conference this year, again at The Salk Institute, and I am pleased to report that it was even more successful.

This field of hybridomas and monoclonal antibodies is a very exciting and promising field of cancer research, and I believe it will lead to a real breakthrough soon in our knowledge of cancer, its causes, treatment, and eventual cure. One of the leading scientists in the field, Dr. Hilary Koprowski, of The Wistar Institute, in Philadelphia was at the conference and he told me he believes it the most exciting development in many years. He feels it is one of the most effective tools at our disposal in the fight against cancer, especially as we become more able to tailor the monoclonal antibodies to the specific antigens on cancer cells. He is conducting experiments at The Wistar Institute in Philadelphia and told me he has achieved very encouraging results.

I also had the great pleasure in December of 1982 of awarding the first Hammer Cancer Prize to two distinguished scientists, Dr. Ronald Levy of Stanford Medical School, and Dr. G. T. Stevenson of Tenovus Research Laboratories in Southhampton, England. Dr. Levy and Dr. Stevenson shared the $100,000 award for their separate but complimentary work using hybridomas and monoclonal antibodies in cancer research and treatment. As you are aware, it was Dr. Levy who last year successfully treated a patient suffering from a form of lymphoma and achieved remission after every other form of treatment had been tried unsuccessfully. The patient is still in remission, and we had the pleasure of having him attend the luncheon at which the award was given. These awards are to be made annually for the next nine years.

Of course, I have not yet had the opportunity to award the one million dollars I have pledged to the scientist or scientists who discover a "cure" for cancer similar to the vaccine discovered by Jonas Salk in treating polio. But I continue to hope I will be able to do so one day. With estimates of 440,000 Americans expected to die from cancer this year, we cannot afford to lag in our search for the knowledge that will one day enable us to conquer this most dreaded disease.

I had hoped to present this report in person to you, for your submission to the President. However, my travel schedule makes that impossible. I hope it will be of interest and look forward to any comments you may have.

With best wishes,

Sincerely,

Armand Hammer

Attachment

The past year has been one of challenge and excitement for the National Cancer Program: excitement generated by quantum leaps in the understanding of basic cancer cell growth, and by the new research tools now available to scientists; challenge posed to the National Cancer Institute (NCI) to pursue these new avenues of research in a time of level budget and increasing research costs.

The NCI has responsed innovatively to these research vistas and to many other aspects of its mandate. Over the year is has acted in a number of areas:

Community Clinical Oncology Program (CCOP)

As acceptable therapies for cancer care are extended into the community, it will be important to develop newer and better treatment protocols as quickly as possible. The Community Clinical Oncology Program was designed to support clinical research in community settings, with community oncologists providing leadership. Each CCOP will affiliate with at least one cancer center or cooperative group and place a minimum number of patients each year into clinical trials. Some 200 CCOPs will be set up under cooperative agreements throughout the country.

Nutrition

Recent research has indicated that diet may have a great deal to do with the risk of developing cancer. Many carcinogens occur naturally in foods, and foods may also contain anticarcinogens—agents that may reverse or halt the cancer process. Other food components may influence cancer risks indirectly. Over the past year, the NCI has increased its efforts in the field of nutrition research to delineate these risks more precisely. It is analyzing a report prepared for it by the National Academy of Sciences and is encouraging new applications for research grants in nutrition. Epidemiologic studies that help pinpoint relationships between diet and cancer are continuing. The NCI is also considering the advice of the National Cancer Advisory Board (NCAB) that a special task force be set up within NCI to set priorities for a national research agenda on nutrition. Finally, the NCI has launched a number of clinical trials with chemopreventive agents that appear, in preliminary studies, to protect against cancer.

Cancer in Minorities

Wide disparities in both the incidence and survival rates for blacks and other minority groups, compared with whites, have been a source of great concern to the NCI for some time. In 1981, the NCI established a cross-institute working group to strengthen programs that will add to our data base and focus greater attention on early detection, better treatment, and preventive measures among minority populations. Over the past year, major steps were taken in these areas. Among them were studies designed to pinpoint environmental and host factors responsible for differences in cancer risk, ongoing activities to improve the training of minority group health professionals, the development of publications and public education programs for Hispanics and blacks, and the support of an international conference at the Pan American Health Organization in August 1982.

Protocol Data Query (PDQ)

As part of its program to extend cancer care into the community more effectively, and to disseminate improvements in cancer therapies more quickly, the NCI last year instituted its computerized PDQ system, or Protocol Data Query. This is a data base for information on cancer treatment research, including clinical trials in progress. Developed in cooperation with the International Cancer Research Data Bank of NCI, the new PDQ system will ultimately provide instant information to physicians and patients via computer terminals anywhere in the country. The first phase of PDQ went on line on October 1, 1982, with its data available through the MEDLARS network maintained by the National Library of Medicine, accessible from some 1,800 locations throughout the country. In its later phases, the PDQ system will contain more extensive information about treatment procedures worldwide.

Hybridoma Research and the Frederick Cancer Research Facility

Just recently, new research methods have added immeasurably to the understanding of cancer and of basic cell biology. Hybridomas and monoclonal antibodies are among the most exciting of these new research tools, and their clinical application has already yielded promise.

Growing hybridomas in the laboratory—by fusing a specific antibody-producing cell with an "immortal" cancer cell—lets investigators clone endless lines of pure, or monoclonal, antibodies. The promise of monoclonal antibodies is that they may be labeled with radioactive tags for use in diagnosis and detection or to monitor progress. There is also the hope, when precise antibodies are developed against specific cancers, that the antibodies can be "armed" with anticancer drugs to destroy cancer cells within the body. Some significant clinical successes have already been achieved with these monoclonal antibodies in the treatment of some cancers.

Other new tools—recombinant DNA, or genetic engineering, among them—have increased the ability to probe basic cellular processes. To add impetus to these very important studies and to decrease overall NCI laboratory costs, the NCI last fall redesigned the operations and management of its Frederick (Maryland) Cancer Research Facility. Research there is under way in the fields of molecular genetics, genetic engineering, hybridomas and monoclonal antibodies, oncogenic viruses, physical and chemical carcinogenesis, immunology, cancer cell biology, and biological response modifiers.

In summary, the President's Cancer Panel has examined a number of NCI's responsibilities and functions during the year. The Panel has also looked at the needs of the U.S. scientific community and the public. As chairman of the Panel, it is my view that the NCI is meeting its mandate fully. Further, it is being very ably managed by its director, Dr. DeVita, and he and his staff are performing in an excellent fashion.

Major Management Improvements

The responsibility of the National Cancer Program is to "develop and expand, intensify, and coordinate research programs" and to use "existing research facilities and personnel...for accelerated exploration of opportunities in areas of special promise." In keeping with this mandate, the NCI has, over the past several years, instituted a number of major management improvements. During the past year these improved procedures were in place, and working. They included: centralization of the budget formulation and corporate decision-making processes in the Office of the NCI Director; major corrections in the research contracting processes, including extensive uniform review by nongovernment experts, and concept review to assure that high priority items are funded and that less effective programs are phased out at appropriate times; analysis of each of the NCI's 1,150 contracts with redistribution of funds from terminated projects to the research grants pool; and, as mentioned above, cost reductions and improved management effected by the reorganization of the Frederick Cancer Research Facility.

With the full support of the NCI Director and his staff, the Panel undertook what it believes to be one of the most significant actions in its history.

To meet with research scientists in their home communities, to facilitate open discussion of the processes by which NCI operates, and to air the concerns of both the advocates and the adversaries of NCI, the Panel last year went "on the road."

Regular meetings of the panel were held in major research centers in Los Angeles, Boston, and Seattle. We believe this has been so rewarding and beneficial to all concerned that we shall continue to hold such meetings "on the road," and continue to invite concerned scientists to attend them. We are planning to hold meetings next year in Houston and in Chicago.

Following are some of the major concerns discussed at these meetings. some representative responses, and one of the major actions taken:

Bernard Fisher, M.D., a Panel member in 1982 until he was succeeded by William P. Longmire, Jr., M.D., posed a series of questions at the Boston and Los Angeles meetings, based on the conduct of NCI peer review and grant award procedures.

He asked:

- Does present research establish a fixed population of scientists, or does it create "transient investigators?"
- Do the mechanics of writing grant applications and progress reports interfere with research?
- Are there aspects of the peer review system that could be improved upon?

Two of the major concerns and recommendations voiced in answer to these questions by the scientists invited to the Boston meeting were:

- Bookkeeping tasks have become extraordinarily burdensome, and grant applications tend to be funded, rather than scientists.
- The National Institutes of Health should fund more, rather than fewer, applicants so that more research ideas will be supported.

Many of the same concerns were voiced by the scientists who attended the Panel's Los Angeles meeting. An additional proposal was made there that a small proportion of funds be allocated to approved research institutions to fund innovative pilot projects by young investigators with high promise, in a system of "decentralized" peer review. Limits on the total amount of grant money awarded to a single investigator and limits on the number of grants awarded to a single laboratory were also suggested.

At the Panel's Seattle meeting in September 1982, held during the 13th International Cancer Congress, the agenda topic was "New Scientific Directions for the National Cancer Program," with an international group of eight invited scientists as discussants.

Major emphases on research into smoking control and in diet and nutrition were urged by one scientist. Others stressed the need for continuing research in genetics and molecular biology, immunology, and virology, and particularly in cell differentiation and regulation. Others sounded the need for continuing multidisciplinary research, particularly in diagnostics.

Dr. Vincent T. DeVita, Jr., NCI Director, underscored the dilemma of the National Cancer Program today: we are faced, more now than at any other time, with a great diversity of good ideas at a time when we have a flat budget. He noted, though, that the NCI is now supporting many more investigators on fewer dollars than a decade ago.

Dr. DeVita also announced that as a result of the dialogue with the scientific community in Boston and Los Angeles earlier in the year, the NCI will begin to develop a new Outstanding Investigator Award. This will be designed to support the investigator, based on his track record, and will "probably" be a 5-year renewable award to be given without regard for the scientist's age.

It will be designed to encourage investigators to take on long-term projects often considered risky in terms of immediate results, and will be recompeted and reviewed at appropriate intervals. Dr. Harold Amos, a member of the Panel, will head the subcommittee to design this award with NCI staff so it can be presented to the National Cancer Advisory Board by October 1983.

Attachment H

Report of the Chairman to the President,

October 1982 - September 1984

October 1982-September 1984

President's Cancer Panel

Report of the Chairman

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institutes of Health

NIH Publication
No. 85-2609
March 1985

President's Cancer Panel

National Cancer Program National Cancer Institute

November 9, 1984

The Honorable George A. Keyworth
Director, Office of Science and
Technology Policy
The White House
Washington, D.C.

Dear Jay:

As Chairman of the President's Cancer Panel, it is my responsibility to report to the President at intervals on the status of the National Cancer Institute. I am greatly helped in the work of the Panel by my two distinguished colleagues, Drs. William P. Longmire and Dr. John A. Montgomery, both of whom have devoted much time and energy to Panel activities. Dr. Elliott H. Stonehill of the National Cancer Institute serves as Executive Secretary of the Panel and has been invaluable to us in this capacity. It is a privilege to work with these dedicated professionals.

I have prepared the attached report which I would appreciate your bringing to the attention of the President and other appropriate officials in the White House.

It is an honor for me to serve the President in this capacity, and I believe we can report with confidence that progress under his Administration is continuing in our fight against this dread disease.

Since I have been Chairman, I have instituted a policy of taking the Panel to visit Cancer Centers throughout the country, a departure from previous Panel custom. This has been a most successful venture, welcomed by the cancer community, and resulting in some practical recommendations for improvements in our National Cancer Program. I am pleased to report that our recommendations have been adopted by the National Institutes of Health. We intend to continue the practice of regional Panel meetings in the next two years.

Some of the most significant advances in recent years have been the identification of cancer causing genes called oncogenes, the identification of a virus responsible for AIDS, the development of the Physician Data Query (PDQ) system, and, an area of great personal interest to me, the expanded use of monoclonal antibodies in the diagnosis and treatment of many kinds of cancer with very encouraging results.

I continue to hold the belief that use of monoclonal antibodies in diagnosis and treatment of various kinds of cancers will lead to a real breakthrough in our search for a cure for cancer.

The work at the National Cancer Institute under the management of Dr. Vincent T. DeVita, Jr. is impressive.

Since the last time I reported to you on the Cancer Panel, the second Hammer Cancer Prize has been awarded. As you may recall, two years ago I announced an annual prize of $100,000 to the individual or individuals who were deemed to have contributed the most to advancing medicine towards a cure for cancer, along with a one million dollar award to the scientist or scientists who finds a cure for cancer. Unfortunately, I have not been able to make the million dollar award yet, but the 1983 award was given to four distinguished scientists for their work in the exciting new field of oncogenes, which are the genes thought to cause cancer after they are activated by some as yet unknown process. The 1982 award went to scientists who had done important work with monoclonal antibodies. Thus, the Hammer Cancer Prize has in the last two years recognized work in what many feel are the two most promising fields of cancer research today, monoclonal antibodies and oncogenes, both of which hold great promise for a breakthrough in our understanding of and eventual cure for cancer. This year's awardee has not yet been selected, but I am confident the caliber of the winner or winners will match that of the previous years.

I continue to support exciting and promising work being done at the Salk Institute in the field of monoclonal antibodies, led by the Nobel Prize Winner Dr. Renato Dulbecco. I have sponsored conferences bringing together leading scientists in

the field from over twenty countries throughout the world. Included among the attendees was one of this year's Nobel Prize winners for medicine, Dr. Georges Kohler, who, along with Dr. Cesar Milstein, discovered the hybridoma process by which monoclonal antibodies are able to be produced with purity and in such great quantities.

The report has been prepared with the hope that it will be useful to the Administration in illustrating the progress that is being made in the fight against cancer, a subject which I know is of great interest to the President and Mrs. Reagan.

With best personal regards,

Sincerely,

Armand Hammer

Chairman

The President's Cancer Panel is heartened by the progress against cancer made possible by the National Cancer Institute (NCI) and it's implementation of the provisions of the National Cancer Program during the past three years.

As stated in the National Cancer Act of 1971, the mission of the National Cancer Program is to bring about a reduction in the incidence, mortality and morbidity of cancer through support of basic and clinical research. The mission also includes responsibility for cancer control and the communication of new information to researchers, physicians, and health professionals.

There has been significant improvement in the treatment and care of cancer patients, particularly at the nation's great cancer centers, and this excellence in care is being extended to the community level. Encouraging improvement in survival for significant numbers of patients has been obtained. The discovery of oncogenes and the identification of a human cancer-causing virus (HTLV) are among the more significant findings. There has been considerable progress in cell biology and molecular genetics that brings us closer to understanding the fundamental processes that cause cancer.

Departing from previous procedures, the President's Cancer Panel held its meetings at several of the nation's cancer centers, to examine regional conditions and issues regarding the role of the centers in their geographic regions and in reaching the goal of reducing cancer mortality and eventually ridding mankind of this most terrible scourge.

This report will address issues in each of these important areas.

SCIENTIFIC PROGRESS

The NCI has launched new intensive education and information programs directed at the general population to increase understanding of the significance of nutrition and lifestyle in the causation and prevention of cancer. Smoking and dietary changes, as well as environmental exposures, are among the important factors targeted in programs supported throughout the country.

The support of basic research by the NCI has produced impressive new gains in understanding genetic mechanisms of some cancers. Prominent results have been obtained by researchers in NCI laboratories in collaboration with virologists, molecular biologists, epidemiologists, and physicians throughout the world.

At the laboratories of the NCI, Dr. Robert Gallo isolated and characterized a human T-cell leukemia/lymphoma virus, HTLV-I, the first proven human cancer virus. HTLV viruses are now being studied intensively to determine the mechanism by which they initiate cancer, and how to protect humans from their effects.

More than twenty oncogenes have been identified both in cancer cells and in normal cells. It is now recognized that, while oncogenes exist in all humans, they are expressed only in those cells that have become cancerous. In my Chairman's Report for 1982, I described the progress and promise for monoclonal antibodies, which have since become universally recognized as vital to fundamental biological research. It is expected that further research will reveal the mechanism whereby the expression of the malfunctioning oncogenes can be reversed with the use of "armed" monoclonal antibodies targeted to the cancer-causing proteins produced by the oncogenes.

ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

The National Cancer Institute moved quickly in 1983 to provide new funding for basic research on acquired immune deficiency syndrome (AIDS). A scientific task force was established to mobilize and integrate intramural and extramural research programs. The appearance of a form of cancer, Kaposi's sarcoma, as a secondary development in many AIDS patients, made the disease significant to cancer research. In May 1983, Dr. Gallo reported the discovery of HTLV in a number of AIDS patients. Researchers throughout the world, working with NCI scientists, discovered HTLV in AIDS patients in Europe, Africa, Asia and North America. In March 1984, Dr. Gallo demonstrated conclusively that AIDS is caused by a variant HTLV, specifically HTLV-III. Current research is directed toward the development of a vaccine and a rapid, reliable test to detect the virus in blood.

DIAGNOSTIC IMAGING

Within the past two years, the NCI has awarded 95 grants to further develop new diagnostic imaging techniques soon to replace current procedures. The new methods can more effectively discriminate internal structures and functions, are less invasive, and provide more information than methods currently in use. These techniques include nuclear magnetic resonance, digital subtraction angiography, positron emission tomography, and advanced developments in the use of ultrasound. These procedures will improve cancer detection, diagnosis, and assessment of therapy.

RESEARCH SUPPORT

The President's Cancer Panel has the responsiblity to identify any impediments that may delay achievement of the goals of the National Cancer Program. Toward this end, under my chairmanship, the Panel held six regional hearings between March 1982 and October 1983, to learn the views of scientists throughout the country regarding the NIH

peer review system. Public meetings were held in Boston, Los Angeles, Seattle, Houston, Chicago, and New York City.

At each of those meetings, I was accompanied by the Panel members, initially Drs. Harold Amos and Bernard Fisher, and subsequently Drs. William P. Longmire and John A. Montgomery. Dr. DeVita and other NCI and NIH representatives also participated in the meetings.

In each city, the speakers indicated that fine-tuning of the peer review system was required, and suggestions were made to modify aspects of the process. The Panel received many suggestions. Most important and cogent were the proposals to institute a responsive appeal system, to improve the composition of study sections and site visit groups, and to provide opportunities and support for paradigmatic changes in science.

High-risk or unorthodox research must be encouraged, since it often leads to significant results. This concept was endorsed by the President's Cancer Panel and, at our behest, NCI has established a new award mechanism, the Outstanding Investigator Grant (OIG). The OIG provides seven years of support for the pursuit of innovative projects by successful applicants.

At the conclusion of the six regional meetings, the President's Cancer Panel submitted a report of its findings and recommendations to the Director of the NIH. I am pleased to report that the Panel's proposals have all been implemented this year by the NIH Division of Research Grants.

NATIONAL CANCER INSTITUTE MANAGEMENT

The momentum of science and medical research depends significantly on appropriate facilities and sophisticated equipment. Currently there is inadequate support for construction and modernization of the physical facilities for research at scientific and medical centers in the nation. The annual NCI allocation for extramural construction purposes has been limited to one million dollars for each of the past three years, which is woefully inadequate.

The critical need for major renovations at many non-federal research facilities has long been a concern of mine. Therefore, when a report was made to the Panel recommending that a study be done of the construction needs of the cancer community, I personally was happy to contribute $75,000 toward the funding of such a study, the remaining $75,000 being contributed by the American Cancer Society. This $150,000 study is being done by a medically qualified independent consulting firm and will be available early next year, when it will be presented to the National Cancer Advisory Board, and made available to the Administration for study and, hopefully, implementation. The study is at no cost to the government, but I believe it will have a valuable impact on the cancer program.

CONCLUSIONS

As Chairman of the President's Cancer Panel, it is my view that the NCI is meeting its mandate to further the National Cancer Program, and continues to make outstanding progress.

The Panel has embarked on a new two-year program. During 1984 we have examined the role, the functions and the effectiveness of the various types of cancer centers such as the basic science center, the consortium center and the comprehensive cancer center. Each seems to be fulfilling a specific need.

The basic science centers provide the opportunity for cross-fertilization and coordination of the all-important basic cancer research. The consortium centers emphasize the delivery of current cancer treatment information, investigation of methods to improve cancer care and extend cancer control programs.

The comprehensive cancer centers are supported to permit their personnel and facilities to engage in all of these fields, basic science, clinical information and treatment, and cancer control. Evidence has been presented to suggest that the guidelines for the establishment of a center might be modified to meet the needs of certain geographic regions (Appalachia) or population groups (blacks, Hispanics). Such centers could enhance research efforts and clinical cancer care in certain regions and among certain groups that show evidence of the need for substantial improvement.

We have embarked on an examination of the country by geographic region, ascertaining in each area the unique character of the population, the disease characteristics, and the effectiveness of local initiatives. Participating with us in this review are state and municipal officials, cancer center and university staff, and voluntary and private sector health care personnel. These hearings help to identify both the strengths and weaknesses of the National Cancer Program, and thus give us the opportunity to seek out needed adjustments.

November 9, 1984

Attachment I

Report of the Chairman to the President,

January 1 to December 31, 1985

January 1 to December 31, 1985

President's Cancer Panel

Report of the Chairman

U.S. Department of Health and Human Services

Public Health Service

National Institutes of Health

National Cancer Institute

NIH Publication
No. 86-2609
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President's Cancer Panel

National Cancer Program National Cancer Institute

February 13, 1986

The President
The White House
Washington, D.C.

Dear Mr. President:

As Chairman of your Cancer Panel, it is both my duty and my privilege to report to you on the status of the National Cancer Institute (NCI). Enclosed is my latest report. My two distinguished colleagues on the Panel, Dr. William P. Longmire and Dr. John A. Montgomery, both have been of enormous assistance in this effort. Dr. Elliott Stonehill of the National Cancer Institute has served as Executive Secretary of the Panel, and his efforts have been most helpful to the Panel.

I would like to point out a few highlights of the report. The first and foremost is the work, of which you are already aware, of Dr. Steven A. Rosenberg of the NCI using lymphokine-activated killer cells (LAK) and interleukin-2 (IL-2) in a most promising new treatment of cancer patients. Dr. Rosenberg's work continues to show favorable results, and I believe that this may be a major breakthrough in our efforts to stop the ravages of cancer. With the addition of money to fund a substantial number of clinical trials around the country using Steve's protocol, we could move the cancer effort a quantum step forward, saving many lives which otherwise would be lost. I do hope you and your advisors will give most serious consideration to this possibility. In 1985 I contributed over $500,000 to push this work forward at other cancer centers, but much more money is needed. You can be sure I will continue my personal efforts to make this treatment widely available throughout the country.

One of those efforts was a most successful conference which I sponsored in September 1985, at the Salk Institute in La Jolla, bringing together the leading experts in the field of so-called "biological" approaches to cancer treatment. Discussions were held concerning not only the LAK and IL-2 treatment, but tumor necrosis factor (TNF), monoclonal antibodies, and interferon, all of which use natural products of the body to fight disease and which can be applied to cancer treatment with very promising results. The experts at the conference were very encouraged with the reports they heard and exchanged information which should help move research farther at an expanded rate. The NCI has established a special research program to intensively explore applications of these substances called biological response modifiers.

In the important area of prevention and control of cancer, the NCI has programs on reduction in smoking, on dietary modification, on early detection of cancer, and on the accelerated and widespread application of the latest cancer treatment regimens. Although the effect of these programs may not be evident immediately, they should substantially reduce cancer deaths in the long term. It is very important that these programs continue to be supported by the NCI.

My colleagues and I hope the information in this report will prove useful and informative to the Administration and will be studied carefully.

As always, Mr. President, be assured of my deep gratitude for your confidence in me in designating me as Chairman of your Cancer Panel, and my continued dedication to effectively carrying out the responsibilities of that position.

With best personal regards,

Sincerely,

Armand Hammer

Chairman

1985 CHAIRMAN'S REPORT TO THE PRESIDENT

During 1985, the President's Cancer Panel witnessed very exciting and remarkable progress in cancer research in this country. These advances were made at the National Cancer Institute (NCI) in Bethesda and in affiliated laboratories and hospitals nationwide, in research programs supported by the NCI.

Continuing the successful approach initiated in 1981, when I was first appointed Chairman of the President's Cancer Panel, we visited five important regional cancer centers in the Nation this year. These were major academic and clinical facilities in Seattle, Honolulu, Philadelphia, Baltimore and New York. My Panel comembers, Dr. William P. Longmire and Dr. John A. Montgomery, and I observed the progress, problems and accomplishments at these centers, focusing attention on the most important and innovative developments in cancer research and steps taken by the NCI to achieve its goal of a 50 percent reduction in U.S. cancer deaths by the year 2000. The Director of the National Cancer Institute, Dr. Vincent T. DeVita, Jr., and appropriate members of his staff, accompanied us during these visits.

However, I feel that a 50 percent reduction by the year 2000, which would mean approximately 200,000 would still die each year for the next 14 years, while feasible, is not sufficient. In view of the progress made with enhancing the body's immune system to fight cancer at the National Cancer Institute and other cancer centers such as Memorial Sloan-Kettering, M.D. Anderson Hospital in Houston, Dana Farber's Boston Center at Harvard, the Jonsson Center at UCLA and others, I believe this goal is too low and we should be aiming at the substantial eradication of cancer by the year 2000.

Dr. Lloyd Old of Memorial Sloan-Kettering, one of the most respected cancer specialists in the U.S., recently told me that more progress had been made in the cancer field in the last several months than in the previous 25 years he has been in research. So the means to achieve our goals may be available, if we can only take advantage of them in an effective way.

This report will address the status of the National Cancer Program and its multiple facets as we have viewed them this past year.

Cancer Treatment

Substantial progess has been made in the treatment of cancers since the passage of the National Cancer Act and the establishment of the National Cancer Program in 1971. These advances are evidenced by a reduced mortality rate for breast cancer and greatly improved survival for testicular and ovarian cancers, childhood leukemias, and aggressive lymphomas.

However, we are still faced with the difficult task of improving the mortality from the most commonly occurring cancers, the so-called "solid tumors," i.e., lung, colon, breast, stomach, and pancreas.

The most promising and dramatic advance in cancer treatment this year was reported by Dr. Steven A. Rosenberg at the NCI. For the past decade, his research in immunology has explored mechanisms used by normal lymphocytes to attack and destroy cancer cells. He has demonstrated that a patient's own white blood cells can be stimulated by interleukin-2 (IL-2) to attack and destroy the patient's tumor cells.

These IL-2 armed white cells, called LAK or lymphokine-activated "killer cells," destroy tumors for months after administration in some cases, until the patient is clear of detectable cancer. It is important to recognize that this treatment has demonstrated effectiveness in 17 of 41 patients with the common "difficult to treat" solid tumors, such as lung, kidney, and colorectal cancers, and melanomas. Dr. Rosenberg's early results, using the adoptive immunotherapy procedure with LAK cells and IL-2, have been published in the prestigious, critically reviewed *New England Journal of Medicine* and have attracted worldwide attention. Steps are under way to confirm and extend these results in other centers.

The patients whose cancers have responded to Dr. Rosenberg's treatments have benefitted from a rapid series of scientific developments, which represent an excellent example of the speed with which exciting discoveries and developments are presently occurring in our knowledge of cancer and cancer treatment.

Dr. Robert Gallo and his coworkers isolated and characterized IL-2, originally named the "T-cell growth factor," in 1976. Dr. Tadatsuga Taniguchi of Osaka, Japan, reported in the March 1983 issue of the *New England Journal of Medicine* the discovery of the gene in T-lymphocytes responsible for the production of interleukin-2, and by means of genetic engineering was able to produce the substance in large amounts sufficient to be used by Dr. Rosenberg, and by others, in treatment of cancer patients.

It now seems that there are a number of substances that occur naturally in the body to maintain normal growth and development which may be utilized to stimulate

the body's natural defenses against cancer. The NCI has established a special research program to explore intensively the therapeutic applications of these naturally occurring substances called "Biological Response Modifiers." In addition to IL-2, this group includes thymosin, interferon, bombesin, and the tumor necrosis factor (TNF). Dr. Old is the chief proponent of TNF, and he started clinical trials at Sloan-Kettering. He thinks there may be some connection between TNF and IL-2. The use of recombinant DNA technology, referred to above, has made pure IL-2 and interferon available in sufficient quantities to conduct cancer treatment studies in a nationwide program.

Clinical trials of monoclonal antibodies have progressed this year at a heightened rate, following promising results in patients with chronic lymphocytic leukemia (CLL), T-cell lymphoma, colorectal and pancreatic cancer, and disseminated malignant melanoma. Current research involves the use of toxic substances linked to monoclonal antibodies which may then be used to kill specifically the targeted tumor cells. This type of therapy, combined with surgery, has been used successfully in the treatment of cancer of the liver, a cancer that has been largely unresponsive to previous treatments. A new sensitive diagnostic procedure uses monoclonals linked to radionuclides as detectors of extremely small tumors.

The Panel has recognized that collaboration among surgeons, radiotherapists, chemotherapists, and immunotherapists continues to improve the outlook for cancer patients. Combination therapy permits the use of less radical surgery when operations are supplemented by chemotherapy and/or radiation for patients with breast, rectal, prostate, and extremity cancers. Lumpectomy with radiation for early-stage breast cancer now appears to be an equivalent treatment to modified radical mastectomy, and salvages the breast.

In 15 years, breast cancer treatment has undergone dramatic revisions. Mutilating operations and poor survival are giving way to less extensive operative procedures and alternative treatment regimens, which preserve patients' bodies and prolong life of better quality. A former member of the President's Cancer Panel, Dr. Bernard Fisher at the University of Pittsburgh, won the prestigious Lasker Prize this year for his research work, done with NCI support, on the treatment of breast cancer.

Early treatment with chemotherapy has also demonstrated some encouraging results in rectal, head, and neck cancers, and childhood sarcomas. Surgery is now being used in a new way to remove lung and liver metastases and to successfully cure some patients with advanced colon cancer and sarcomas. An adjuvant study in colon cancer with very positive results is presently being repeated. Significant progress has also been made in therapy which overcomes drug resistance in certain metastatic cancers. Moreover, reseachers have recently discovered important biochemical mechanisms involved in the metastatic process, and for the first time, a model system is available which enables a scientific approach to combatting deadly metastases.

Prevention and Control of Cancer

Programs have been initiated over the past decade for cancer prevention, detection, and treatment techniques and have been disseminated to the widest possible population. In 1985, the NCI established several new programs to foster information transfer from the laboratory bench to the patient's bedside. A network has been developed which links basic science laboratories, cancer centers, cooperative clinical research groups, community oncologists, and practicing physicians. There is now wide access to PDQ, the new computerized data base which provides information on the latest cancer treatment directly to physicians nationwide. These networks have expanded through cooperation with state and local governments and private industry.

In 1985, the NCI expanded its research in chemoprevention and nutrition to identify agents capable of preventing or reversing the progression of cancer. This research will further identify dietary components that either induce or inhibit cancer. Folic acid, for example, is being studied in women with cervical dysplasia to try to prevent cervical cancer, and a low-fat diet is being studied as a preventive measure for breast cancer in women at increased risk. The NCI is supporting 25 clinical trials with chemopreventive agents or dietary factors believed to interfere with cancer progression in people at high risk for certain cancers. In addition, major prevention awareness programs are under way to reduce the incidence of several major cancers. These focus on the reduction of fat in the diet, and on smoking cessation.

In 1985, the incidence of lung cancer in white males decreased significantly for the first time, which correlates with the decline in smoking over the past 20 years. A reduction of 50 percent in smoking by the year 1990 alone, can lead to the saving of 75,000 lives annually by the year 2000. The public mood seems to be in the direction of smoking less. Lung

cancer in American females, however, continues to increase, and is clearly related to increased smoking.

The NCI believes that diet and nutrition may be related to a significant number of cancer deaths and that screening and early detection could substantially reduce mortality for women with breast cancer. The NCI believes that the maximum national use of state-of-the-art cancer treatment would substantially reduce the mortality rate from cancer at some sites. Gains in treatment methodology, already reflected as improvements in survival rates for many cancers, can reasonably be expected to continue over the next 15 years.

To fulfill the NCI's goal of reducing cancer mortality by 50 percent by the year 2000, the Institute believes the following objectives must be met in four areas: a 50 percent reduction in smoking by 1990; dietary modification; early detection of cancer through effective screening; and accelerated and widespread application of the latest cancer treatment regimens. The Director of the NCI has established a national schedule, with annual benchmarks and ongoing monitoring systems, which I believe can assure the desired objectives.

The overall relative survival rate reported in 1985 for all cancer patients in this country has been estimated at approximately 50 percent. The public attitude toward cancer is one of fear and pessimism, in spite of steady progress in its management. Cancer is really over 100 different diseases. Many of them are curable by early available treatment, while others are not.

Cancers with the highest five-year relative survival rates are: thyroid, testis, endometrium, melanoma, female breast, bladder, Hodgkin's disease, and prostate. Unfortunately, survival continues to be poor for patients with pancreatic, lung, esophageal, and stomach cancers.

Human T-Cell Leukemia/ Lymphoma Virus (HTLV)

New associations of HTLV retroviruses with human diseases continue to be discovered in the laboratories of Dr. Robert Gallo and his associates. It is believed that the number of cancers caused by viruses has been underestimated in the past.

Over 15,000 cases of Acquired Immune Deficiency Syndrome (AIDS) have been reported in this country. The spread of this virus has been so rapid in high-risk groups that almost 90 percent of factor VIII-recipient hemophiliacs have been exposed to the virus.

A condition known either as pre-AIDS, lymphadenopathy syndrome, or AIDS-related complex is associated with early HTLV-III infections. During 1985, the NCI and the National Institute of Allergy and Infectious Diseases (NIAID) collaborated in developing treatments for AIDS patients, and several new drugs which show promise in early trials at the NCI and NIAID are about to be tested on a national scale.

Discovery of HTLV-III as the causative agent of AIDS created a demand for large amounts of the virus to enable the mass production of materials for screening tests and for potential vaccines. The Frederick Cancer Research Facility of the NCI produced the virus in sufficient quantities to allow the development of an economical and widely available assay which now protects the Nation's blood supplies. Licenses to produce and market the screening tests are held by several private industrial concerns.

Oncogenes

During the Panel's visits to the cancer centers and at meetings of the National Cancer Advisory Board, we have been presented with considerable evidence that cancer cell growth is probably controlled by oncogenes. Oncogenes are altered versions of normal genes involved in early embryonic development. In the cancer process, these dormant genes become active again due to the action of viruses, chemicals or radiation, or by gene rearrangement. Intensive studies are under way to characterize the 24 oncogenes and their protein products identified to date. The presence of oncogenes can be detected and the amount of their gene products measured by recombinant DNA and monoclonal antibody technologies.

Research at the NCI has identified oncogene products which are directly related to factors that are known to activate the unrestricted growth of cells. The production of abnormal proteins by these oncogenes may also enable cancer cells to metastasize throughout the body. Most cancer deaths result from metastases, not primary tumors.

One oncogene discovered by NCI scientists was found this year also to be a specific marker for cystic fibrosis (CF). This diagnostic oncogene will enable doctors to identify the 10 million Americans who carry the hidden recessive gene for CF, and to prevent the potential appearance of new cases. Cystic fibrosis is the most common fatal genetic disease in the Western world. There are at least 30,000 patients in the United States.

Conclusions

As Chairman of the President's Cancer Panel, I have examined the National Cancer Program in-depth in Bethesda and across the Nation. My colleagues and I have examined the basic research efforts, the clinical applications, and the progress being made toward prevention and elimination of those diseases collectively called cancer. One result of our regional Panel meetings has been an increased awareness of the diversity of the problems in various sectors of our Nation, and at the same time an appreciation of the great resources which are available to people through

the cancer centers and through the efforts of the National Cancer Institute.

It has been satisfying to see the magnificent outpouring of new scientific discoveries this past year, a harvest of true riches derived from the seeds planted in basic science supported by the Federal Government through the National Cancer Program. It is my view that the NCI, under its capable Director, Dr. Vincent T. DeVita, Jr., is working toward the NCI mandate to reduce the mortality and morbidity rates from cancer and is making great strides toward complete control of these diseases.

We as a Nation are spending over $400 billion annually on medical care, a great fraction of which is ultimately borne by the Federal Government. The bulk of this expenditure is for conditions that can be conquered or eliminated by research. I do not feel it is in the best interests of the Nation to spend only 1 percent of the cost of medical care on the only course open to us for the elimination or reduction of that cost. I believe the Nation would profit greatly if the Office of Management and Budget and the Congressional Budget Office increased expenditures for cancer research by two- or threefold. I believe we could see an almost immediate benefit from expanding the clinical trials of Steve Rosenberg's LAK and IL-2 protocol across the country. Such an expansion would cost approximately $20 million, but its benefits could be incalculable, both in saving lives and in lessening the economic costs of cancer to society as a whole. Dr. DeVita has authorized six centers to start these clinical trials, and the NCI is appropriating $2.5 million for this work. Although this is a good beginning, more funds will be needed in the future.

Dr. George Keyworth, before his retirement, was impressed by his meeting with Dr. Steven Rosenberg, which I arranged a year ago. Dr. Keyworth said in May 1985, "When Dr. Rosenberg has achieved successful results in the treatment of 20 cancer patients, I will speak to President Reagan and urge him to add $20 million to the NCI budget for the establishment of clinical trials at centers throughout the country using Dr. Steven Rosenberg's protocol." Dr. Rosenberg now has successful results with 17 patients. Mr. President, let's not wait any longer.

At present, our Nation's physical facilities for cancer research and medical education are in dire need of updating and replacement, as was found in a thorough study I helped to fund this past year and submitted to Congress and the White House. New laboratory and clinical research opportunities presently exist which can and should be made possible through increased support.

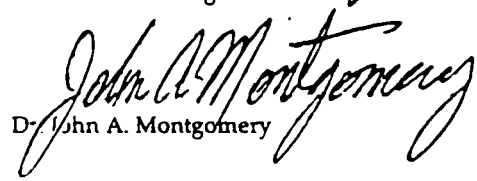
I believe under the present circumstances that this country is deriving the maximum benefit from its cancer research budget, but we should not delay the effort to maximize the best and most modern research efforts in the best and most modern physical facilities that this country can obtain.

This report has been prepared with the cooperation and approval of my colleagues, Dr. William Longmire and Dr. John Montgomery.

Dr. Armand Hammer, Chairman
The President's Cancer Panel

Concurred:

Dr. William P. Longmire



Dr. John A. Montgomery

President's Cancer Panel

National Cancer Program National Cancer Institute

February 13, 1986

The Honorable George Bush
President of the Senate
Washington, D.C. 20510

Dear Mr. President:

As required by Section 415 (b) of the Health Research Extension Act of 1985, I am submitting herewith, as Chairman of the President's Cancer Panel, a copy of my Annual Report to the President of the United States. Section 415 (b) also asks that a copy be sent to the Speaker of the House; this is being done.

Because of your keen interest in our cancer research activities, I believe you will find this report of great interest as, according to one of our top researchers, Dr. Lloyd Old of Sloan-Kettering Cancer Center, more advances were made in cancer research in 1985 than in the past 25 years.

I shall also send copies of this report to certain key members of the Senate who might have a special interest in it.

With best personal regards,

Armand Hammer

AH:fa

Enclosure

President's Cancer Panel

National Cancer Program National Cancer Institute

Executive Secretary:
Dr. Elliott H. Stonehill
National Cancer Institute
Bethesda, MD 20205
Phone: 301-496-1148

February 13, 1986

The Honorable Thomas P. O'Neill
Speaker of the House of Representatives
Washington, D.C. 20515

Dear Mr. Speaker:

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Armand Hammer

AH:fa

Enclosure

President's Cancer Panel

National Cancer Program National Cancer Institute

February 19, 1986

The Honorable Otis R. Bowen
Secretary
Department of Health and Human Services
Washington, D.C. 20201

Dear Mr. Secretary:

I am pleased to enclose herewith a copy of the report I have submitted to the President covering the status of the National Cancer Program. As Chairman of the President's Cancer Panel, it is my responsibility under law to periodically submit such reports to the President, as well as to the Congress. Copies have therefore also gone to the President of the Senate and the Speaker of the House, as well as selected members of Congress.

I hope you will find the report of interest, particularly the reference to the work being done at the National Cancer Institute by Dr. Steven Rosenberg. As Secretary of the Department of Health and Human Services, you have every reason to be proud of the fine work being done at the National Cancer Institute under the leadership of its distinguished Director, Dr. Vincent T. DeVita.

With warmest good wishes,

Sincerely,

Armand Hammer

AH:ec

Enclosure