ANNUAL REPORT
OF
PROGRAM ACTIVITIES
NATIONAL CANCER INSTITUTE
Fiscal Year 1982

Office of the Director
Division of Extramural Activities
Division of Resources, Centers & Community Activities

NATIONAL CANCER INSTITUTE

Annual Report

October 1, 1981 through September 30, 1982

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OFFICE OF THE ASSISTANT DIRECTOR

OFFICE OF THE DIRECTOR

PROGRAM ACTIVITIES REPORT

October 1, 1981 through September 30, 1982

The Office of the Assistant Director (AD) administers the functions of the President's Cancer Panel, which convened four meetings during the year. The Panel has served as a forum for both the scientific community and public, and has affected both the initiation of new program priorities and implementation of existing priorities. The AD serves as the Executive Secretary to the Panel.

In addition to meetings held in the Washington/Bethesda area, during 1982 the President's Cancer Panel conducted public meetings on the east coast at the Harvard University School of Public Health, and on the west coast at the University of California in Los Angeles. At these meetings the Panel examined alternatives and options proposed by scientists regarding possible modifications of the peer review and grants award mechanisms at the NCI and the NIH.

The AD is also Director of the Office of Medical Applications of Cancer Research (OMACR) and maintains liaison with the NIH Office of Medical Applications of Research (OMAR). During 1982 OMACR processed numerous evaluations of patent applications from grantees and contractors, and also supported Consensus Development programs and technology transfer activities at the NIH. In November, 1981, NCI personnel participated in the planning and promulgation of a 3-day, Consensus Development Conference on CT Scanning of the Brain held at the NIH.

Other activities of the Office of the AD this year have included establishment and co-chairmanship of the NCI Radiation Coordinating Group, and participation and liaison with the Interagency Radiation Research Committee, chaired by the Assistant Secretary for Health. The planning and implementation of a new telephone accessible information system has also been undertaken, with the aim to provide protocol data relative to the cancer therapy clinical trials currently in progress. The Office of the AD has coordinated and supervised the integration of resources into a computer system referred to as PDQ (Protocol Data Query System) intended to be of benefit to both physicians and patients as well as to researchers in cancer treatment.

Program Activities Report
Fiscal Year 1981-82
Editorial Office of the National Cancer Institute

The Board of Editors reviewed 662 manuscripts submitted for publication in JNCI during the 12-month period July 1, 1981, to June 30, 1982. These manuscripts were from the following sources:

National Cancer Institute: 58 (34 accepted, 5 rejected, 19 pending)
Other research institutions: 604 (177 accepted, 185 rejected, 242 pending or withdrawn)

Although the total number of manuscripts submitted shows a decrease from the previous 12-month period (-13%), this decline in submissions appears to be reversing. The number of manuscripts received during the 6-month period from 1 January through 30 June 1982 shows a 5.4% increase over the number received during the same period in 1981. Despite the decline in total submissions, the number of manuscripts submitted by NCI researchers showed a 5% increase over the number submitted last year.

Of the 604 manuscripts received from sources outside the National Cancer Institute, 213 were from authors in other countries. As shown in table 1, authors from 29 foreign countries submitted manuscripts for publication in JNCI.

Volume 67 (July-December 1981) contained 1,434 pages and volume 68 (January-June 1982), 1,044 pages, for a yearly total of 2,478 pages.

The printing and binding of JNCI were performed under contract through the Government Printing Office. Volume 67 was printed by the McFarland Company of Harrisburg, Pennsylvania. In October 1981, a 2-year contract was awarded to Waverly Press, Inc. of Easton, Maryland, and they began publication with the February 1982 issue. Both printers produce excellent work and have been able to meet the high standards of quality required by JNCI.

Two special issues of JNCI were published during this period. The November 1981 issue was dedicated to Dr. Mearl F. Stanton, an outstanding research scientist at the National Cancer Institute and a former editor in chief of the Journal. Dr. Stanton's last research paper and a guest editorial examining his work on fiber carcinogenesis were featured in this issue. The July 1982 issue featured the proceedings of the Seventh Food and Drug Administration Science Symposium. This symposium was on photochemical toxicity and examined the toxic, allergic, and carcinogenic aspects of light-induced chemical reactions. Emphasis was placed on predicting the effects of photosensitive responses in humans.

In an effort to improve the effectiveness of JNCI in meeting the needs of its readers, a survey is being made to evaluate the Journal and determine what areas, if any, should be changed and what new areas should be added. The initial survey will comprise the NCI laboratory and section chiefs who currently receive the Journal.

Four NCI Monographs were published and four were in production during the 1 July 1981-30 June 1982 period. Pending receipt of manuscripts, no dates have been set for three other monographs. The status of each is as follows:

No. 56: Sarcomas of Soft Tissue and Bone in Childhood; September 1981

No. 57: Surveillance, Epidemiology, and End Results Program: Incidence and Mortality Data: 1973-77; October 1981

No. 58: Carcinogenic and Mutagenic N-Substituted Aryl Compounds; March 1982

No. 59: Cancer Mortality in the United States: 1950-1977; May 1982

No. 60: Research Frontiers in Aging and Cancer: International Symposium for the 1980's; July/August 1982

No. 61: Third International Symposium: Cancer Therapy by Hyperthermia, Drugs, and Radiation; August 1982

No. 62: Third Symposium on Epidemiology and Cancer Registries in the Pacific Basin; December 1982 (expected date)

No. 63: Biological Response Modifiers; December 1982 (expected date)

Forty-Five Years of Cancer Incidence in Connecticut: 1935-1979

The Use of Small Fish Species in Carcinogenicity Testing

Photobiologic, Toxicologic, and Pharmacologic Aspects of Psoralens

In March, a term contract for publishing NCI Monographs was awarded to the McFarland Company of Harrisburg, Pennsylvania. This printer is known for high quality performance on schedule. Monograph No. 62 will be the first under the term contract. This company also was awarded the contracts for No. 59 and 61 under the individual bid system by the Government Printing Office.

The position of Editorial Assistant under the Monograph Editor has been unfilled for the past year because of lack of qualified candidates for this temporary part-time position.

Table 1. Countries of Origin of Manuscripts Submitted to JNCI 1981-82

Argentina	1	Italy	13
Australia	9	Japan	68
Austria	1	Netherlands	7
Belgium	5	Norway	1
Bulgaria	1	Poland	4
Canada	20	Romania	1
China	1	Scotland	2
Denmark	2	Singapore	1
England	9	South Africa	4
France	18	Sweden	9
Democratic German Republic	1	Switzerland	1
Federal Republic of Germany	7	Taiwan	2
Greece	1	United States	449
India	4	U.S.S.R.	3
Israel	15	Yugoslavia	2

EQUAL EMPLOYMENT OPPORTUNITY OFFICE

OFFICE OF THE DIRECTOR

NATIONAL CANCER INSTITUTE

Summary Report

October 1, 1981 - September 30, 1982

The Personnel Management Branch and the Equal Employment Opportunity Office met with the executive staff and the principal administrative officers to thoroughly explain the Federal Equal Opportunity Recruitment Program (FEORP). The program was officially implemented during the month of January 1982. An EEO handbook was established and issued to all NCI supervisors and managers.

OFFICE OF ADMINISTRATIVE MANAGEMENT
OFFICE OF THE DIRECTOR
NATIONAL CANCER INSTITUTE

Program Activities Report
October 1, 1981 - September 30, 1982

The Office of Administrative Management (OAM) coordinates and manages all administrative activities of the Institute and is headed by the Associate Director for Administrative Management who also serves as Executive Officer. The Office is composed of seven branches; Management Analysis Branch, Administrative Services Branch, Personnel Management Branch, Research Contracts Branch, Grants Administration Branch, Grants Financial and Data Analysis Branch, and Financial Management Branch.

Some notable activities of the OAM during Fiscal Year 1982 include:

- Reorganization - A reorganization brought the Grants Administration Branch and the Grants Financial and Data Analysis Branch into the OAM from the Division of Extramural Activities, thereby consolidating all NCI business management functions.

- Position Review - Coordinated an Institute-wide position review.

- Special Management Initiatives - A series of management initiatives was undertaken covering travel policy, processing of interagency agreements, support vs. research contracting, renovation and construction, funding plans, problem grants and contracts, overtime audit procedures, cash awards, Frederick Cancer Research Facility operating policies. These initiatives were developed by committees of NCI staff from OAM branches and divisional administrative staff.

- Publication - Initiated a publication titled Administrative Notebook to improve intra-Institute communication on administrative and policy matters.

Individual branches of the office achieved the additional accomplishments described below.

Administrative Services Branch (ASB)

The ASB serves as the Administrative Office for all of the components of the Office of the Director, including the Office of Administrative Management, Office of Cancer Communications, Office of International Affairs, and the Office of Program Planning and Analysis. It is also responsible for office services, property management, mail and files, international travel, domestic travel policy, and the annual travel plan for the entire Institute and for space management, especially in leased buildings, and serves as the NCI coordinating point for cross cutting administrative issues.

- Property Management - Increased the number of custodial areas from 59 to 74 in order to monitor property/equipment and completed physical inventories of NCI property. Each area will be inventoried accurately on an annual basis.

- Travel - Information for managing NCI foreign travel and OD domestic travel have been computerized, resulting in a reduction of person hours needed to produce the quarterly foreign travel report.

- EPMS - The Branch coordinated for NCI the transition from the old employee performance appraisal system to the new EPMS and arranging the procurement of training for affected employees and the establishment of a monitoring system for tracking implementation.

- Space - An Institute-wide space analysis was conducted and recommendations made to the NCI Executive Committee to improve space utilization and facilitate program consolidation.

Financial Management Branch (FMB)

The FMB serves as principal advisor to the Institute in the financial management aspects of the planning, formulation, execution and evaluation of its programs. It collaborates with the Office of Program Planning and Analysis in the development and coordination of the National Cancer Plan with the budget plans and monitors the execution of the Institute's financial management program.

- Personal Services Forecast - Redesigned information system to include special pay categories for Commissioned Officers and Visiting Fellows.

- FTE Reports - Modified FTE reporting system to include summation of data by Division and a "what if" capability.

- Budget Formulation Model - Modified Budget Formulation and Presentation Support processing system to include data available from NIH prepared Allotment Ledger Master tape.

- Gift Fund - established a special conditional gift fund in response to the new NIH manual issuance 1160-1.

- Construction - assisted in the development of the NCI manual issuance on use of funds appropriated for construction of facilities.

- Transfers - effected several transfers among the Divisions requiring a change in the budget projection model. Effected necessary documentation for the National Toxicology Program and National Institute of General Medical Sciences transfers.

- Financial Reports - worked with DFM to develop a summary report of all Service and Supply Fund reports for greater efficiency and accuracy.

Research Contracts Branch

RCB participates in developing policies on Institute research contract programs; develops guidelines, procedures and controls to promote compliance with policy and sound contracting practices; provides contract management services for all Institute research contracts; and designs, maintains and operates automated Institute contract management information systems.

- Management Improvements - During FY 82 RCB devoted considerable effort to improving its contracting activities. As a result of the 1980 Office of Inspector General's (OIG) Review of NCI Contracting Activities, the Office of Procurement Assistance and Logistics (OPAL), DHHS developed, in collaboration with the Public Health Service (PHS), the National Institutes of Health (NIH), and the NCI, a corrective action plan which was endorsed by the OIG in October 1981.

  The purpose of the plan was to specify and track implementation of a series of agreed upon improvements in contracting practices. It incorporated quarterly monitoring by NIH, PHS and OPAL to inform the Secretary and Inspector General of actions taken. The final OPAL report which was received in April 1982 notes that excellent progress has been made by NCI in improving its contracting operations. Continuation of quarterly monitoring was not found to be warranted, but OPAL plans a final review for late in FY 1983.

- Peer Review - The Branch worked closely with staff of the Division of Extramural Activities and program staff of other Divisions to improve contract proposal review procedures initiated in 1981. Concept review by Boards of Scientific Counselors, strong technical evaluation by independent review groups and more complete involvement by the NCAB were facilitated.

- FCRF Recompetition - The contract for the operation of the Frederick Cancer Research Facility (FCRF) has been the largest managed by HHS since it inception in 1972. In an attempt to maximize competition for continuation of contractor activity, NCI segregated the existing single contract into five major components: research, operations and technical support, animal holding, computer services, and library services. Two of these were set aside for small businesses. As a result of this initiative, NCI received multiple proposals in all areas, and, as of this writing, anticipates award of several contracts in lieu of the single contract utilized for the past 10 years.

- Systems Automation - Implemented two automated systems to assist contract specialists and branch managers in tracking and completing work requirements. These systems are expected to lead to substantially improved pre- and post-award contract administration.

Grants Financial and Data Analysis Branch (GFDAB)

GFDAB is responsible for maintaining grants financial data, the analyses necessary to provide funding guideline recommendations, preparation of budgets and advising on grants financial policy decisions, and for making grants financial data available to requestors. It also maintains an automated system of essential data on NCI contracts and cooperative agreements.

- Contract Monitoring System (CMS) - GFDAB assumed responsibility for the maintenance of the CMS from the Research Contracts Branch. Apart from ongoing monitoring of the CMS contract, GFDAB has initiated measures to ensure that the CMS will be a more accurate and useful reporting system for financial and administrative purposes by reconciling financial data with that of DFM.

  Two subsystems were developed in conjunction with the RCB to serve the needs of both program and contracting officials. The CAS is a post-award reporting system used to account for deliverables while the Milestone Tracking System is a pre-award system in which the status of each contract is identified from initiation of Project plans to award of the contract.

- Integrated System - Under development for consolidated financial reporting for grants, contracts and cooperative agreements.

- Funding process - Worked with program and administrative staff to produce an orientation and reference paper on the grants funding process to facilitate and clarify the funding selection process. Specific procedures to be followed were outlined and a request form for funding exceptions was developed which is used by the NCI Executive Committee in exception decisions.

- Special studies: Two prepared for Executive Committee management meetings addressing issues which have become significant in times of tight budgets and increasing competition for research grant dollars: a detailed analysis and comparison of program projects (POIs) and traditional (ROIs) grants; and an exploration of the impact on research grants of the tight budgets and various funding options.

Grants Administration Branch (GAB)

The GAB performs all business activities attendant to the administration of all NCI grant and cooperative agreement programs. It participates with the Division Directors and their staffs in the formulation and execution of grants policy, develops the Institute's position on grants and cooperative agreement management issues, and negotiates the amount of grant and cooperative agreement awards. This year, NCI issued approximately 5,000 award notices for over 3,600 grants and cooperative agreements totaling $549 million.

- Award Preparation - After a year of work with DRG and DFM, award production control was transferred from DRG to NCI. This required redelegation of approval and obligation authorities to division directors and to the Grants Management Officer. Three sets of computer terminals were installed to facilitate local preparation of awards. The system is being converted one phase at a time and will be fully independent by next year. The change allows flexibility in this stage of the award process and permits the preparation and issuance of an award as quickly as one day, one week at most. The average time between preparation and issuance had been three weeks. The new process also permitted NCI to replace preparation of "Approval Lists" with a more efficient certification process.

- Microfiche Project - In order to reduce records storage space, and to improve staff access to and control of records, installed microfiche equipment in the Records Management Unit to test the feasibility of using microfiched grant files as working documents. Has proved workable for the normal basic research grant. Format for the more complicated, multi-budgeted grants under development. Other uses for microfiche are also being explored, such as microfiching sensitive issue folders as insurance against loss.

- Personnel - A new position of Internal Auditor was established for the purpose of conducting management reviews of the quality of grants administration as documented in official files, identifying weaknesses and developing procedures to assure consistent overall quality of grants administration.

- Internal Management Review - In collaboration with Branch staff, the Internal Auditor developed criteria for review of GAB administration of Program Project (P01) grants in selected programs. Recommendations were developed for improved GAB grants management procedures in areas identified by the study.

- External Management Review - Site visits to conduct reviews of the business management of NCI grants were made to nine institutions, both non-profit and for-profit.

- Community Clinical Oncology Program (CCOP) - Participated in developing an RFA to insure that neophyte Federal grantees will meet the criteria to receive cooperative agreements by offering options to expedite grants to CCOP participants.

- Issuances and Publications - Prepared an NCI Manual Issuance establishing Institute Alert System policy for handling allegations, formal or informal, of wrongdoing by recipients of NCI grant and contract support. Continued update of NCI Policy Manual and GAB Operations Manual. Revised and published booklet titled NCI Grants Process for use of grantee community in understanding grants process.

- Scientific Review and Evaluation Awards (SREA) - Conducted an in-depth review and analysis of all aspects of and potential uses for Chairman's Grant data. Working with the Grants Review Branch, DEA, computer data base was expanded to include information specifically pertinent to DEA needs, to improve useful access for Institute staff, and to improve administrative operations. Developed procedural manual for all aspects of SREA administration, including voucher auditing, account reconciliation and record maintenance.

Personnel Management Branch (PMB)

The PMB exercises appointing authority and provides central personnel management services for the entire NCI including policy development, training, workforce planning, recruitment, employee development, salary administration, and Equal Employment Opportunity in collaboration with the EEO Coordinator.

- Recruitment and Pay for Shortage Category Position - Resolved long-standing problem in connection with recruitment and retention of GS-648, Therapeutic Radiologic Technicians/ Technologists. PMB staff negotiated successfully with OPM to (1) increase special pay rates; (2) issue qualification standards to provide uniformity in qualifying candidates; and (3) establish twelve ceiling exempt student stipend positions for radiation therapy training to alleviate recruitment problems. These achievements are significant particularly in light of very stringent requirements established by OPM and the need to meet increased program needs for this kind of technical support.

- Initiated Publication - Personnelity - for distribution to all NCI staff on a periodic basis to provide highlights of significant personnel matters and trends. The NCI EEO Manager contributes articles for the publication on EEO related items.

- Experts and Consultants - In response to a DHHS study of NCI Expert and Consultant authorities, revised policy and established improved operating procedures to assure better processing, documentation and use of this special authority. HHS adopted several PMB practices/procedures to serve as models to other agencies in the administration of their Expert Programs.

- Processing and Automation - Processed approximately 8,000 personnel actions in the TDCS during the fiscal year. Initiated a comprehensive review of TAPS data with the Divisions to assess the system and make it a more useful management tool. Coordinated the review and purging of approximately 2200 OPF's for NCI employees.

- Position Review - As a result of the Department-mandated, two-year classification review, PMB desk audited, established and/or redescribed 245 positions within NCI. PMB undertook a comprehensive review of its positions which resulted in restructuring to support current grades, upward mobility, and provision of specialized training.

- Summer Employment - Coordinated the annual NCI Summer Employment Program which employed 188 students. Representation in hiring represents a strong NCI commitment to the employment of minorities and women. Of the total number of students hired, 3 were Hispanic, 13 were Black, 15 were Asian, 1 was an American Indian and 113 were women.

- Recruitment Activity - Coordinated 15 recruitment trips which included minority and non-minority colleges, universities, job fairs, career days, and special conferences. Worked closely with NCI EEO office to assure optimal recruitment strategies for FEORP.

- Administrative Career Development Program - Coordinated the reinitiation of the Administrative Career Development (ACD) Program and assured that operating procedures were in compliance with HHS and OPM requirements. Developed supporting documentation and monitored the full range of activities leading to the final selection.

- PMB Role in NIH Activities - Senior PMB staff members played a key role in various NIH personnel management and EEO initiatives, such as leading pilot studies, contributing to major revisions in personnel policy/procedures and representing the NIH personnel community on key task forces.

Management Analysis Branch (MAB) became the new name for what was formerly titled the Management Policy Branch. The change better reflects the responsibilities of the Branch. It advises on the development of general administrative policies and procedures; designs and conducts management studies; analyzes and advises on organization proposals; prepares papers and reports on general management issues; maintains a management issuance system; advises on development of regulations for Institute programs; and assists in development of automatic data processing applications for management purposes.

- Overtime Audit - Developed NCI procedures for auditing compliance with HHS regulations, to include special training sessions for timekeepers.

- Electronic Communications - Lead role in collaboration with the Office of Program Planning and Analysis (OPPA), NCI in developing procedures, training sessions, and experiments with electronic mail using WYLBUR system which improved electronic communications.

- Data Processing - Lead role in cooperation with OPPA in arranging experiment for contract supported training in data processing using the NIH WYLBUR system.

- Intramural Site Visits - Developed Institute policy guide for scientific peer review of NCI intramural research activities.

- Construction/Renovation - Initiated and provided support for collaborative effort with NIH Division of Engineering Services to address serious problems in laboratory renovation and construction.

- Consultant Services - Developed recommendations for streamlining HHS/PHS consultant services clearance procedures.

- Manual Issuances

  1. Procedures for Overtime Approval NCI-2300-630-4
  2. Development of Construction Budgets and Classification of Construction-Type Projects NCI-2600-103-17.
  3. NCI Manual System NCI-1710.
  4. Alert System to Deal with Sensitive Grant and Contract Problems Within NCI NCI-1752.
  5. Organization Change NCI-1121.
  6. EEO Incentive Positions NCI-2300-330-1.
  7. Release of Information to the Public NCI-1181-1.
  8. Commissioned Officer Travel NCI-1530.
  9. Processing Personnel Actions NCI-2300-296-1.
  10. Preparation of PHS Commissioned Officers Personnel Actions NCI-2300-296-2.
  11. Procedures for Effecting Actions for Visiting Programs NCI-2300-296-3.
  12. Guest Worker Program NCI-2300-302-1.
  13. Employment of Experts NCI-2300-304-1.
  14. Employment of Consultants NCI-2300-304-2.
  15. Training NCI-2300-410.

- Information and Instruction Memoranda

  1. Implementation of Audit Procedures for Overtime Administration, NCI MAB-82-1.

  2. Admittance or Examination of Foreign Nationals at the Clinical Center OD-82.

- Reorganization - MAB facilitated the following formal reorganizations:

  - Office of the Director

    - The Office of Administrative Management received the transfer of the Grants Administration Branch and Grants Financial and Data Analysis Branch from the Division of Extramural Activities.

  - Division of Cancer Treatment

    - Established a Radiation Research Program providing an organization focal point for present and future initiatives in radiation research.

    - Completed the phase-out of the Baltimore Cancer Research Program.

    - Established the Laboratory of Experimental Therapeutics and Metabolism in the Developmental Therapeutics Program.

  - Division of Cancer Biology and Diagnosis

    - Established the Laboratory of Tumor Immunology and Biology to study the diagnostic possibilities of monoclonal antibodies/immunologic markers.

    - Abolished the Laboratory of Immunodiagnosis in the Immunology Intramural Research Program.

  - Division of Resources, Centers and Community Activities

    - Created a Biometrics and Operations Branch to provide a statistical, epidemiological and operations research capability for the Division.

  - Division of Extramural Activities

    - Transferred the Grants Administration Branch and Grants Financial and Data Analysis Branch to the OD, NCI.

    - Established the Administrative Management Branch as an independent organizational segment within the Division.

OFFICE OF CANCER COMMUNICATIONS
OFFICE OF THE DIRECTOR
NATIONAL CANCER INSTITUTE

Program Activities Report
October 1, 1981--September 30, 1982

The National Cancer Act Amendments of 1974 require that the "Director of the National Cancer Institute (NCI) shall provide and contract for a program to disseminate and interpret on a current basis for practitioners and other health professionals, scientists and the general public, scientific and other information respecting cause, prevention, diagnosis and treatment of cancer."

NCI disseminates information in three categories:

1. Scientific information used and produced by investigators.

2. State of the art information for use of health professionals and the public.

3. Administrative and program information used by NCI and other organizations within the National Cancer Program.

The Office of Cancer Communications (OCC) (J. Paul Van Nevel, Director) is a major source of information for the public (including cancer patients and people at risk of developing cancer) and a substantial source for health professionals. It carries out traditional communications support activities for NCI. Within the National Cancer Program it assumes the role of coordinator of cancer communications, and develops new initiatives to help meet responsibilities stemming from the Act, to provide the public and health professionals with useful information about cancer.

OCC's traditional activities include responding to press inquiries; preparing news releases, press summaries, announcements, and background statements for use by the press; and assisting in press room operations at major cancer-related scientific meetings. The OCC develops reports and publications, speeches and congressional testimony, reports required by law, special reports for the byline of NCI's Director, and a wide variety of publications for public and professional audiences.

The OCC develops exhibits aimed primarily at health professionals and scientists. They are used at scientific and professional meetings each year, and provide audiences with information on cancer and how to tap resources available through NCI and other organizations.

The office also responds to public inquiries: those requiring both customized and non-customized written responses, and controlled and congressional inquiries. The office distributes publications, and replies to inquiries by regular telephone and to a special toll-free number. It provides backup service to 21

OCC maintains awareness of communications activities of all participants of the National Cancer Program, assuring that there is a minimum of unneeded duplication, and identifying and filling gaps in communications programming.

The OCC operates a national Cancer Information Clearinghouse that maintains awareness of cancer-related informational and educational materials and services produced or used by the cancer community. The Clearinghouse responds to requests for information about available informational and eduational materials and services, promotes the use of existing informational and educational materials and services, and identifies areas where needed materials and services do not exist.

OCC's approach to information dissemination is to reach out to target audiences through intermediary groups which have best access to the chosen audiences. The types of intermediary organizations with which OCC is involved are: cancer related (cancer centers, cancer societies); non-cancer related (fraternal organizations, medical societies, community groups, etc.); and the mass media. Organized dissemination projects are under way in the areas of smoking information, breast cancer information, and coping with cancer. Other areas of special emphasis are: (1) pretesting and evaluation of all communcations projects; (2) communication with minority audiences; (3) an internship program for graduate students in journalism, communications, etc.; and (4) support for 21 Cancer Information Service offices located around the country.

As part of the development of needed communications resources, OCC sponsors a six-month graduate internship in health communications. Outstanding graduate students are selected for varied communications appointments involving science writing, information sciences and health education programs. Interns are assigned to work with professional staff and are given writing, editing and other technical tasks. Interns are encouraged to participate in a specially designed seminar series and to develop special projects during their term.

INFORMATION PROJECTS BRANCH

The Information Projects Branch is responsible for designing, implementing, and evaluating programs to disseminate cancer information. As such, it has undertaken a variety of projects to reach various target audiences with specific health messages.

Smoking Education Programs

The Information Projects Branch (IPB) is engaged in a number of projects intended to help smokers who want to quit, either directly or through health professionals; assist school officials and others interested in education to develop smoking cessation programs for youth; develop approaches to utilize the workplace and education materials aimed at high-risk minority audiences; and stimulate smoking-related efforts through the print and audiovisual media. These activities are being developed and implemented in cooperation with other public and private health organizations so that these smoking programs will contribute to an overall coordinated effort.

The following projects related to smoking are under way for health professionals:

1. "Helping Smokers Quit" kit. Intended for use by physicians with patients who want to quit smoking, these kits have been prepared and distributed to more than 150,000 physicians and other health professionals. The availability of the kits is promoted by direct mail, presentations at medical conventions, and print ad and editorial coverage in medical and dental newsletters.

2. "Let's Help Smokers Quit" kit. This kit was designed by the American Dental Association and OCC for use by dental professionals (dentists, hygienists, and assistants) with patients who want to quit smoking. The kit is an adaption of the "Helping Smokers Quit" kit developed for physicians. The focus of this program is oral health care, effects of smoking on periodontal disease, and smoking's cosmetic effects.

3. "Helping Smokers Quit" program. The American Pharmaceutical Association and the National Cancer Institute are working together to design a smoking cessation program for pharmacists' use in counseling patients who would like to quit smoking. The program (similar to the quit smoking kits designed for physicians and dentists) is in development and is not yet available.

4. The Smoking Digest. The Digest was published in 1978 for program planners, leaders and activists. It summarizes and examines recent information on attitudes about smoking, cessation techniques, smoking information campaigns, smoking legislation, and the tobacco industry. The Digest is being revised.

The following project is under way for young people:

Smoking Programs for Youth. To fill a gap in the existing literature on smoking education for young people, OCC has prepared this comprehensive state-of-the-art report. An offshoot of The Smoking Digest, this booklet discusses the issues related to adolescent smoking, and summarizes policies, curricula, and counseling programs related to smoking prevention/cessation in primary and secondary schools.

The following projects are under way for minority groups:

As a result of the DHHS Office on Smoking and Health's Planning Conference on Smoking and Health in Minority Communities, OCC has initiated the following activities:

1. Promotion of the "Helping Smokers Quit" kit to minority physicians.

2. Translation and Promotion of "Clearing the Air." The NCI pamphlet "Clearing the Air" is a compilation of methods and techniques for giving up cigarettes. OCC has actively promoted its availability in lay and professional publications with Hispanic and black readership. In addition, the booklet and a supporting poster have been translated into Spanish, with appropriate adjustments in format and graphic design, and widely promoted.

Breast Cancer Education Program

The goal of the breast cancer education program is to increase public awareness and improve attitudes about breast cancer in order to:

1. Increase detection practices, including: thorough monthly breast self-examination; routine breast exam by a health professional; instruction in breast self-examination techniques by health professionals; mammography when recommended and appropriate.

2. Reduce delay time in seeking medical consultation for breast cancer symptoms.

3. Improve the ability to deal effectively with the medical and psychosocial aspects of breast disease should a symptom be discovered.

The audience for the program is all women over the age of 18, with materials prepared and tested especially for women who are at increased risk to breast cancer and who tend to have lower levels of knowledge about the subject.

Program materials offer a variety of printed and audiovisual materials, including:

1. The Breast Cancer Digest, A Guide to Medical Care, Emotional Support, Information Programs and Resources, was developed for health professionals, educators, and the media. The Digest covers the medical, psychosocial, and educational aspects of the disease including detection, diagnosis, treatment, rehabilitation, and breast reconstruction.

2. Breast Cancer, We're Making Progress Every Day (formerly entitled "Progress Against Breast Cancer") was designed for use by business, service clubs, religious organizations, unions, and other interested groups. The educational package includes: a slide-tape or videocassette program which provides an overview of progress being made and what people can do to take advantage of it; a take-home pamphlet for every member of the audience, which summarizes the information contained in the slide-tape presentation and sources of additional information; two posters; a User's Guide to help persons organizing the program; and a print ad.

3. "BSE-in-Hospitals Program" was designed to help nurses teach their hospitalized women patients how to perform breast self-examination (BSE) and to encourage these women to practice BSE monthly following their hospitalization. The program has been endorsed by the American Nurses Association. Materials include a "Coordinator's Guide," a three-part slide-tape or videocassette program, a brochure for nurses, a pamphlet for patients, four posters, and a certificate of completion for nurses.

4. What You Need to Know About Cancer of the Breast is a pamphlet designed for breast cancer patients. It discusses symptoms, diagnosis, rehabilitation, emotional issues and questions to ask the doctor. It is also available in Spanish.

5. Breast Exams: What You Should Know is a booklet for the public, describing a variety of breast cancer screening methods including physical examination, breast self-examination, and mammography.

6. Breast Cancer: A Measure of Progress in Public Understanding is a management summary of a national survey on public knowledge, attitudes, and practices related to breast cancer. The survey was conducted among a national probability sample of women and men and a supplemental sample of urban black and Hispanic women.

7. Questions and Answers About Breast Lumps is designed for women who have questions about breast lumps. The pamphlet discusses some of the most common noncancerous lumps, diagnostic procedures, treatment, and cancer risks. Step-by-step instructions in breast self-examination are also included.

8. If You've Thought About Breast Cancer, written by Rose Kushner contains information about topics including symptoms of breast cancer, detection, diagnosis, treatment, rehabilitation, and breast reconstruction.

9. If You've Had Breast Cancer offers suggestions on followup care for mastectomy patients.

10. Breast Reconstruction: Creating a New Breast Contour After Mastectomy discusses techniques used in breast reconstruction, advantages and disadvantages of the procedure, and other factors concerned with breast reconstruction.

Coping with Cancer

The goal of the Coping with Cancer program is to provide those with cancer and their family members the opportunity to gain a sense of control over their lives by providing them with information on the disease, its treatment, and psychosocial aspects. Program materials emphasize the following:

1. A diagnosis of cancer does not have to be a death sentence. More individuals than ever before are living with the disease.

2. Living with cancer is frequently accompanied by physical, psychological, emotional, and/or social problems that patients, family, and friends must cope with in order to live with quality.

3. There are useful coping behaviors and strategies that those with cancer and their families can employ.

4. Often, problems in coping with cancer and other chronic diseases are not unique, but are common to many patients and families. However, the applicability of a coping approach depends on the individual patient and his or her circumstances.

The primary audience for the program and the main focus for its materials are those with cancer and their families. The secondary audience includes health

professionals and others to whom the patient and family go to for care, information, and support.

The following materials are available for adults with cancer and their families:

1. Eating Hints--Recipes and Tips for Better Nutrition During Cancer Treatment is a collection of helpful, practical information on making mealtime more pleasant for the patient. Tips for coping with common eating problems and tasty recipes are included in this cookbook-style publication.

2. Chemotherapy and You--A Guide to Self-Help During Treatment addresses problems and concerns associated with chemotherapy treatment. Emphasis is on explanation and self-help. Includes a glossary of terms.

3. Radiation Therapy and You--A Guide to Self-Help During Treatment addresses problems and concerns of patients in radiation treatment. Emphasis is on explanation and self-help. Includes a glossary of terms.

4. Taking Time--Support for People with Cancer and the People Who Care About Them is a sensitively written booklet for persons with cancer and their families, addressing the feelings and concerns of others in similar situations and how they have learned to cope.

5. Control of Cancer Pain is a fact sheet addressing medical and non-medical modalities of dealing with pain related to cancer.

6. What You Need to Know About Cancer is a series of pamphlets discussing symptoms, diagnosis, rehabilitation, emotional issues and questions to ask doctors. The series consists of one general pamphlet and 24 site-specific pamphlets.

The following materials are available for young people with cancer and their families:

1. Young People with Cancer: A Handbook for Parents was written in cooperation with the National Candlelighters Foundation. It includes information on the most common pediatric cancers, treatments, and side effects. Special consideration is given to the emotional impact of cancer on patients and family members.

2. Help Yourself: Tips for Teenagers with Cancer was produced in cooperation with Adria Laboratories, Inc. It includes a booklet and an audiotape designed to provide information and support to adolescents with cancer. Issues addressed include reactions to diagnosis, relationships with family and friends, school attendance, and body image. A User's Guide for health professionals is also available.

3. Hospital Days, Treatment Ways, a coloring book developed for children with cancer, explains procedures the young patient may experience in the hospital environment.

4. Diet and Nutrition: A Resource for Parents of Children with Cancer contains suggestions for dealing with nutrition problems arising from pediatric cancer or its treatment. Includes special diets and an attractive poster for convenient display in the kitchen.

5. Maintaining a Normal Life (Proceedings of the First National Conference of Parents of Children with Cancer) was compiled in cooperation with the National Candlelighters Foundation. Presentations delivered at the 1978 conference include the following areas: discipline, nutrition, treatment developments, practical problems, parental roles and relationships, and remarks from a panel of teenagers with cancer.

6. The Leukemic Child, a booklet written for parents, describes one mother's experience in caring for a child with leukemia.

7. What You Need to Know About Wilms' Tumor; Child Leukemia--see two pamphlets in the "What You Need to Know About Cancer" series (item 6 in section above).

The following materials are available for health professionals and others who provide support and information:

1. Coping with Cancer--A Resource for the Health Professional is a reference work on the psychological and social aspects of cancer. It summarizes issues faced by cancer patients of all ages and their families and provides practical guidance to caregivers in responding to patient and family needs. Support programs available throughout the country are described. References for further reading and an easy-to-use subject index are included.

2. Students with Cancer--A Resource for the Educator, a booklet for educators of young students with cancer, is designed to answer questions pertaining to the student's participation in school activities.

3. NCI Patient Materials Catalog contains annotated citations of 40 patient and professional information materials available free of charge from NCI. Includes an order form.

4. Coping with Cancer--An Annotated Bibliography of Public, Patient, and Professional Information and Education Materials provides annotated citations of 300 print and audiovisual materials for patients, health professionals, and the public.

5. Services Available to Persons with Cancer--National and Regional Organizations is a reprint from the October 10, 1980, Journal of the American Medical Association. The article was written to acquaint the physician with national and regional organizations with services available to help patients with the psychological, social, and economic problems related to their having cancer.

6. Help Yourself: Tips for Teenagers with Cancer: User's Guide is a short leaflet produced in cooperation with Adria Laboratories, Inc.,

summarizing the content included in the "Help Yourself" patient booklet and audiotape.

Pretesting and Evaluation Program

1. The Health Message Testing Service

The Health Message Testing Service (HMTS) completed its fifth year as a service to test broadcast and print health messages. Approximately 74 television and 20 radio public service announcements (PSA's) were tested through the broadcast component of the service. Twenty-five brochures and 10 posters were tested as part of the print component of HMTS.

In FY 1982, funds to support the service were contributed by the National Cancer Institute; The National Heart, Lung and Blood Institute; and the Office of Health Information and Health Promotion, DHHS. This year's message sponsors included: Office on Smoking and Health; National Institute on Alcohol Abuse and Alcoholism; National High Blood Pressure Education Program; USC Cancer Information Service; Office of Public Affairs, DHHS; American College of Obstetricians and Gynecologists; Health Care Financing Administration; Social Security Administration; and the New York State Department of Health.

Funding for this year also was used to conduct a final analysis of the data from broadcast testing. This analysis examined 58 television PSA's to determine what factors within the message contributed to high test scores. In addition, a review of the literature for developing effective PSA's was conducted. A working group of experts in communication research, advertising and PSA production was gathered to comment on these reports and make recommendations on what can be shared from this project. Based on the recommendations from this group, the HMTS staff are currently preparing a booklet on planning, producing, and implementing public service announcements, which incorporates the results of the broadcast HMTS project.

For print testing, two articles are being prepared for communication research journals, which describe the methodologies developed for testing print formats and what we have learned from print testing.

This was the final year for evaluation set-aside funding for this project, and testing will no longer be available to other agencies.

2. Pretesting and Evaluation Activities

Pretests conducted as part of OCC program development this year included: the breast cancer poster, the adolescent coping tapes and materials; Lo Que Usted Debe Saber Sobre el Cancer (What You Should Know About Cancer); What Black Americans Should Know About Cancer; Examenes de los Senos: Conocimientos Practicos (Breast Examinations: Practical Knowledge). Also user satisfaction surveys were completed for Chemotherapy and You, Radiation Therapy and You, and Taking Time.

Several special projects also were completed this past year. They include the second content analysis of daily newspaper coverage of cancer, a content analysis of daily newspaper coverage of the Laetrile clinical trial results, analysis of scientific press coverage of Laetrile trial results, and an analysis of black newspaper coverage of cancer. The first phase of the national survey of public knowledge, attitudes and practices related to cancer was completed this year. This involved conducting approximately 16 focus groups with various segments of the population to discuss their knowledge and perceptions about cancer. This phase was undertaken to isolate relevant survey topics, develop researchable hypotheses, and provide both content and language direction for the survey questionnaire.

OCC provided technical assistance to the American College of Obstetricians and Gynecologists; the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases; and the Department of Agriculture. In addition a seminar was given at Columbia University's School of Public Health on the Health Message Testing Service Project. A paper entitled "Breast Cancer Education: An Approach to Program Planning and Evaluation" was published in the Proceedings of the Conference on Issues in Cancer Screening and Communications, Buffalo, New York.

Cancer Communications Network

The Cancer Communications Network (CCN) has been established by the Division of Resources, Centers and Community Activities (DRCCA) for the purpose of assuring that accurate, up-to-date information on cancer cause, prevention, early detection, diagnosis, treatment, rehabilitation and continuing care is readily available and accessible to the public and health professionals. The CCN contracts were recently recompeted for an additional three years of funding and currently consist of 19 regional offices funded by NCI. Two additional offices receive no funds from NCI but actively participate in the information exchange that occurs throughout the network.

Each network office is responsible for:

1. Establishing a Communications Office to plan, administer, promote, develop support materials for and evaluate activities undertaken by the contract staff;

2. Developing and maintaining a resource directory of agencies and services available to cancer patients and their families within the defined service area of the center;

3. Establishing and operating a toll-free telephone service (the Cancer Information Service or CIS) for immediate access to answers on cancer-related questions from the public; and

4. Identifying, developing, implementing and evaluating a limited number of special projects to meet specific cancer information/education needs within the service area.

Work continued on the national evaluation of the Cancer Information Service portion of the network's operations. The quality assessment program has undergone pretesting, and the standardized call record form will be pretested soon.

The national Publicity and Promotion Task Force continued to advise NCI on promotional materials developed for the network. Revisions of the National Plan for Publicity and Promotion of the Cancer Information Service were completed. The document is now used as background and guidance for the network and for NCI. The task force is currently undertaking the development of a marketing plan for the Cancer Information Service, which will be completed in the next fiscal year. Two Public Service Announcements (PSA) were developed for the network by NCI, one of these in conjunction with the "Decade of Discovery," a celebration of the first 10 years of the National Cancer Program. This PSA was cosponsored by the Candlelighters Foundation, Inc. It was a finalist in a national competition. Other PSA's produced by various CIS offices were replicated by NCI for use by the entire network.

The Staff and Volunteer Training Task Force has been established to develop a uniform staff and volunteer training program for use by the network. This task force will review all training programs currently in operation and use this information, coupled with new information, to develop a standard program.

At the end of this fiscal year, more than 800,000 callers have been served by the Cancer Information Service since its inception. The CIS currently averages 11,500 calls each month, with over 135,000 total calls this fiscal year.

Examples of special projects currently under way throughout the network include a series of leaders forums, a Seniors Team Up Against Cancer health education project, a Pap smear education program for high-risk women, cancer risk self-assessments, a cancer program for older citizens, cancer education programs targeted towards the black and Hispanic communities, an information dissemination campaign for rural audiences, and many newsletters, radio programs, and mass media campaigns providing cancer information and education to various target audiences. In addition, the Psychosocial Cancer Counseling Line (PCCL) has been developed by one office to meet the psychological and emotional needs of cancer patients and their families.

Because of a similarity in activities and skills with the CCN programs, the Office of Cancer Communications has played a major role in the management and support of the network since its inception in 1974. The Information Projects Branch serves as the designated coordination and liaison point between OCC and DRCCA. The Branch provided support to the Cancer Communications Network in two broad areas during the past year.

1. Management and Staff Support—At the request of DRCCA, a special arrangement was established in which a member of the branch staff (Thomas Kean) was assigned half-time to the DRCCA to serve as Project Officer for the network. In addition, one OCC intern has been assigned to the network for the past 1-1/2 years. All secretarial support for the CCN is currently provided by OCC, as is all space housing CCN program staff.

2. Technical Advice and Support--The branch continued to provide direct support to the network offices in the areas of advice on program and materials development (including pretesting), publicity and promotion, and advance notice of national publications and broadcast programing that cites or promotes the network and its services. Staff members from the Information Projects Branch of OCC currently serve on the Publicity and Promotion Task Force and the Evaluation Task Force of the CCN. These task forces act as advisory groups to the CCN program staff.

Minority Program

The thrust of the OCC minority program this year was to ensure that ample cancer information materials were available to users and to involve key outside organizations to help OCC plan for the future.

In this regard, the branch:

- Translated into Spanish and promoted "Clearing the Air," "Everything Doesn't Cause Cancer," and other materials.

- Completed an evaluation of and made appropriate revisions to "What Black Americans Should Know About Cancer" and "Lo Que Usted Debe Saber Sobre el Cancer."

- Planned a comprehensive national study entitled "Survey of Public Knowledge, Attitudes, and Practices Related to Cancer" to be started in FY 1983. This first-of-a-kind study will enable member organizations of the National Cancer Program, including NCI, to better plan, develop, implement, and evaluate public information and education programs on cancer. The results of this survey will be disseminated widely to health program planners, health educators, physicians and others in a position to influence public understanding of cancer.

- Responded to recommendations of the Hispanic Outreach Task Force and is now developing new Hispanic programs based on the recommendations. These programs involve gathering data on Hispanics and cancer, developing new audiovisual and print materials, and creating specialized promotional activities.

The staff of the Information Projects Branch at the beginning of the year consisted of Robert W. Denniston, branch chief; Barbara D. Blumberg, Carol S. Case, Thomas J. Kean, Nancy McCormick-Pickett, and Rose Mary Romano, program staff; Dorothy Kipnis and Sylvia Pines, support staff; and interns Andrea Eastman, Karen Vogel, Kathleen Duffy, and Joann Ferguson. In May 1982, Mi-Hyang Nam, summer student, returned for a third summer, and in July, Rose Soodak (secretary) joined the staff.

REPORTS AND INQUIRIES BRANCH

The Reports and Inquiries Branch responds to inquiries from the public, cancer patients, and the news media, and disseminates information on research findings and National Cancer Institute activities. Information dissemination occurs in a

variety of forms, including reports and other publications, speeches and congressional testimony, magazine articles, and news releases and fact sheets for the news media.

Reports Section

As in recent years, inquiries from the news media continued at a high level, reflecting interest in all areas of cancer research and activities of the National Cancer Institute and the National Cancer Program (NCP). Section staff responded to approximately 2,000 inquiries from journalists, representing daily and weekly newspapers, magazines, and the electronic media, as well as newspapers and magazines for physicians and scientists. In addition, section staff initiated contacts with the media on numerous occasions to remind them of upcoming meetings, press conferences, or major reports. NCI administrators and scientists were interviewed for news and comment programs of the major television and radio networks, as well as local stations throughout the country and news organizations from many countries of the world.

The Reports Section prepared nine notes to reporters and editors, announcing a new report from the Surveillance, Epidemiology and End Results (SEER) Program, the reorganization of the Division of Cancer Cause and Prevention, several NCI staff appointments and awards; and one news release on bioassay results on selenium sulfide and Selsun shampoo.

Results of Phase I clinical testing of interferon were announced at the annual meeting of the American Society of Clinical Oncology (ASCO). Section staff handled the press conference, press room, and prepared a detailed description of the findings from all NCI-sponsored clinical trials of interferon. Three press summaries were prepared on NCI scientists' research reported at the annual meeting of the American Association for Cancer Research (AACR), two on work presented at the ASCO meeting, and one for the annual meeting of the Federation of American Societies for Experimental Biology (FASEB).

Press inquiries continued at a high level on potential and known risks for cancer, breast cancer, interferon, Laetrile, cancer statistics, Kaposi's sarcoma, experimental cancer therapies, chemoprevention, nutrition, the new Community Clinical Oncology Program, and other NCP programs, priorities and budget. Reporters and researchers for television networks, film companies, and major newspapers continued major surveys of progress in cancer research. Critical reports included a Washington Post five-day series on the NCI drug development program, and an ABC-TV "20-20" program on the "War on Cancer." In response to a complaint, the National News Council conducted an investigation of the Post series and asked the NCI for a review of the errors in the article. Reports Section staff worked with NCI scientific staff to prepare a detailed review, and the National News Council subsequently found that the series was flawed.

To respond more effectively to high numbers of requests about evolving NCI research studies, section staff prepared "Fact Sheets" and "Updates" on the following topics: testicular cancer therapy; Kaposi's sarcoma; biological response modifiers; viruses and cancer; a family prone to lymph gland cancer; drug infusion chemotherapy; cancer following medical irradiation; neutron beam radiotherapy; a diagnostic glossary; accomplishments of the NCI intramural program; effects of radiation on cell samples in a cancer-prone family; nitrate

use among Kaposi's sarcoma patients; alcohol consumption and esophageal cancer; cancer patient survival; a genetic mechanism for cancer formation; the cloning of gamma interferon; families prone to lung cancer; mortality among petroleum refinery workers; and NCI clinical trials of interferon.

In addition, section staff also prepared statements on NCI research on soft tissue sarcoma, and chronologies on methyl-CCNU research and diethylstilbestrol education efforts, three Messages from the NCI Director, question-and-answer sheets on the National Cancer Act and NCI smoking activities, an NIH News and Features story on bombesin research by NCI scientists, and Special Communications on DES, neurofibromatosis, stretching Federal research dollars, publication of Decade of Discovery: Advances in Cancer Research 1971-1981, and receipt of the 1981 Antonio Feltrinelli International Prize by a long-time NCI grantee.

Section staff participated in the preparation of materials for Congress. Specific projects included the traditional statements for both the House and Senate appropriations hearings, as well as testimony for reauthorization hearings, hearings on NCI's drug development program, and input for DHHS testimony on the drug development program, smoking and health, and the Atomic Bomb Compensation Act of 1982.

Staff also prepared the 1981 report of the National Cancer Advisory Board (NCAB) and the NCI Director's annual report to the Congress.

Six speeches for the NCI director and one for the acting NIH director were prepared in the section, as was a major briefing book for the DHHS Secretary. Section staff also began updating a major NCI publication, Cancer Rates and Risks.

Several short articles on cancer research findings were prepared for the NCI Director, including an editorial for ACS Cancer News, and a chapter on "Modern Therapy" for a book on cancer being published by the American Cancer Society. Forty-six articles of interest to the NCI and NIH communities were prepared for the NIH Record from October 1, 1981 through the end of June 1982.

At the end of the fiscal year, permanent staff in the section were Pat Newman, section chief; Farrell Wolfson, Florence Karlsberg, Eleanor Nealon, Linda Anderson, Alice Hamm, Harriet Page, and Lorraine Kershner (writers); Amelia Champion and Anne Gooding (editorial assistants); Elsie Cleveland, a full-time secretary who joined the section in January 1982; and part-time clerk-typist Marilyn Pazornik. Four science writing interns trained in the section, as part of the OCC internship program: Aubin Tyler and Thomas Hager (to January 1982) and Ann Menting and Mary Plaut (beginning July 1982). Nathan Rosen, summer student, returned to the section for a second summer.

Public Inquiries Section

The Public Inquiries Section answers written and telephone inquiries about cancer from patients, their families, concerned members of the public, students, health and other professionals, members of Congress and other government components. With the assistance of a contractor, Biospherics, Inc., the section prepares responses to the written inquiries, and operates the Cancer Information

Service, a toll-free telephone operation that acts as a backup to the Institute's Cancer Communications Network. Publications also are distributed with the letters and telephone calls, and in answer to bulk orders from health professionals, hospitals, cancer organizations, and other health groups.

The philosophy underlying the program is that Americans are entitled under the National Cancer Act to the most recent and accurate information about cancer research, causes and treatment. The section provides information that combines standard, prepared materials with information tailored to the specific needs of each letter or telephone call.

In FY 1982 (the last four months are projected), the section responded to an estimated 291,100 written and telephone inquiries and distributed 15.2 million publications. This volume reflects the American public's continuing need for reliable information about cancer and interest in the national effort to achieve control over the disease.

In comparison with the fiscal year ending September 30, 1981, the most noteworthy change in the current year is the increase in the total number of written and telephone inquiries, up an estimated 10,500 from the total of 270,500 in FY 1981. This is an average increase of about 1,700 per month. Calls to the national toll-free information service increased from 44,674 to more than 49,500, a rise averaging about 400 calls per month.

Estimates projected to the end of FY 1982 include 5,880 custom letters (individually prepared responses to letter and telephone inquiries)--down from 8,859--and 268,524 non-custom inquiries (requests that can be answered by sending publications alone) up from 192,684 in FY 1981. "Controlled" letters, received or referred from members of Congress, the White House and other government offices, continued at the annual level of 220.

In the period from FY 1978 to 1982, the volume of custom mail has gradually decreased from 14,000 annually to the current estimate of 5,880. Factors associated with this trend are the increasing promotion and use of the Institute's toll-free telephone information service and the development of new publications and information sheets that satisfy inquirers' information needs.

The overall increase in inquiries and distributed publications can be traced to promotion of NCI publications and information services. This has included titles about the most common types of cancer, particularly cancers of the breast, lung, and colon. Patient education materials like Chemotherapy and You, Radiation Therapy and You, Taking Time, Eating Hints, What You Should Know about Cancer, and Breast Exams: What You Should Know have approached distributions of 300,000 each. The most popular items are Why Do You Smoke? (630,000) and Clearing the Air (nearly 500,000). From September 1974 through February 1982, NCI distributed a total of 36,418,688 copies of various anti-smoking publications.

The electronic media and many of the large-circulation magazines have informed the public about the availability of cancer information from NCI. This included repeated attention in Family Circle, Ladies Home Journal, Woman's Day, Redbook, Better Homes and Gardens, plus most of the weekly news magazines and newspapers. Available materials and services also were identified in a growing

number of scientific, medical and nursing journals, not only in the cancer field, but in other areas of medicine as well. For example, they included Journal of Respiratory Diseases, Journal of Urology, Progress on Cardiovascular Diseases, and American Journal of Clinical Nutrition. At the other end of the spectrum, cancer information has appeared in small local journals of all types, including church and health newsletters.

With this kind of exposure, much of the American public has access to cancer information. The result is that the inquirer is more sophisticated and more demanding than a few years ago. Questions seem more informed and incisive. The inquirer wants an honest and full answer and expects the best in current information.

The people who call or write to the Institute are gratifyingly articulate about their problems, whatever their educational level. Roughly half are patients, family members and friends, plus a growing number of persons who are worried that they may have cancer, or might get it someday. Up to 40 percent of the inquirers--students, professionals and others--want information or publications. Most are in the health or counseling field, although these inquirers also include attorneys, teachers, and insurance specialists. Inquiries come from all over the States, with the most from the most populous ones. Letters arrive from a growing list of foreign countries: Australia, Belgium, Brazil, Canada, Colombia, Denmark, England, Holland, Italy, Japan, Mexico, Peru, Poland, Russia, Spain.

The most common topics of interest are breast cancer, followed by other major types of cancer and questions about how to find good treatment. Some inquirers ask about the hazards of asbestos, smoking or sunbathing. Some complain about the slowness of finding a cancer cure, others accuse the medical profession of trying to withhold a cure, but most appreciate the Institute's programs. An analysis of responses to a critical series about the Institute in a Washington newspaper showed little impact in the letters and calls. Regularly, some 20 letters of thanks are received a month.

The statistics show that people are calling more and writing somewhat less. This year's calls are about 10 percent higher than last year's total. Calls are heaviest between 11 a.m. and noon; 40 percent of calls are under 3 minutes long, and another 48 percent, 4 to 10 minutes. About 1/5 of the calls are referred from other CIS offices.

Along with the publication titles, the national CIS telephone number has been widely publicized in the media. Altogether, 175,000 calls have been received since the service was founded. The callers represent about 20 percent of total inquirers, up from 17 percent last year. The service is staffed by trained health or counseling professionals 16 hours a day, seven days a week. They operate eight lines, including two for Alaska and Hawaii.

The publications are housed in a warehouse where more than 300 titles are grouped by topic.

Because of the size and complexity of the program, a number of quality control procedures have been instituted. Blind calls are regularly made to the CIS;

reports on the calls are made to the staff, as feedback to improve performance. Such items as how long it takes for the telephone to be answered, the attitude of the telephone specialist, and the appropriateness of the answer are evaluated. Telephone logs are checked each day as a means of gauging correctness of replies. A weekly control check is made in the contractor's warehouse of new publication deliveries, and their entry into the TRS-80. At the end of May 1982, approximately 18 million publications were stored in the warehouse.

This past year, the Public Inquiries Section was responsible for developing a number of publications and fact sheets. They include: If You've Had Breast Cancer,...A Guide to Followup Care for Breast Cancer Patients, Biopsy Choices--One Step or Two, A Guide to Mastectomy, A Guide to Radiation Therapy As Primary Treatment for Breast Cancer, Questions and Answers About Pain Control: A Guide for People with Cancer and Their Families, Adjuvant Chemotherapy for Breast Cancer, Research Report: Cancer of the Prostate, and Control of Cancer Pain.

A new information approach, "Message from the Director," was initiated during the year. Timely one-page messages from the NCI Director to increase public understanding of the cancer problem were inserted in letter replies to written inquiries. Section staff prepared seven of these pages. The staff also prepared three NIH-syndicated "Search for Health" columns: "Cancer Prevention," "Non-Hodgkin's Lymphomas," and "Advances in Childhood Leukemia." Three Research Reports--Bone Cancer and Other Sarcomas, Hodgkin's Disease and the Non-Hodgkin's Lymphomas, and The Leukemias--also were written by section staff.

The staff consisted of the chief, Robert J. Avery, Jr., who also served as project officer of the Biospherics contract; Betty MacVicar, writer and assistant project officer; Karen Schlick, who was promoted from secretary to public affairs specialist in the fiscal year, and Sheila Stempler, secretary. Mary Frances Boak, an information writer in the section since 1971, retired in January and was replaced by Joan Chamberlain, who came to NCI from a similar position in the National Center for Health Services Research.

Two graduate student communications interns--Jeanine Brumbeau from the University of Maryland and Pamela Frankel from Tulane University--joined the section in July 1981 and served until December 1981. In April 1982, Mary Sullivan, from the University of Virginia, joined the section for a six-month period. Leah Cates, from the University of Missouri, began an internship in July 1982.

INFORMATION RESOURCES BRANCH

The Information Resources Branch is responsible for various supporting services for the Office of Cancer Communications (OCC) and the National Cancer Institute (NCI). The branch is composed of two sections: the Document Reference Section and the Graphics and Audiovisuals Section. Each of the two sections has specialized service responsibilities.

The Document Reference Section (DRS) is an in-house information center with the responsibility for OCC's needs for scientific, technical, and public information library/reference services. The DRS has access to major on-line data bases and performs searches upon request for OCC staff and for other NCI offices on an as-needed basis.

The Graphics and Audiovisuals Section (GA/V) manages graphics and printing services for the OCC and other NCI components. The GA/V also has a number of specialized functions including the NCI Exhibits Program, "Current Clips" (NCI's clipping service), NCI document clearance control, graphic services (slides, photographs, etc.), photo resources, NCI Speakers Bureau, Freedom of Information Act/Privacy Act coordination, Special Communication/Message from the Director (announcements), purchasing and the management of printing and reproduction services.

Cancer Information Clearinghouse

The Information Resources Branch is also responsible for the Cancer Information Clearinghouse, a major information resource for data on public and patient educational materials. The Clearinghouse is contractor-operated (CSR, Inc.). During FY 1982, numerous significant changes in the project have been proposed and will be carried out during FY 1983.

Among these changes is the elimination of all professional education materials from the collection. Previously, the Clearinghouse served organizations that needed data on public, professional and patient educational materials.

Other significant changes include: (1) the stopping of all formal published topical bibliographies (during 1982 an estimated 220,000 were distributed by the OCC); (2) the purging of all materials not directly considered to be "materials-in-use," e.g., resource materials and texts; (3) the purging of all "non-current" materials, i.e., earlier than 1978; (4) intensive promotion of the availability of the Clearinghouse data base; and (5) intensive evaluation of user satisfaction and studies to assure that the Clearinghouse is meeting its objectives by assessing quantitative measures of performance.

During June 1982, the OCC developed a new work statement leading to formal solicitation for a new contract. The RFP (Request for Proposal) was issued in late summer with procurement expected by April 1983. The "new" Cancer Information Clearinghouse will be quite different: smaller, narrowly specialized, non-publishing and responsive through data base searches.

Communications Internship Program

During FY 1982, the OCC recruited nine communications interns. During previous calendar years the program had averaged 16 interns per year. These are outstanding graduate students selected from the nation's schools of public health, information science and journalism. The names and assignments of each of these interns are contained in the respective sections of the annual report.

The internship is undergoing change: an evaluation of the program's effectiveness and objectives was scheduled to be conducted during July-September by contacting former interns and having OCC supervisors rate the efficacy of the program. Further, the recruiting materials were reviewed and updated. The promotion of the internship was shifted from contacting schools to media-oriented public service advertising in publications reaching professors and potential candidates in schools. There has been increased emphasis on reaching minority candidates (Hispanic) with special skills in language and knowledge and

interest in the health practices of the culturally disadvantaged. Intern-planning offices have become target receivers of OCC intern recruiting materials. Intern position descriptions have been revised and membership on the selection panel is being broadened.

These changes will contribute to the development of a stronger program for recruiting and selecting intern candidates.

Document Reference Section

DRS, the in-house library of the OCC, has continued its growth of services to OCC staff this year. Additional data bases have been obtained, particularly in the public affairs areas; backlog cataloging of the book collection was completed and cataloging of new books accomplished; the data base representing the indexed DRS collection has grown by nearly 5,000 items to a total of 43,000 items.

The DRS is a central informational resource of the OCC and the Institute. Support materials (both published and unpublished) are collected, indexed and made available to specific users. Included in this user group is the NIH scientific community as well as professionals working in public information areas. The in-house collection is comprised of public/press inquiry records, news clips, bioscientific publications, audiovisuals and other significant documents. The automated, bibliographic data base, composed of data records for DRS collection items, may be searched free-text or by controlled vocabulary index terms.

In addition to its own data base, DRS has access to other major commercially-available, health-relevant, data bases. They include those sponsored by the National Library of Medicine (MEDLINE, CANCERLINE, CLINPROT, etc.), Bibliographic Retrieval Services (Pre-Med, SSIE, Medoc, etc.), System Development Corporation (Psychological Abstract, ERIC, Agricola, etc.) and Lockheed-Dialog (Exerpta Medica, Pharmaceutical News Index, Science Citation Index, etc.). Access to journalistic data bases such as the New York Times Information Bank, Newsearch, National Newspaper Index and NEXIS allows the DRS to support the Institute with data especially useful in public information work.

The DRS has performed more than 3,000 computerized searches and 1,000 manual searches this fiscal year. These searches have aided health communicators, scientist-administrators and public information specialists in responding to inquiries and developing information projects.

Patti Dickinson continued as section chief. Kathi Canese, a student at State University of New York at Albany, assigned to the DRS as an information intern from July 1981 until December 1981, resigned to take a position as an information specialist with Public Technology, Inc., in Washington, D.C. Judy Lim-Sharpe, a professional librarian, joined the staff as a full-time permanent employee in February. Dolores Leshy joined the staff in June as an information intern. Ms. Leshy, a student at University of California, Berkeley, worked with the NCI archives and on-line systems. Susan Grodsky, a full-time temporary professional librarian, resigned her position in June to take a position with System Development Corporation, Santa Monica, California. Johanna de Voest joined the staff in June as a clerical assistant/summer aide. Ms. de Voest is a college student at Montgomery College, Rockville, Maryland.

Graphics and Audiovisuals Section

The Graphics and Audiovisuals Section provides a variety of services to OCC and the NCI.

Printing management services involve more than 300 titles of public information materials and other NCI publications. This work involves coordination of graphics and printing services as well as arranging for distribution by direct mail from the printer.

New table top exhibits were developed on specific information programs. Twelve new panels were prepared to supplement panels in existing large exhibits, to allow promotion of educational materials on specific programs. A new exhibit structure was prepared on the programs of the OCC for the White House Conference on Aging. Exhibits were shown at 12 professional meetings. More than 75,000 publications were distributed at those meetings. Printed materials were provided for the National PTA, Montgomery County Health Department Health & Fitness Fair, NIH Nutrition Education Project, Valley Hills Mall, Hickory, North Carolina Health Fair, and National Consumer Education Week.

NCI's "Special Communication" is a service for rapid disseminating of information. The special communication can be sent selectively to medical and voluntary groups, professional societies, and persons in allied health professions. During FY 1982, nearly one million individuals and groups were reached via 12 special communications.

Nearly three million publications were distributed for NCI by Supermarket Communications Systems, Inc., in bulletin board distribution facilities located in 4,500 supermarkets and discount stores throughout the United States. The Consumer Information Distribution Center in Pueblo, Colorado, distributed approximately 300,000 copies of English and Spanish NCI publications.

More than 250 nonresearch materials including publications, audiovisuals, and speeches were processed by the section for official clearance. Assistance was provided to all NCI program areas in obtaining printing and audiovisual services. Section staff also handled arrangements for a number of special events, including award ceremonies and tours.

Over 250 requests under the Freedom of Information Act were received and processed. Approximately 1,200 Privacy Act requests were handled during the year.

A daily newspaper clipping service of items of NCI interest was provided to the professional staff, Cancer Information Service offices, and members of the President's Cancer Panel and the National Cancer Advisory Board. Section staff screened eight newspapers and a number of mass-circulation and scientific magazines and journals.

The staff of the section included Margaret Layton, section chief; Arlene Soodak-Cohen, visual information specialist; Maralyn Farber Berlin, NCI freedom of information coordinator; public information specialists Anthony Anastasi and Edith Gaub; and Beverly Gamble, secretary. Ms. Gamble is responsible for purchasing activities for OCC.

OFFICE OF INTERNATIONAL AFFAIRS
OFFICE OF THE DIRECTOR
NATIONAL CANCER INSTITUTE

Program Activities Report
October 1, 1981 - September 30, 1982

INTRODUCTION

The prevention and control of cancer depends upon knowledge of causation, identification of population risk groups, availability of early detection measures, and the means for effective intervention. Marked differences in the geographic, environmental, occupational, and social conditions of people suggest that these variations may critically influence the incidence and course of many if not most types of cancer in a given area. Thus, the efforts of world specialists engaged in cancer research are stimulated and enhanced through international interaction, by collaborative studies and by the exchange of scientific results. Through its participation in the international cancer scientific community, the National Cancer Institute (NCI) ultimately benefits from the rapid advances in basic research throughout the world and their application to the clinical management, control, and prevention of cancer. The ultimate gain from such collaborative cancer research efforts is a tangible improvement in the quantity and quality of health services to millions of people the world over.

The contribution of NCI to the international struggle against cancer includes: (1) the continuing support of cancer research in foreign countries by highly qualified scientists; (2) the support of cooperative research programs, principally under bilateral agreements with foreign governments, institutions, and organizations; (3) maintenance of liaison and research collaboration with international organizations and agencies that have well-defined objectives in cancer research and cancer prevention; (4) the support of training of foreign scientists in the United States as well as of the interaction of American scientists with colleagues in foreign laboratories; and (5) the management and operation of an International Cancer Research Data Bank for promoting and facilitating, on a worldwide basis, the exchange of information for cancer research, care and management of patients, and cancer control and/or prevention.

RECENT SCIENTIFIC ADVANCES

A joint study between NCI scientists and a visiting Hungarian developmental chemotherapist led to the confirmation of the role of the tripeptide, glutathione, in resistance of the tumor cell to alkylating agents. Experiments have been completed on a substance that inhibits the biosynthesis of glutathione, making the tumor cell less resistant to an anticancer agent. These results demonstrate that it is possible to completely sensitize the resistant cancer cell to the cytotoxic effects of anticancer drugs, in this case L-phenylalanine mustard (commercially named melphalan and L-PAM) which is used in the treatment of breast cancer.

An NCI-supported study in Israel was completed recently on the time course of natural killer (NK) cell activity in mice fed the carcinogen, DMBA. The NK cell is one type of natural cell-mediated immunity in the body. Very soon after the administration of DMBA, the number of spleen cells of treated animals was decreased to about 50% of normal. The NK activity was decreased significantly. Splenocytes were restored to normal value about 3 months following DMBA exposure and, in most animals, prior to tumor development. The NK activity, however, remained depressed throughout the entire carcinogenesis latency period. A further significant decrease in NK activity occurred in those animals in which primary tumor developed. This additional NK depression is apparently secondary to tumor development and mediated by suppressor cells.

An American-Japanese workshop highlighted the epidemiologic and clinical findings related to T-cell leukemias and lymphomas, indicating that they appear to occur in clusters of high incidence in certain prefectures in Japan. There is further indication that those malignancies may be associated with a human retrovirus, Human T-Cell Leukemia Virus (HTLV), recently isolated by an NCI intramural scientist. Independently, the Japanese have isolated a similar, if not identical virus, Adult T-Cell Leukemia Virus (ATLV).

The monograph series of the International Agency for Research on Cancer (IARC), entitled "Evaluation of the Carcinogenic Risk of Chemicals to Humans," continues to be the authoritative source of current information on environmental chemicals. This program is supported, in part, by the NCI, and NCI scientists participate with international experts in the analysis of data and the preparation of texts for these important references.

Based on the positive experience with the Japanese-developed anticancer agent, aclacinomycin A, Phase I clinical trials have been completed, and a large scale Phase II study was begun in the United States. There is evidence of good activity of the agent in leukemias and lymphomas; however, no activity is demonstrated against solid tumors. As well, American evaluation of PEP-bleomycin has begun, based on Japanese and European clinical data. This analog of bleomycin has demonstrated low pulmonary toxicity and has yielded very good results in the treatment of testicular cancer.

One of the more than 300 compounds supplied to NCI by the European Organization for Research on the Treatment of Cancer (EORTC), for potential use as anticancer agents, is the drug teroxirone, obtained from the German pharmaceutical firm of Henkel. Its efficacy in the treatment of a variety of cancers is being determined by the NCI in Phase I studies. The NCI acceptance of teroxirone for clinical trial was based principally on the results of European studies of its pharmacology and toxicology in preclinical tests.

Preclinical testing is underway in the United States of Italian-produced chemical analogs of Adriamycin and Daunorubicin. Interest in the analogs is based on their being less cardiotoxic and their anticancer efficacy in a broader spectrum of tumor systems.

An increase in chromosome length and gene amplification is the indication of hamster cell resistance to the effects of such mutagenic substances as colchicine and methotrexate. An American-Soviet genetics team advanced this pattern of cellular behavior when they isolated and characterized

a protein from colchicine-resistant cells. The amount of protein fluctuated with the degree of resistance of the cells and their chromosome length. When the chromosome was longest, the quantity of protein was greater than when the chromosome was shorter. This information could be of significance, as an indicator, for the more precise selection of those drugs for therapy whose activity will not be resisted by the diseased cell.

A product of American-Chinese collaboration is the utility in Chinese investigations of a technique, learned in the NCI, for producing, in hybridomas, monoclonal antibodies to aflatoxin B_1. These monoclonal antibodies and those to aflatoxin B_1-DNA adducts are being used to measure exposure to aflatoxin B_1, its effect on cell metabolism, and induced DNA damage in Chinese populations at high risk of developing liver cancer. In addition to finding aflatoxin B_1-DNA adducts in liver samples taken from Chinese donors in high-risk areas, American and Chinese collaborators have identified autoantibodies to the DNA adducts. The implication of these findings is that another lead exists for understanding further the mechanism(s) of human carcinogenesis as well as the early detection of liver cancer, and perhaps other types of cancer, using these biochemical markers.

Exchanges between American and Japanese scientists collaborating on studies of tumor promoters revealed the discovery of a new, highly potent class of tumor promoters that occur naturally in the indole alkaloids teleocidin and lyngbyatoxin. The source of the latter is an edible seaweed. Both compounds exert their influence through binding on cell membrane receptors.

BILATERAL AGREEMENTS AND OTHER COUNTRY-TO-COUNTRY ACTIVITIES

Cooperative cancer research programs under formal government-to-government treaties and other forms of Bilateral Agreements comprise a major segment of the international activities of the National Cancer Institute. The first of these cooperative cancer research agreements was established on 23 May 1972 with the signing of the USA-USSR Agreement for Cooperation in the Fields of Medical Science and Public Health. Subsequently, additional bilateral programs were formalized between the NCI and the Japanese Society for the Promotion of Science (1974); the Institute of Oncology, Warsaw, Poland (1974) under the USA-Polish People's Republic Agreement; in 1975 with the French Institut National de la Sante et de la Recherche Medicale (INSERM) under an earlier NIH Agreement with INSERM; the Cairo Cancer Institute (1976) under the aegis of the Agreement between the USA and the Arab Republic of Egypt; the Ministry of Science and Technology of the Federal Republic of Germany (1976); the Cancer Institute (Hospital), Chinese Academy of Medical Sciences, under the USA-People's Republic of China Accord for Cooperation in Science and Technology (1979); the National Cancer Institute of Milan and the Institute of Oncology of Genoa, Italian Republic (1980); and the National Institute of Oncology, Budapest, Hungarian People's Republic (1981).

The following sections relate to NCI's bilateral activities and the progress that has been achieved through these cooperative efforts.

Cooperation with the Soviet Union

The six original program areas -- since inception of the USA-USSR Health Agreement in 1972 -- were modified, restructured, and/or merged during the Sixth USA-USSR Meeting on the Problem of Malignant Neoplasia in Bethesda, September 1981. Thus, the scientific areas of Cancer Treatment, Carcinogenesis and Cancer Prevention are the foci for continuing collaboration between American and Soviet cancer specialists.

An NCI exchange scientist, during his November 1981 visit to Moscow's All-Union Oncologic Scientific Center, was able to engage in productive discussions in cancer chemotherapy, especially from the view of detailed analysis of raw data and clinical rounds for observation of Soviet patients entered into a parallel study of tamoxifen as an adjuvant in the surgical treatment of breast cancer. Preliminary data indicate positive treatment results with this agent, and the patient accrual under the study should yield promising data. The NCI provides the tamoxifen and research counsel for this parallel study.

The NCI has been provided with additional quantities of the Soviet drug, histar, for completion of preclinical testing in xenograft systems following demonstration of positive histar activity in L-1210 leukemia, B-16 melanoma, and CD8F mammary tumor. As well, the Soviets are preparing samples for NCI testing of three compounds of natural origin and their indication of potential use as anticancer agents. These are the antibiotic, bacuchiol; and the lichen products, chrysophanol and cynodontin.

During their January-February 1982 visit to the NCI and other US cancer centers, two Soviet chemotherapists joined American colleagues in the design and development of a protocol for a "Phase I Clinical and Pharmacologic Trial of Platinum Diammine (1,1-cyclobutane-dicarboxylato (2-)-O,O')." The agent is commonly referred to as CBDCA. The objectives of the Soviet study are: (1) establishing the maximum human tolerable dose of CBDCA; (2) evaluation of its toxicity in patients with previously treated and untreated malignancies; (3) antitumor activity of CBDCA; and (4) its clinical pharmacokinetics. The Pharmacologic Committee of the USSR Ministry of Public Health approved the use of CBDCA in Soviet patients; CBDCA has been provided to USSR scientists by NCI and the evaluation of the protocol is underway in the USSR and the Baltimore Cancer Research Center.

Meetings of American-Soviet working groups in the program areas of Carcinogenesis and Cancer Prevention will be convened in Moscow in the Fall of 1982. Prime consideration will be given to work plans for research activities considered to be mutually beneficial.

Cooperation with the Hungarian People's Republic

Based on the exchanges with a delegation of Hungarian cancer researchers visiting the United States, in December 1978, and Americans visiting Hungary, in June 1979, proposals had been exchanged for initiation of joint research between scientists of the two nations. Subsequently, on 23 February 1981, a Memorandum of Understanding for a Cooperative Cancer Program was signed by the Director, NCI, and the Director, National Institute of Oncology,

Budapest, HPR. Priorities for scientific activity are given to studies in the areas of: (1) cancer epidemiology/etiology; (2) experimental pathology; (3) immunology with emphasis on the leukemias and hematologic research; and (4) cancer therapy and developmental therapeutics.

Implementation of activities, under this agreement, followed in September 1981 as two American immunologists journeyed to Budapest and the NCI received three Hungarian specialists, each for 6 months.

The American immunologists devoted their time to exchanges of information on: (1) conditions under which receptors for immune globulins are shed from the cell surface and the nature, structure, and function of the shed receptors vis-a-vis those that are bound to the cell surface; (2) natural killer (NK) cell activity in normal human donors and NK activity in patients with various types of cancer, especially breast and lung cancers; (3) analyses of NK cytotoxicity and its possible utility for determining the prognosis in cancer patients; (4) the production of high levels of alpha and gamma interferon from human peripheral blood leukocytes; and (5) the production of a wide variety of monoclonal antibodies. They participated, as well, in a meeting on "Signals and Signal Processing in the Immune System."

An experimental chemotherapist from the National Institute of Oncology, Budapest, spent her 6 months in the NCI Laboratory of Medicinal Chemistry and Biology engaging in studies designed to investigate the resistance of murine tumor cells to alkylating agents utilized as anticancer drugs. Her work and that of her NCI colleagues has confirmed the role of the tripeptide, glutathione, in resistance of tumor cells to alkylating agents. She completed in vitro studies with buthionine sulfoximine, an inhibitor of glutathione biosynthesis. These studies have demonstrated that it is possible to completely sensitize the resistant cancer cell to the cytotoxic effects of an anticancer drug such as L-phenylalanine mustard (L-PAM), commercially known as melphalan. L-PAM is one of the effective drugs, used in combination with others, for the treatment of breast cancer. Additionally, she devoted considerable effort toward the development of amino acid specific, synthetic-pelleted diets for use in these experiments. She contributed significantly to the evaluation of an Alzet osmotic minipump for continuous intraperitoneal infusion of agents such as buthionine sulfoximine and anticancer agents, thus affording a concentrating effect of antitumor agent at the cancerous site.

The transplantation biologist/tumor immunologist from the National Institute of Hematology and Blood Transfusion, Hungary, spent his initial 4 months in the Sidney Farber Cancer Institute (SFCI). His efforts were devoted to joint research on developing, in endothelial cells (EC), monoclonal antibodies active against T-cells and monocytes. His approach was to collect endothelial cells from the umbilical cord and to amass the antigens acting against the monoclonal antibodies. Based on his research activities at the SFCI, the Hungarian scientist concluded that EC are rich in their expression of HLA-A, B and C antigens, but their expression of HLA-DR is anomalous. EC also share myelomonocytic surface antigens, My-7, Mo-3 and Mo-4. The relevance of these findings to transplantation is enhanced by initial observations that Mo-4 is also expressed in human kidney endothelium as shown by immunoperoxidase reactions. He became acquainted with the method for phenotyping leukemic cells by means of monoclonal antibodies and, by virtue of an SFCI gift

of a series of monoclonal antibodies, he has begun phenotyping leukemias and lymphomas in his laboratory in Budapest. Because of the SFCI interest in the Hungarian study on HLA-antigen distribution in gypsies and in the incidence of various diseases in this ethnic group, the Hungarian scientist has provided the SFCI with more than 30 blood samples of Hungarian gypsies for typing the complement phenotypes.

An experimental pathologist/chemotherapist from the Semmelweis Medical University, Budapest, spent 6 months at the Roswell Park Memorial Institute (RPMI) to study methods of tumor disaggregation -- mechanical and enzymatic -- to yield single cancer cell suspensions. At the same time, he developed cell separation methodologies for biochemical, biologic, and morphologic characterization of the various tumor subsets derived from the human tumor cell suspensions. The subsets, then, were tested for their sensitivity to anticancer drugs. Among the 17 tumors studied, there were great differences in the number of cells obtained by disaggregation. Considering the disaggregated samples as the base, the recovery rate ranged from 30.7 to 82%, with mean values of 49% and 56.3%, respectively, for mechanically and enzymically disaggregated samples. In the six cell fractions of a Percoll gradient, intracellular concentration of the anticancer agent, Ara-C, and ^{3}H-thymidine was higher in the fractions with more viable cells. The effect with a platinum derivative drug was the opposite, in that results suggest an intensive binding to non-viable cells. These experiments are continuing at RPMI and in Budapest.

Cooperation with the People's Republic of China (PRC)

During its meeting on 19 November 1980, in the PRC, the USA-PRC Joint Committee on Medicine and Public Health approved the joint cancer proposal which is included in Annex 2 to the USA-PRC Protocol for Cooperation in the Science and Technology of Medicine and Public Health. The American-Chinese cooperative cancer effort, thus, includes studies of the epidemiology, early detection and diagnosis, treatment and multidisciplinary studies of esophageal cancer.

Under the aegis of the USA-PRC Agreement and during the interval of September-October 1981, five American scientists visited the People's Republic of China -- two for periods of 2 weeks; two each for 4 weeks; and the fifth for a period of 6 weeks. One of these, a biochemist/pharmacologist, traveled for the purpose of participating in workshops and teaching Chinese colleagues in the methods of organic and medicinal chemistry for the design and development of anticancer drugs, their preclinical testing, and potential utility in treating esophageal and other cancers. He was provided with abundant information on Chinese antineoplastic agents such as the alkaloids harringtonine and homoharringtonine, which are found useful by the Chinese in acute or chronic granulocytic leukemia, AML, and malignant lymphosarcoma. He learned of quite a few folk remedies for cancer, not verifiable but worthy of scientific surveillance, among which are herbal derivatives of some 35 different plants readily available in the PRC.

In this context, another of the American visitors participated in scientific exchanges in pharmaceutical institutes, principally, on Chinese development of anticancer drugs and their utilization of products of natural origin in the treatment of cancer. Chinese antineoplastic agents were made available to him for return to the NCI for testing. Among these was pingamycin,

an antibiotic shown by the Chinese to be effective against hepatoma and cancers of the cervix and breast. A promise was made by officials of Beijing Institute of Antibiotics to send all novel and unique compounds to the NCI for testing.

The third American, a biochemist/nutritionist, engaged in scientific exchanges on the relationship of dietary selenium to the incidence of esophageal and other cancers and interacted with Chinese on matters related to chemical carcinogenesis. While in Xi Chang, Sechuan Province, he had opportunities to observe the Chinese effort on Keslan disease, a cardiomyopathy prevalent in children and endemic to areas where soil selenium is extraordinarily low. A dearth of dietary selenium appears to be associated with the incidence of esophageal cancer in regions of high risk. Based on these exchanges, a joint American-Chinese study has been initiated on the efficacy of dietary supplementation as a prophylactic and/or cancer preventive measure. Beta-carotene, selenium and other nutrient substances are being tested in some 20,000 Chinese persons in geographic regions of high risk.

Early detection of cancer, with particular emphasis on cytogenetic-epidemiologic, as well as pathomorphologic analyses and technologies, were among the scientific topics pursued by the last two American visitors.

In compliance with the provisions in the 1980 USA-PRC cancer accord, the NCI has received three Chinese principals, for protracted periods of one year each, for study and joint research in the NCI and other American cancer centers. An epidemiologist from the Wuhan Medical College and another epidemiologist from the Xarbin Medical University are pursuing study/research programs under the mentorship of the staff of NCI's Field Studies and Statistics directorate, within the Division of Cancer Cause and Prevention. During their first 4 months, February through June, they devoted their time to becoming acquainted with NCI's programs in analytic epidemiology, biometrics and medical statistics as well as to learning how to use computer terminals and the language of the computer.

The third of the Chinese visitors, a thoracic surgeon from Beijing, has been pursuing activities related to observation and training in: (1) surgical management of thoracic and esophageal malignancies; (2) bronchoscopy and other endoscopic procedures; (3) the use of lasers in hematoporphyrin-derivative photoradiation therapy; and (4) image intensification of the fluoro- and endoscopic site.

Prior to the adoption of the 1980 USA-PRC collaborative cancer program, a joint NCI-Cancer Institute (Beijing) study was initiated in the area of biochemical epidemiology. The research embodies the collection and cultivation, in China, of human fetal tissues (liver, esophagus, stomach, and bronchi) for use in the identification of biochemical markers that may be associated with cancers of these organ sites. In tissue samples brought to the NCI by the Chinese collaborator, aflatoxin B_1-DNA adducts have been isolated from liver samples taken from donors in cancer high-risk areas. This was done by use of monoclonal antibodies to aflatoxin B_1, a technique developed by NCI scientists and taught to the Chinese.

Cooperation with the Arab Republic of Egypt

This effort between the NCI and the National Cancer Institute of Cairo University continued under the Special Foreign Currency Program (PL 480). This study includes three ongoing programs: treatment of bladder cancer, cytopathology of bladder cancer and cooperative clinical studies, under the Southwest Oncology Group (SWOG), for the treatment of breast cancer, head and neck cancers, adult lymphomas, and childhood lymphoma.

In 1981, the results of a joint American-Egyptian study, initiated in Egypt in 1976, were published on the evaluation of urinary cytology as a screening method for the early detection of bladder cancer in a rural community where the parasitic disease, schistosomiasis, is endemic. Additionally, the study included the identification of a high-risk group related to schistosome infestation and the determination of the prevalence of urinary bladder carcinoma and its precancerous lesions in that population. The definition of the high-risk group, in this study, proved to be valid since all tumors were detected among farmers at high risk; and, no tumors were detected among the control groups of the rural population. In farmers, who work daily in the field, the schistosomal infestation, with frequent reinfection, is most intense. Nonfarming villagers, living in the same rural community, get milder forms of infestation often related to accidental contact during swimming or washing. This is considered to be epidemiologic evidence of the relationship between schistosomiasis and urinary bladder cancer.

Urine cytology, in this experience, proved to be an effective method for population screening. The yield of the screening was 11 cases of histologically confirmed carcinomas among 8,744 individuals screened. All 11 cases were in the high-risk group; none were detected in the two low-risk control groups. A yield of 2 per 1,000 of high risk was obtained. This would also constitute a 4/10,000 of all rural population. And, knowing that about half of the population is below the age of 20, the prevalence rate could be estimated as 8/10,000 of the adult rural population.

Thus, the American and Egyptian scientists successfully concluded a joint project and demonstrated that a screening program is productive, if conducted in and restricted to high-risk groups. In this instance, it is especially true in view of the available resources including limited funds, manpower, and medical facilities.

In May 1982, two senior Egyptian investigators were invited to participate in the International Workshop on the Influence of the Environment on Leukemia and Lymphoma Subtypes.

A pathologist from the Cairo University will spend 6 months in the Laboratory of Pathology, National Cancer Institute, to receive advanced training in hematology and to study the use of marker techniques in lymphoma investigations.

US-Japan Cooperative Cancer Research Program

The Etiology Program Area covers cancer epidemiology, chemical carcinogenesis, viral and biological carcinogenesis and molecular biology. The main aims are to clarify the cause of human cancers and to determine the mechanism of carcinogenesis. It is anticipated that cancer prevention may evolve from the progress made in solving the etiology of cancer.

In November 1981, a seminar entitled "Carcinogenesis and Gene Expression in Liver Cell Culture" was held in Hawaii. Discussions dealt with patterns of expression of various genes during carcinogenesis, especially hepatocarcinogenesis. Changes in expression of various genes were reflected by the production of enzymes and proteins which were not found in the normal liver. The change is so pleiotropic that the mechanisms of some of these changes would be intrinsically relevant to the carcinogenic process. It became clear that there are three kinds of liver cells in culture and the specificity of each cell population was discussed to learn more about hepatocarcinogenesis. There were 9 Japanese, 8 American and 1 French investigators participating in the meeting.

A conference on "Intestinal Metaplasia and Stomach Cancer" was held in March 1982 in Shimodu, Japan. At this conference many aspects of intestinal metaplasia were considered. New histological and biochemical enzymatic techniques as well as new methods for histochemical and immunological procedures were presented. An interesting finding on the relationship between mesenchymal and epithelial tissue was presented; namely, that stroma can influence and guide the development of epithelial tissues. Although there was no agreement on whether intestinal metaplasia is a precursor lesion for stomach cancer or only an associated condition, some speakers are of the opinion that a definite precursor relationship could be demonstrated. Others believe that there is no causal relationship between intestinal metaplasia and stomach cancer. Since the causes of stomach cancer are very complex, it is reasonable to expect that some cancers can be formed by a process not related to the formation of intestinal metaplasia. However, the association of intestinal metaplasia with many cases of stomach cancer appeared to be strong. The conference was an effective catalyst in stimulating new ideas among the 13 Japanese and 6 American scientists who participated.

During the year, 5 Japanese scientists and 2 American investigators were selected as Exchange Scientists and engaged in collaborative research activities in laboratories in Japan and in the United States on projects in viral oncology and chemical carcinogenesis.

In the Cancer Biology Program Area, a conference on "Cell Interaction and Cancer" was held in November 1981 in Kyoto, Japan. Presentations covered a diverse series of topics ranging from cell-to-cell adhesion in primitive cell systems to studies of the pathology and biology of human cancer cells. Discussion on differentiation of tissue mast cells and the growth of leukemia cells in microenvironments, cell-binding sites of collagen, heparin, and other macromolecules, and regulatory proteins on transformed cells, drew considerable attention from the participants. Following the 3-day meeting the final session on "Cell Interaction" was opened to the public, drawing about 100 Japanese professionals and graduate students, in order to disseminate the latest advances in molecular biology in relation to cancer.

In November 1981, the immunology group sponsored a meeting on the "Analysis of Mechanisms for Induction of Tumor-Specific Immunity and Experimental Approaches to Tumor Immunoprophylaxis and Therapy" at Harvard School of Medicine in Boston, Massachusetts. Topics discussed at the meeting included the antigenic nature of tumor cells, the expression and regulation of tumor antigens, the fundamental immunologic processes in host response to tumors, and preclinical applications of tumor immunology. There were 8 Japanese and 8 American participants with several observers from nearby research centers.

In the Cancer Diagnosis Area, a meeting on the "Application of Cytology Automation in Cancer Cytology and Cell Biology" was sponsored in March 1982 in Hakone, Japan. Six American and 16 Japanese investigators met to discuss the latest information on instrumentation and data analysis, the application of automated cytology in cell biology, a new technological approach for sample preparation and the application of automated cytology in cancer detection.

During the year an American cell biologist spent 3 weeks at the Cancer Institute in Tokyo, Japan, involved in cooperative research, while 3 Japanese scientists visited several cancer centers in the U.S. to discuss research advances in molecular biology and cancer immunology.

The Cancer Treatment Program Area had a particularly active year in sponsoring three meetings. The seventh annual program review meeting entitled "Development and Evaluation of Treatment of Cancer with Combined Modalities" was held in Gettysburg, Pennsylvania, in November 1981. The discussions covered three different topics: the treatment of oat cell carcinoma of the lung in the United States and Japan; new development of methodology in clinical and preclinical investigations, which included the progress of human tumor cloning assay as a predictor for the sensitivity in situ of human tumors to administered drugs; and topics on new antitumor agents, natural and synthetic, now in Phase I and II stages and also those still in preclinical steps of development. At this meeting 16 American and 10 Japanese oncologists presented talks that stimulated considerable discussion on new areas of clinical research.

In October 1981, the first meeting on "Preclinical and Clinical Trials of Tumor Immunology" was held in Maui, Hawaii. Subjects discussed included experimental studies of cancer immunotherapy, possible application of human T-hybridomas for immunotherapy of cancer, monoclonal antibody therapy in man, adjuvant immunotherapy of lung cancer with bacterial cell wall skeleton preparations, current status of interferon therapy and clinical trials using immunotherapy. The discussions were very actively pursued by the 11 Japanese and 6 American clinical investigators.

A group of 12 Japanese and 9 American oncologists met in Tokyo, Japan, in November 1981, to discuss recent advances in the "Treatment of Bladder Cancer". The American delegation included several active members of the NCI National Bladder Cancer Program. The sessions included subjects on superficial cancer of the bladder, deeply invasive cancer of the bladder, metastatic disease, prevention of bladder cancer, conduct of clinical trials and projected cooperative bladder cancer treatment programs. The results of this meeting were fruitful and served to establish a foundation for

further cooperative studies of bladder cancer as well as basic and clinical investigations on bladder cancer. Similar criteria for diagnosis and treatment protocols were developed which would be useful for investigators in both countries in order to facilitate the mutual understanding and utilization of diagnostic, therapeutic and clinical technology. It is now possible to establish collaborative clinical trials between Japan and the United States.

During the year 3 American investigators, a radiation oncologist and 2 urologists, visited Japanese laboratories to discuss recent developments in their respective fields. Also 2 Japanese scientists visited American laboratories to discuss radiation biology and engage in clinical studies.

The Interdisciplinary Program Area sponsored a seminar on "Neural Crest Tumors" in Hawaii in March 1982. At the meeting discussion focused on certain syndromes associated with tumors or familial neoplasia derived from the neural crest and the differences between the two countries in the frequencies of these tumors.

The seminar on "T-Cell Leukemia/Lymphoma--Role of Human Type C Retroviruses" was held in Seattle, Washington, in March 1982. The participants included viral oncologists, pathologists and epidemiologists to discuss the nature of the T-cell leukemias and probable etiologic agents. It was learned that teams of American and Japanese virologists independently isolated and identified retroviruses which are associated with Human T-Cell Leukemia Virus (HTLV) and the Adult T-Cell Leukemia Virus (ATLV), respectively. These are newly identified human retroviruses which seem to be identical or very similar to each other. The viruses are closely associated with mycosis fungoides, Sezary syndrome, and Adult T-Cell Leukemia, which belong to the category of differentiated T-cell lymphoma and leukemia. The viruses have been found to be endemic in the southwestern part of Japan and certain Caribbean islands. The pathogenicity of these viruses seems to be low with a long latent period. Highlights of this meeting will be published in the Journal of the National Cancer Institute.

In June 1982, the NCI-JSPS Joint Steering Committee met in Tokyo, Japan, to review and evaluate the bilateral activities of the past and current year. The Joint Steering Committee also discussed and presented the program activities to sponsor 10 meetings and provide support for the exchange of scientists for the coming year.

During the past year, an American pathologist visited several Japanese laboratories to discuss and plan cooperative studies on leukemias and lymphomas. In addition, one Japanese exchange scientist visited several American cancer centers to study the classification of lymphomas, while another Japanese immunologist studied methods for in vitro sensitization and testing of cytotoxic lymphocytes.

U.S.-Poland Cancer Program

In spite of the political situation in Poland, the exchange of scientists has continued to be effective. During this fiscal year an American nuclear chemist spent 6 weeks at the Institute of Oncology in Warsaw to conduct collaborative research in nuclear medicine and radio-pharmaceutical research

with one of the senior Polish investigators. They investigated possibilities of using microspheres as carriers of radioactive isotopes for treating certain types of cancers, such as liver cancer. Experiments demonstrated the stability of microsphere carriers in animal models.

In the fall of 1981, a Polish tumor biologist visited Stanford University, the University of California at Berkeley and the University of Wisconsin to discuss and learn about the recent advances in radiation biology, cancer immunology and cancer biology. A young Polish biologist from the Institute of Oncology in Warsaw spent 6 months collaborating in DNA polymerase research at the Roche Institute of Molecular Biology, Nutley, New Jersey.

A Polish biochemist from the Polish Academy of Sciences engaged in research on chemical carcinogenesis at the University of California at Berkeley. A senior pharmacologist spent 3 months at the Roswell Park Memorial Institute in Buffalo and at the National Cancer Institute to discuss and engage in collaborative research in biochemical pharmacology and tumor immunology. Also, a young Polish molecular biologist will arrive to spend one year in the Laboratory of Biochemistry, National Cancer Institute, to receive advanced training in molecular biology.

The Director of the Institute of Oncology in Warsaw attended the 13th International Cancer Congress in Seattle, Washington, and visited cancer centers in Seattle, Los Angeles, Houston and the National Cancer Institute to discuss the progress of the Polish National Cancer Program as well as the progress of the U.S.-Poland Cancer Program.

Under the agreement of cooperation between the National Cancer Institute and the National Research Institute of Mother and Child in Warsaw, a pediatrician from the Polish institute observed and studied treatment of childhood cancer in the Pediatric Oncology Branch of the National Cancer Institute.

U.S.-France Cancer Program

The Basic Cancer Research Program Area has responsibility for cooperation in the areas of biological and chemical carcinogenesis, cellular and molecular biology, viral oncology, cancer immunology and hormone research as related to cancer.

In March 1982, the NCI and INSERM Program Coordinators and representatives from the sponsoring agencies met in Bethesda to review, evaluate and discuss policy and program changes. Discussions focused on science policies of the new administration in France, the support of cancer research by the respective agencies, and policy changes. The group agreed to continue to stimulate and support the exchange of scientists, to exchange information on NCI and INSERM research grants, to identify promising areas for new collaborations and to consider possible ways of restructuring the present Basic and Clinical Cancer Research Program Areas.

During this fiscal year 5 American investigators spent periods ranging from 2 weeks to 6 months at French laboratories for collaborative studies in hormone and receptor research, studies on nucleic acids, mutagenesis

and carcinogenesis. There were 4 French investigators who engaged in collaborative research on gene expression, hepatitis virus antigens, viral oncology and antiviral interventions of certain types of cancers.

In the Clinical Cancer Research Program Area the Joint Committee for Clinical Cancer Research met in June 1982 in Paris, France, and convened a review and program planning meeting. The discussions focused on the progress made in cooperative research in clinical studies on breast cancer, treatment of osteosarcoma, biochemical and clinical pharmacology, and hormone therapy of breast cancer. Discussions were also held on the possibility of changes in the program policies taking place during the coming year.

During the year an American epidemiologist spent 6 months collaborating with French investigators on biostatistics and clinical epidemiology. An American endocrinologist spent 2 weeks conferring with French experts on the biochemical effects of estrogen in endometrial cancer. A French pharmacologist is spending a period of 18 months at the Medical College of Virginia to receive advanced training in biochemical pharmacology in order to establish a collaborative effort with his American colleagues upon his return to France.

U.S.-Germany Cancer Program

In the Environmental Carcinogenesis Program Area an epidemiologist from the German Cancer Research Center in Heidelberg, Germany, visited the Environmental Epidemiology Branch, National Cancer Institute, to confer and engage in a case-control study in occupational epidemiology of workers in certain hazardous occupations. He also gained experience in the conceptual aspects of epidemiological investigations, data analysis and the implementation of studies in the network of surveillance and monitoring. He also visited the Department of Environmental Medicine, New York University Medical Center to confer with several senior investigators to plan joint studies on workers in the chemical industry and on the establishment of a system for cancer registration.

A pathologist from the German Cancer Research Center spent 2 months at the Experimental Cancer Registry, National Cancer Institute, to continue his cooperative studies with the Registry staff. Joint studies were conducted to develop a common system of classification and terminology of experimental cancers and tumors to establish a comparable system at the two centers. The newly established registry in Germany will make it possible to exchange materials and specimens for comparative studies.

The Program Coordinators for the Developmental Therapeutics Program Area will meet in Germany in September 1982 to discuss program policies and plan for the exchange of scientists between the two countries, as well as plan for workshops to be held during the coming year to discuss collaborative activities in drug development and clinical studies.

U.S.-Italy Cancer Program

Pursuant to a meeting of American and Italian cancer specialists in April 1979, agreement was reached early in 1980 to pursue joint studies in Cancer Therapeutics and Cancer Prevention. American and Italian Working Groups

for both of these programs have been established, and meetings were held in the fall of 1981.

In Cancer Therapeutics, the following topics were discussed and considered for implementation of collaborative research: (1) Chemotherapy of Stage I-III Breast Cancer; (2) Phase I Studies of Deoxycoformycin in Pediatrics plus Deaminase Monitoring; (3) Phase II Pediatric Studies; (4) Experimental Metastasis Models and Therapy Sensitivity; (5) Fundamental and Clinical Studies of Biologic Response Modifiers; (6) Studies of Pain in Adults and Children, plus Pharmacologic Monitoring.

The Annual Review Meeting was held in Bethesda, Maryland, in November 1981 to review the activities during 1980 and to discuss progress of collaborative clinical studies in biochemical pharmacology, breast cancer treatment, pediatric oncology, studies on metastases, trials with anthracyclines, radiation oncology and the recent progress on biological response modifiers. The Joint Committee on Therapeutics also discussed plans for 1982 and made tentative plans for the next annual meeting on Combined Modalities Treatment to be held in October 1982.

During the year two pharmacologists from the Roswell Park Memorial Institute in Buffalo, New York, visited Italian research centers to discuss and plan collaborative research on the study of model systems to investigate drug metabolism and to obtain the latest information on anthracycline drugs being tested and used in Italy. They also presented lectures on their own research activities.

A young Italian pediatric oncologist visited and observed treatment of childhood cancers at the St. Jude Children's Research Hospital in Memphis, Tennessee, and the Pediatric Oncology Branch at the National Cancer Institute. Another Italian pediatrician spent 2 months at the National Cancer Institute to cooperate on a study of Phase I and II drugs to treat solid tumors and acute lymphoblastic leukemia. He also gained information of dose-limiting toxicity and antitumor activity of drugs currently being used to treat bone sarcomas, neuroblastoma and other childhood cancers.

An Italian immunologist spent 2 months at the Biological Response Modifiers Program, Frederick Cancer Research Facilities of the National Cancer Institute to learn the latest techniques in testing for biological response modifiers.

During the year a young Italian oncologist arrived to spend one year at the Roswell Park Memorial Institute to obtain advanced training in biochemical pharmacology and experimental chemotherapy.

In the Cancer Prevention Program Area, the U.S.-Italy Joint Committee on Prevention met in Bethesda in November 1980 to discuss areas for cooperative research. The general areas include: cancer epidemiology; chemical carcinogenesis; detection and diagnosis; and biologic carcinogenesis. The mechanisms for implementation involve an exchange of scientists, an exchange of information and research resources, and the design and development of joint research projects.

The annual review meeting for the Prevention Program was held in conjunction with the Workshop on Leather, Benzene and Shipyard Workers, which was held in Portofino, Italy, in October 1981. The workshop involved discussion on the development of collaborative studies to identify the environmental determinants of specific cancers. Unique opportunities exist within Italy to assess the impact of certain occupational exposures, particularly benzene, chromates, and dusts in the leather and shoemaking industries. Also the workshop focused attention on the risk of lung cancer among shipyard workers.

Four members of the American delegation also spent additional time after the workshop to visit several leading Italian cancer research centers to give lectures in their specialties and to discuss areas of cooperative research activities.

Another American epidemiologist spent 2 months at the Istituto di Oncologia, University of Genova, Genova, Italy, to discuss and plan for cooperative studies in occupational epidemiology.

A young Italian viral oncologist spent 13 months at the Mt. Sinai Hospital in New York to study the relationships between polyamine biosynthesis and differentiation in an attempt to elucidate the biological role of these compounds in the steps leading to differentiation of the erythroleukemia cells. An Italian biochemist visited for 3 months the Pathology Department of the University of Texas System Cancer Center to learn techniques for the detection of DNA alterations induced by carcinogens. Also he made plans to continue collaborative studies for differential and systematic enzymatic digestion of DNA and the separation and analysis of the DNA fragments. An epidemiologist from the Istituto di Oncologia in Genova spent 3 weeks at the National Institute of Occupational Safety and Health in Cincinnati, Ohio, to study occupational epidemiology.

THE INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM

The ICRDB Program, established by the National Cancer Act of 1971, has developed into an effective, multifaceted system for the rapid exchange of cancer research findings among scientists. This international resource for cancer information is comprehensive and of service to cancer researchers throughout the world. To facilitate the transfer of available cancer research information, the ICRDB Program has: (1) established three online computer databases known as the CANCERLINE system, which enable scientists to retrieve cancer information easily at more than 2,500 locations within the United States and in 13 other countries; (2) developed a series of publications providing complete coverage of cancer research information, in special formats designed for easy use and quick reference; and (3) supported a variety of specialized information collection, analysis, and dissemination activities.

The Computer Databases of the CANCERLINE System

CANCERLIT, CANCERPROJ, and CLINPROT are the three databases comprising the CANCERLINE System.

CANCERLIT contains nearly 320,000 substantive abstracts of information accumulated from published papers and those presented at scientific meetings, symposia, and conferences; books; technical reports; and research theses. CANCERLIT is growing at an annual rate of nearly 45,000 abstracts, selected from over 3,000 biomedical journals. Because of stringent input processing requirements and monthly updating of CANCERLIT, the most recently published research results are quickly available to cancer researchers worldwide. Since early 1980, all new literature entries have been indexed with the Medical Subject Heading (MeSH) vocabulary developed by the National Library of Medicine (NLM), making their retrieval easier during online searching. ICRDB Program screening, indexing, and abstracting activities are performed under contract by the Franklin Research Center in Philadelphia.

Descriptions of some 20,000 current cancer research projects, in 83 countries, are the elements of the CANCERPROJ database, the most comprehensive source available for ongoing cancer research project information. Included are some 5,000 foreign project descriptions collected by an international network of data input coordinators. Until November 1981, collection, input, and quarterly updating of the project descriptions in CANCERPROJ were performed by the Current Cancer Research Project Analysis Center (CCRESPAC) under an interagency agreement with the Department of Commerce. The activity is continuing via interim agreements until a new contract can be awarded.

Summaries of nearly 3,100 experimental cancer therapy protocols are the substance of CLINPROT, the database providing worldwide access to information on new procedures, agents, and combinations of modalities/agents being evaluated for treating cancer patients in major American and foreign cancer centers. 1,500 of these protocols are clinically active while the remainder serve as a unique reference. Collection and input of protocol summaries and quarterly updating of CLINPROT are the contractual function of Informatics General Corporation.

The cancer information contained in the databases of CANCERLINE is available through the computerized biomedical information network of the NLM. NLM's effort in CANCERLINE is supported by an intra-agency agreement.

Foreign access to CANCERLINE has been enhanced by the recent addition of CANCERLINE to the EURONET system operated by a consortium of the major hosts in the European Community offering online scientific and technical information and interactive retrieval services. Arrangements are being completed for the sale of the CANCERLINE databases, worldwide, through the National Technical Information Service (NTIS).

ICRDB Program Publications

CANCERGRAMS are published monthly as current awareness bulletins containing abstracts of recently published literature in 66 major cancer research areas. Each month, CANCERGRAMS are compiled from the most recent acquisitions of CANCERLIT and contain carefully selected and organized abstracts screened from the more than 3,000 biomedical journals contributing to CANCERLIT. They are prepared for publication by scientists at three Cancer Information Dissemination and Analysis Centers (CIDACS) and a network of nearly 100 researcher consultants. Disseminated to some 12,000 scientists worldwide,

CANCERGRAMS enable recipients to keep up with the most relevant portions of the vast cancer literature with minimum time and effort.

Fifteen ONCOLOGY OVERVIEWS are published each year. Each of the OVERVIEWS contains retrospective bibliographies, with abstracts, of recent literature and provides comprehensive coverage of specific topics of high current interest to cancer researchers. Included are the most relevant abstracts published during the past several years on the OVERVIEW topic, providing in-depth coverage of emerging foci of cancer research. OVERVIEWS are prepared by scientists at the CIDACS, with review and editorial commentary by well-known researchers in each topic area. They provide an excellent means of rapidly updating knowledge in burgeoning areas of cancer research.

The COMPILATION OF EXPERIMENTAL CANCER THERAPY PROTOCOL SUMMARIES, now in the 6th Edition, April 1982, is derived from the CLINPROT database and contains over 1,500 summaries of Phase II and Phase III clinical trials currently in progress in cancer centers of the world. The COMPILATION is indexed by tumor, agent, and protocol identification number, and is a useful reference for the practicing oncologist. Protocols that have been closed to patient entry during 1981 are listed by title and include the name of the principal investigator and his or her mailing address. The 6th Edition includes a brief, preliminary list of the Phase I protocols that were activated in 1981. This annual document is prepared, under contract, by Informatics General Corporation.

The DIRECTORY OF CANCER RESEARCH INFORMATION RESOURCES, 3rd Edition, 1981, contains over 900 entries covering the broad spectrum of resources available to health professionals.

The foregoing ICRDB Program publications are printed and distributed by the NTIS under an interagency agreement.

Special Information Activities of the ICRDB Program

Three contract-supported CANCER INFORMATION DISSEMINATION AND ANALYSIS CENTERS (CIDACS) function as information resources in three broad areas of cancer research. These are the CIDAC for Diagnosis and Therapy, University of Texas System Cancer Center, M.D. Anderson Hospital and Tumor Institute, Houston; and the CIDACS for Carcinogenesis and for Cancer Virology, Immunology and Biology, both at the Franklin Research Center, Philadelphia. Each CIDAC is staffed by scientists and served by a consultant network with special expertise appropriate to the fields pertinent to each CIDAC. Within its own subject area, each CIDAC prepares CANCERGRAMS and ONCOLOGY OVERVIEWS, performs custom CANCERLINE searches, and provides scientific guidance to the ICRDB Program.

The CURRENT CANCER RESEARCH PROJECT ANALYSIS CENTER (CCRESPAC) collects and processes ongoing research project information and generates the CANCERPROJ database. A contract will be awarded, following recompetition, to an agency for resumption of the functions and activities previously conducted by the Smithsonian Science Information Exchange under an interagency agreement.

A CLEARINGHOUSE FOR ONGOING RESEARCH IN CANCER EPIDEMIOLOGY is a cooperative project supported jointly by the ICRDB Program, the International Agency for Research on Cancer (IARC) in Lyon, France, and the German Cancer Research Center in Heidelberg, Germany. The CLEARINGHOUSE, located in Lyon, collects, processes, and disseminates detailed data on research related to cancer epidemiology and studies of human cancer causation in countries throughout the world. The CLEARINGHOUSE also prepares lists of epidemiology researchers and resources, responds to technical questions and produces an annual Directory of On-going Research in Cancer Epidemiology.

The LATIN AMERICAN CANCER RESEARCH INFORMATION PROJECT (LACRIP) was developed through the ICRDB Program in collaboration with the Pan American Health Organization (PAHO) and its Regional Library of Medicine (BIREME) in Sao Paulo, Brazil. LACRIP serves as the source for identifying, collecting, and supplying Latin American biomedical literature, summaries of ongoing cancer-related research projects and active therapy protocols in Latin America for inclusion in the CANCERLINE system. PAHO also serves as the center for searching ICRDB databases and providing documents and data in response to requests for information from cancer researchers in Latin America. An automatic SDI service is also provided to cancer researchers and clinicians in Latin America.

Through LACRIP, a series of collaborative clinical studies were developed between 10 cancer centers in the United States and 12 centers in Latin America. LACRIP maintains the clinical data gathered at the Latin American centers and arranges for the exchange of professional staff between centers in order to promote a better understanding of current cancer treatments available in the United States. These activities are now supported completely by NCI's Division of Cancer Treatment following the termination of ICRDB Program support in April 1982.

In cooperation with the International Union Against Cancer (UICC), the ICRDB Program provides partial support for a special COMMITTEE FOR INTERNATIONAL COLLABORATIVE ACTIVITIES (CICA), within the framework of the UICC. One of the CICA activities is the collection of data on ongoing cancer research projects (including clinical protocols) from more than 70 countries. CICA personnel identify and promote collaborative projects among cancer centers and cancer scientists in different countries. CICA periodically publishes an updated International Directory of Specialized Cancer Research and Treatment Establishments, which contains descriptions of more than 700 of the world's cancer centers. An International Cancer Patient Data Exchange System (ICPDES) has been established as part of the CICA project. Present participants include 10 European and 5 United States cancer centers. The ICPDES could result in the establishment of the first internationally recognized and standardized tumor registry, providing comparative data of value, from a multitude of countries, in cancer epidemiology, treatment and prevention.

Scientist-to-Scientist Communication

The ICRDB Program, through the UICC in Geneva, Switzerland, encourages INTERNATIONAL SCIENTIST-TO-SCIENTIST COMMUNICATION through the International Cancer Research Technology Transfer Program (ICRETT). This program promotes direct and rapid transfer of information about new or improved technology or methodology between two or more investigators located in different countries.

This is accomplished by supporting short-term visits for the purpose of conducting brief collaborative research projects by investigators from different countries performing similar research investigations on a cancer problem. Since the inception of the program in 1975, some 600 ICRETT awards have been granted (through July 1982).

In many instances, ICRETT associations between scientists from different countries develop into significant collaborative studies that otherwise might not have had the impetus and resources with which to evolve. For instance, an area of study known as "chrono-oncology" is attracting the attention and interest of many oncologists. The phenomenon relates to optimum timing of drug administration during the daily cycle, the 24-hour temperature pattern of tumors, etc. In this context, a chrono-oncologist from the University of Minnesota journeyed to Chandigarh, India, as an ICRETT awardee to demonstrate radiation therapy and surgery-radiation therapy procedures and methodologies in the clinical management of cancer. He introduced the Indian oncologists to chronobiology (circadian or 24-hour biology cycle) and chronochemotherapy and their relationship to immunobiology and immunotherapy. In the course of his visit he arranged for his group to be consultants and to assist the Indian scientists in the analysis of data emanating from their studies.

Subsequently, an oncologist from Karnataka, India, utilized the resources of his ICRETT award to study in the Chronobiology Laboratories of the University of Minnesota. As such, he and his hosts collaborated on analyzing clinical data obtained in India for the tumor temperature patterns of carcinoma of the cervix. They then studied the effects of adrenocorticotropic hormone (ACTH) as pretreatment for improving the tolerance of Adriamycin when administered at certain hours of the day. The study has now been extended to include tumors of the head and neck.

A Liberian epidemiologist/biometrist observed and learned the principles for organizing a cancer registry during her period of ICRETT study in Dundee, Scotland. Her objective was to develop skills for improving methods in Liberia for the registration of new cancer cases and for follow-up studies of cancer morbidity/mortality.

While in the National Cancer Institute, an ICRETT-sponsored Yugoslav immunologist studied techniques for the isolation, purification, and characterization of lung tumor-associated antigen. There now is a continuous exchange of information between him and his NCI host on the results of the use of this antigen—a glycoprotein containing sialic acid—in the immunodiagnosis of human lung tumors.

With the assistance of his ICRETT award, an epidemiologist from the People's Republic of China visited cancer registry facilities in Birmingham and Oxford, England, and Lyon, France, where he benefited from their design and experience with systems for registration of cancer incidence and follow-up. Of importance to him was familiarization with methodologies used to catalogue and correlate information for use in studies of cancer risk factors and etiology. His training and application of it will be of significance in effective collaboration on problems of cancer epidemiology now in progress under the American-Chinese Cooperative Cancer Program.

DEPARTMENT OF COMMERCE (National Technical Information Service) (Y01-CO-60702)

Title: ICRDB Document Announcement and Dissemination Services

Contractor's Project Director: James Jennings

Project Officer (NCI): Dr. Dianne Tingley

Objective: This agreement supports the printing and dissemination of ICRDB publications, the announcement of these documents to potential users, and maintenance of all ICRDB documents in archival storage for supplying copies on request.

Major Accomplishments: Currently, NTIS disseminates more than 24,000 copies of CANCERGRAMs per month to over 12,000 investigators. In addition 15 ONCOLOGY OVERVIEWs are published yearly, each of which is distributed to an average of 600 investigators. The annual Compilation of Experimental Cancer Therapy Protocol Summaries is disseminated to over 7,000 investigators. NTIS also distributes 5,000 copies of other ad hoc ICRDB publications yearly.

Significance to Biomedical Research and Program of the Institute: This interagency agreement has allowed the ICRDB Program to rapidly fulfill one of its mandated activities, namely, the broad dissemination of biomedical research information on cancer. Through its various worldwide outlets, NTIS performs a valuable service in disseminating ICRDB products to the global scientific community.

Proposed Course: The agreement will continue as described.

Date Agreement Initiated: September 30, 1976

Current Annual Level: $682,133

DEPARTMENT OF COMMERCE (National Technical Information Service, Smithsonian Science Information Exchange, SSIE) (Y01-CO-00708)

Title: Current Cancer Research Project Analysis Center

Contractor's Project Director: Dr. Donald Elliott

Project Officer (NCI): Dr. Hortencia Hornbeak

Objective: The overall objective of this agreement was the operation of a Current Cancer Research Project Analysis Center (CCRESPAC) to support the International Cancer Research Data Bank (ICRDB) Program by coordinating the collection and processing of research project descriptions.

Major Accomplishments: The contractor prepared for publication 55 annually updated Special Listings of Current Cancer Research, which consisted of edited summaries of ongoing research in specific cancer subject areas. Computer tapes containing over 20,000 cancer projects were prepared on a quarterly basis for the regeneration of the CANCERPROJ data base, which is available for online searching and retrieval via the NLM MEDLARS computer system. Continued correspondence and other communications with scientists and clinicians in 83 countries resulted in the addition of over 5,000 non-U.S. research projects to the CCRESPAC information system.

Significance to Biomedical Research and Program of the Institute: This interagency agreement promoted the exchange of cancer research project information among researchers around the world by providing a variety of information products and services tailored to their individual needs. Current awareness of research in progress enables investigators to effectively utilize new concepts and techniques in the design of their own research projects.

Date Agreement Expired: November 30, 1981 (Activity to be continued under a contract to be competitively awarded)

Date Agreement Initiated: December 30, 1974

Final Annual Level: $417,078

FRANKLIN RESEARCH CENTER (NO1-CO-05463)

Title: Screening, Indexing and Abstracting of Published Cancer-Related Literature

Contractor's Project Director: William S. Thompson

Project Officer (NCI): Donna J. Wicker

Objectives: The SIA project collects, abstracts and indexes cancer literature published in professional journals, monographs and reports. This literature collection is the source material for the three primary services of the ICRDB Program: CANCERLIT, CANCERGRAMs, and ONCOLOGY OVERVIEWs.

Major Accomplishments: Approximately 4,000 items are photocopied, abstracted, indexed and keyed onto magnetic tape each month and sent to the ICRDB computer contractor for the final reformatting required to update the computer database. The items are collected from approximately 3,000 journals, and are abstracted from articles written in over 20 languages within 30 days of the receipt of each journal issue.

Significance to Biomedical Research and Program of the Institute: The SIA project is a multifaceted activity that provides rapid scanning of the world's cancer literature followed by processing that permits rapid, easy access to narrow cancer topics within a fraction of the time a scientist would normally have to spend retrieving the same material in a library. Access to the complete collection is possible via the CANCERLIT database or, following further processing, via the secondary publications ICRDB produces in narrow cancer subject areas.

Proposed Course: The contractor will continue the activity as described.

Date Contract Initiated: June 30, 1977

Current Annual Level: $1,699,934

FRANKLIN RESEARCH CENTER (NO1-CO-14343)

Title: Cancer Information Dissemination and Analysis Center (CIDAC) for Carcinogenesis

Contractor's Project Director: Dr. L. Gerald Parchman

Project Officer (NCI): Dr. Dianne E. Tingley

Objectives: The CIDAC provides scientific input necessary to produce information products and services for cancer researchers, and provides guidance to the ICRDB Program, in the area of carcinogenesis.

Major Accomplishments: The CIDAC regularly produces 21 monthly CANCERGRAMs, current awareness bulletins containing abstracts of recently published literature. In 1982, a compilation of abstracts of carcinogenesis-related review articles appearing during calendar year 1981 was published as a supplement to the CANCERGRAMs, under the title "Recent Reviews in Carcinogenesis." Five ONCOLOGY OVERVIEWs, retrospective bibliographies with abstracts concerning high interest topics in carcinogenesis research, are published annually. Videotapes of a CIDAC-sponsored symposium on "Relationship of Carcinogen Action on DNA to Cell Transformation," held on November 18, 1980, are still circulating to many requesters and have been well received. The CIDAC also performs custom searches of the CANCERLINE data bases in response to requests for information; submits monthly Highlight Reports, pinpointing significant new developments in carcinogenesis research; and assists in database quality control.

Significance to Biomedical Research and Program of the Institute: The CIDAC serves as a valuable resource for the NCI and the worldwide cancer research community in the area of carcinogenesis. The CANCERGRAMS collectively provide comprehensive coverage of this entire field, quickly alerting researchers to new findings with minimal expenditure of effort,

and thereby allowing them more time for productive research. ONCOLOGY OVERVIEWs enable researchers to rapidly update their knowledge in emerging areas of research concentration.

Proposed Course: The contractor will continue production of CANCERGRAMs and ONCOLOGY OVERVIEWs and provision of information services.

Date Contract Initiated: May 4, 1978

Current Annual Level: $284,925

FRANKLIN RESEARCH CENTER (NO1-CO-14356)

Title: Cancer Information Dissemination and Analysis Center (CIDAC) for Cancer Virology, Immunology and Basic Cancer Biology (VIB)

Contractor's Project Director: Dr. L. Gerald Parchman

Project Officer (NCI): Dr. Dianne E. Tingley

Objectives: The CIDAC provides scientific input necessary to produce information products and services for cancer researchers, and provides guidance to the ICRDB Program, in the area of cancer virology, immunology, and basic cancer biology.

Major Accomplishments: The CIDAC regularly produces 24 monthly CANCERGRAMs, current awareness bulletins containing abstracts of recently published literature. Five ONCOLOGY OVERVIEWs, retrospective bibliographies with abstracts concerning high interest topics in basic cancer research, are published annually. Videotapes of a CIDAC-sponsored symposium/workshop on "Mechanisms of Metastasis," held on January 28, 1981, are still circulating to many requesters, and have been well received. The CIDAC also performs custom searches of the CANCERLINE data bases in response to requests for information; submits monthly Highlight Reports, pinpointing significant new developments in basic cancer research; and assists in data base quality control.

Significance to Biomedical Research and Program of the Institute: The CIDAC serves as a valuable resource for the NCI and the worldwide cancer research community in the area of cancer virology, immunology, and biology. The CANCERGRAMS collectively provide comprehensive coverage of this entire field, quickly alerting researchers to new findings with minimal expenditure of effort, and thereby allowing them more time for productive research. ONCOLOGY OVERVIEWs enable researchers to rapidly update their knowledge in emerging areas of research concentration.

Proposed Course: The contractor will continue production of CANCERGRAMs and ONCOLOGY OVERVIEWs and provision of information services.

Date Contract Initiated: June 22, 1976

Current Annual Level: $289,624

FRANKLIN RESEARCH CENTER (NO1-CO-85403)

Title: Cancer Information Dissemination and Analysis Center (CIDAC) for Chemical, Environmental and Radiation Carcinogenesis

Contractor's Project Director: Dr. L. Gerald Parchman

Project Officer (NCI): Dr. Dianne E. Tingley

Objectives: The CIDAC provided scientific input necessary to produce information products and services for cancer researchers, and provided guidance to the ICRDB Program, in the area of carcinogenesis.

Major Accomplishments: The CIDAC regularly produced 21 monthly CANCERGRAMs, current awareness bulletins containing abstracts of recently published literature. Twenty-eight ONCOLOGY OVERVIEWs, retrospective bibliographies with abstracts concerning high interest topics in carcinogenesis research, were published. As a pilot project to explore new methods for enhancing the transfer of cancer research information, the CIDAC, on November 18, 1980, conducted and videotaped a symposium on "Relationship of Carcinogen Action on DNA to Cell Transformation." The videotapes have been circulated to many requesters, and have been well received. The CIDAC also performed custom searches of the CANCERLINE data bases in response to requests for information; submitted monthly Highlight Reports, pinpointing significant new developments in carcinogenesis research; and assisted in database quality control.

Significance to Biomedical Research and Program of the Institute: The CIDAC served as a valuable resource for the NCI and the worldwide cancer research community in the area of carcinogenesis.

Date Contract Expired: April 6, 1982 (These activities are being continued under contract No. NO1-CO-14343)

Date Contract Initiated: May 4, 1978

Final Annual Level: $242,916

FRANKLIN RESEARCH CENTER (NO1-CO-85404)

Title: Cancer Information Dissemination and Analysis Center (CIDAC) for Cancer Virology, Immunology and Basic Cancer Biology (VIB)

Contractor's Project Director: Dr. L. Gerald Parchman

Project Officer (NCI): Dr. Dianne E. Tingley

Objectives: The CIDAC provided scientific input necessary to produce information products and services for cancer researchers, and provided guidance to the ICRDB Program, in the area of cancer virology, immunology, and basic cancer biology.

Major Accomplishments: The CIDAC regularly produced 24 monthly CANCERGRAMs, current awareness bulletins containing abstracts of recently published literature. Twenty-eight ONCOLOGY OVERVIEWs, retrospective bibliographies with abstracts concerning high interest topics in basic cancer research, were published. As a pilot project to explore new methods for enhancing the transfer of cancer research information, the CIDAC, on January 28, 1981, conducted and videotaped a symposium/workshop on "Mechanisms of Metastasis." The videotapes have been circulated to many requesters, and have been well received. The CIDAC also performed custom searches of the CANCERLINE data bases in response to requests for information; submitted monthly Highlight Reports, pinpointing significant new developments in basic cancer research; and assisted in data base quality control.

Significance to Biomedical Research and Program of the Institute: The CIDAC served as a valuable resource for the NCI and the worldwide cancer research community in the area of cancer virology, immunology, and biology.

Date Contract Expired: June 18, 1982 (These activities are being continued under contract No. NO1-CO-14356)

Date Contract Initiated: June 22, 1976

Final Annual Level: $289,624

HERNER AND COMPANY (NO1-CO-05465)

Title: Acquisition, Indexing and Keyboarding of Cancer-Related Meeting and Dissertation Abstracts

Contractor's Project Director: Lois Lunin

Project Officer (NCI): Donna J. Wicker

Objective: The AIK project collects, indexes and keys abstracts presented at meetings which describe cancer research projects. The project also indexes and keys abstracts from Dissertation Abstracts, a secondary journal that summarizes doctoral theses. These abstracts are part of the source material for CANCERLIT, CANCERGRAMs and ONCOLOGY OVERVIEWs.

Major Accomplishments: Approximately 1,000 items are processed each month and forwarded to the ICRDB computer contractor for the final reformatting required to update the computer database. The abstracts are collected from major biomedical conferences such as the American Association for Cancer Research, the American Society of Clinical Oncology and the Federation of American Societies for Experimental Biology.

Significance to Biomedical Research and Program of the Institute: The AIK project provides rapid, easy access to cancer research information presented at meetings. This information can be retrieved by searching the CANCERLIT database in any narrow topical area of cancer.

Proposed Course: The contractor will continue the activity as described.

Date Contract Initiated: August 12, 1980

Current Annual Level: $122,825

IIT RESEARCH INSTITUTE (NO1-CO-05468)

Title: Computer Support for Cancer Information Dissemination

Contractor's Project Director: Peter B. Schipma

Project Officer (NCI): Dr. John H. Schneider

Objective: The purpose of the contract is to establish and operate a Computer Support Center (CSC) for the ICRDB Program.

Major Accomplishments: The contractor performs a wide variety of computer operations necessary for the creation and maintenance of ICRDB databases, preparation of ICRDB publications, maintenance of special mailing lists, statistical reporting and special tasks identified by the Program.

Significance to Biomedical Research and Program of the Institute: The computer support provided by the contractor is of central importance to the entire spectrum of ICRDB products and services, whereby the Program is able to fulfill its mandate to actively promote the dissemination of cancer research information on a worldwide basis.

Proposed Course: No significant change.

Date Contract Initiated: June 27, 1975

Current Annual Level: $593,817

INFORMATICS, INC. (NO1-CO-05509)

Title: Preparation and Updating of Clinical Protocol Summaries

Contractor's Project Director: Mr. Richard Amacher

Project Officer (NCI): Mr. Barry Goldfarb

Objectives: This contract provides the capabilities for collecting, processing and disseminating ongoing cancer therapy protocol summaries to clinicians and investigators throughout the world.

Major Accomplishments: Informatics prepares annual updates of the Compilation of Experimental Cancer Therapy Protocol Summaries. The 1982 sixth edition contains over 1,500 summaries of Phase II and Phase III clinical trials currently in progress worldwide. This edition also includes a brief, preliminary list of several Phase I protocols activated during 1981 and a list of protocols closed to patient entry during 1981. Magnetic tapes containing the summaries of all protocols (3,200) are provided for the quarterly regenerations of the CLINPROT online database.

Significance to Biomedical Research and Program of the Institute: Both the Compilation and the CLINPROT data base are valuable information resources for apprising practicing oncologists of the latest developments in cancer treatment research. The availability of the principal investigator's or group chairman's address and telephone number on all protocol summaries facilitates the interaction of clinicians and investigators with common interests.

Proposed Course: Plans call for the continuation of this contract through December 1982, including annual updating of the Compilation.

Date Agreement Initiated: December 14, 1979

Current Annual Level: $214,614

INFORMATICS, INC. (NO1-CO-14361)

Title: Technical Support Services for the International Cancer Research Data Bank (ICRDB) Program

Contractor's Project Director: Richard Amacher

Project Officer (NCI): Dr. J. Wesley Simmons

Objectives: This project provides a broad range of technical support activity to all projects within the ICRDB Program and to related information activities within DCCP.

Major Accomplishments: Support relating to exhibits at major meetings for cancer researchers (e.g., ASCO and AACR) has contributed significantly to the enhancement of user awareness of the ICRDB Program. Updates of the CANCERGRAM and Compilation mailing lists were made to preclude unnecessary mailing of ICRDB publications.

Significance to Biomedical Research and Program of the Institute: This project makes available to the ICRDB Program for short- and long-range special projects, as needed, personnel and expertise in the areas of publications preparation, promotion of user awareness, evaluation of user services, and scientific analysis. This support is essential to fulfillment of the ICRDB Progam mandate for active collection and dissemination of cancer research information.

Proposed Course: The present contract will continue, with special efforts devoted to formal evaluation of ICRDB products and services, and increasing awareness of ICRDB services.

Date Contract Initiated: August 31, 1981

Current Annual Level: $284,223

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER (NO1-CO-55195)

Title: Clearinghouse for On-going Work in Cancer Epidemiology

Contractor's Project Director: Dr. Calum S. Muir

Project Officer (NCI): Dr. John H. Schneider

Objective: This contract provides a special mechanism for intensive collection and dissemination of information about current cancer-related epidemiology projects.

Major Accomplishments: The Clearinghouse, located in Lyon, France, continually identifies and contacts new sources of epidemiology research project descriptions. Project descriptions are collected, edited, and published annually as the Directory of On-going Research in Cancer Epidemiology, as well as provided on magnetic tape for entry into the CANCERPROJ data base. The 6th edition of the Directory (1981) contained 1,313 project descriptions collected from 80 countries.

Significance to Biomedical Research and Program of the Institute: By serving as a resource for epidemiological data and establishing communication among epidemiology researchers worldwide, the Clearinghouse promotes international awareness and cooperation which contributes to more productive research in this area.

Proposed Course: Work will continue as described.

Date Contract Initiated: February 25, 1975

Current Annual Level: $124,303

INTERNATIONAL MEDICAL INFORMATION CENTER (NO1-CO-75362)

Title: Development and Implementation of Mechanisms for Interaction between the ICRDB Program and Asian Countries.

Contractor's Project Director: Masanobu Fujikawa

Project Officer (NCI): Dr. John H. Schneider

Objective: This project was established to enhance the coverage of Asian cancer literature by the ICRDB Program, and to facilitate communication with Asian cancer researchers.

Major Accomplishments: The contractor provided annually more than 1,000 cancer-related abstracts or annotations for input to the CANCERLIT database, screened from approximately 150 Asian-language journals and proceedings of Asian cancer meetings (mostly Japanese).

Significance to Biomedical Research and Program of the Institute: Through CANCERLIT, this activity made available to researchers worldwide cancer-related findings which might otherwise pass unnoticed because of the Asian language barrier.

Date Contract Expired: November 29, 1981 (Screening of the most significant Asian literature was continued under a modification to contract No. N01-CO-05463)

Date Contract Initiated: November 30, 1976

Final Annual Level: $129,964

NATIONAL ACADEMY OF SCIENCES (NAS) (N01-CO-75384)

Title: Support of Activities of the U.S.A. National Committee for the International Union Against Cancer (UICC)

Contractor's Project Director: June Ewing

Project Officer (NCI): Barry M. Goldfarb

Objective: This contract serves the dual purposes of: 1) providing for one representative body (acting on behalf of the various U.S. cancer organizations and foundations) to deal with issues and policies on the International Union Against Cancer (UICC); and 2) supporting Committee participation in the UICC-sponsored International Cancer Congress held every four years.

Major Accomplishments: Planning for the XIII International Cancer Congress held in Seattle in September 1982 was completed.

Significance to Biomedical Research and Program of the Institute: This contract supports the representative body which develops and presents the issues and policies of the United States cancer research community to the UICC, and through support of International Cancer Congresses promotes the productive exchange of research information among researchers throughout the world.

Proposed Course: Plans call for continuation of this contract through March 1983.

Date Contract Initiated: April 1, 1977

NATIONAL LIBRARY OF MEDICINE (1-Y01-CO-50003)

Title: Joint NLM/NCI International Cancer Research Data Bank

Contractor's Project Director: Dr. Henry M. Kissman

Project Officer (NCI): Donna J. Wicker

Objective: The agreement with the NLM permits the generation, maintenance and operation of the three ICRDB databases (published literature, research projects, clinical protocols) on the NLM computer, and for the dissemination of the information in these collections to institutions subscribing to the NLM computer services.

Major Accomplishments: The NLM currently maintains approximately 320,000 abstracts of published literature, 20,000 descriptions of research projects and 3,200 summaries of clinical protocols for the ICRDB Program. Each year a total of 20 updates or regenerations are performed to update or correct the records in these three files. It is estimated that approximately 24,000 searches were run against CANCERLINE in 1981.

Significance to Biomedical Research and Program of the Institute: In consonance with the National Cancer Act of 1971, this interagency agreement has given the ICRDB Program the cost savings benefit of using an existing organization with capabilities to reformat, process, and make the results of cancer research available to more than 2,500 locations throughout the world via an existing telecommunications network resident at NLM. These locations include medical schools, medical research institutions, regional medical libraries and hospitals throughout the United States, and several countries outside the United States.

Proposed Course: Plans call for the continuation of this agreement through September 1983.

Date Contract Initiated: July 1, 1974

Current Annual Level: $325,000

PAN AMERICAN HEALTH ORGANIZATION (NO1-CO-65332)

Title: Latin American Cancer Research Information Program

Contractor's Project Director: Dr. Jorge Litvak

Project Officer (NCI): Dr. J.W. Simmons

Major Accomplishments: The contractor has supplied several hundred cancer-related articles and meeting abstracts from Latin America for inclusion in CANCERLIT. There has been a steady input of cancer research projects and clinical protocols for inclusion into the CANCERPROJ and CLINPROT data bases respectively. At present there are over 350 cancer research summaries from Latin America in CANCERPROJ.

Significance to Biomedical Research and Program of the Institute: LACRIP is an important resource for the ICRDB Program in that it supplies project descriptions, clinical protocols and journal articles for the databases (CANCERPROJ, CLINPROT and CANCERLINE) that would otherwise not be included, and provides a centralized mechanism for dissemination of cancer-related information to a large number of countries.

Proposed Course: This contract will continue, at a reduced level, through July 1984.

Date Contract Initiated: May 24, 1976

Current Annual Level: $234,118

UNION INTERNATIONALE CONTRE LE CANCER (UICC) (NO1-CO-65341)

Title: International Scientist-to-Scientist Information Exchange Program

Contractor's Project Director: Dr. Anders Englund

Project Officers (NCI): Barry M. Goldfarb, Dr. Robert R. Omata

Objective: The purpose of this program is to promote direct and rapid person-to-person transfer of information about new or improved technology or methodology between investigators from different countries who are working in areas of basic, clinical or behavioral research, in order to further the progress of cancer research.

Major Accomplishments: This contract promotes international cancer research collaboration by providing International Cancer Research Technology Transfer (ICRETT) awards which enable two cancer researchers from different countries to jointly carry out brief research projects. From the inception of this program through December 1980, 476 exchanges (average period sponsored, 3 weeks) have been granted.

Significance to Biomedical Research and Program of the Institute: Scientists are afforded the valuable opportunity for on-the-spot collaboration necessary for comparing the results of parallel or related research and developing or improving techniques. These interactions frequently lead to continuing exchange of research information, which in turn leads to a more productive collaborative effort.

Proposed Course: This contract activity will continue at approximately the same level through March 1984.

Date Contract Initiated: December 4, 1975

Current Annual Level: $104,640

UNION INTERNATIONALE CONTRE LE CANCER (UICC) (NO1-CO-75377)

Title: Liaison and Implementation Projects in Support of the NCI, International Cancer Research Data Bank (ICRDB) Program

Contractor's Project Director: Dr. G. P. Warwick

Project Officer (NCI): Barry M. Goldfarb

Objective: Through its Committee on International Collaborative Activities (CICA), the UICC provides liaison and implementation projects in support of the International Cancer Research Data Bank (ICRDB) Program.

Major Accomplishments: This effort has resulted in collection and processing of information on over 6,000 unpublished current cancer research projects. This information is made available worldwide through the CANCERPROJ data base. The CICA has also established, as a pilot program, an International Cancer Patient Data Exchange System (ICPDES) whereby information covering the entire patient care spectrum is collected in an internationally standardized manner, with participation by 5 major U.S. and 10 foreign cancer centers. As of July 1981, over 23,000 case reports had been entered, covering breast, colorectal and laryngeal cancers, and Hodgkin's and non-Hodgkin's lymphomas.

Significance to Biomedical Research and Program of the Institute: CICA activities have been of major significance in making the ICRDB Program truly international in scope. Active efforts to establish liaison with and obtain data from cancer centers and individual investigators around the world have stimulated increased communication and cooperation among researchers, as well as more effective utilization of clinical research data.

Proposed Course: Patient data collection will continue through the ICPDES, and efforts are underway to re-establish a European data processing center in addition to the one located in Houston. A new edition of the International Directory of Specialized Cancer Research and Treatment Establishments, last published in 1978 and listing 679 such centers located in 80 countries, is scheduled for release in September 1982.

Date Contract Initiated: April 1, 1977

Current Annual Level: $277,377

UNIVERSITY OF TEXAS SYSTEM CANCER CENTER (NO1-CO-14347)

Title: Cancer Information Dissemination and Analysis Center (CIDAC) for Cancer Diagnosis and Therapy

Contractor's Project Director: Dr. Eugene McKelvey

Project Officer (NCI): Dr. Dianne E. Tingley

Objectives: The CIDAC provides scientific input necessary to produce information products and services for cancer researchers, and provides guidance to the ICRDB Program, in the area of cancer diagnosis, therapy and rehabilitation.

Major Accomplishments: The CIDAC regularly produces 21 monthly CANCERGRAMs, current awareness bulletins containing abstracts of recently published literature. Five ONCOLOGY OVERVIEWs, retrospective bibliographies with abstracts concerning high interest topics in clinical cancer research, are published annually. The CIDAC performs custom searches of the CANCERLINE data bases in response to requests for information; submits monthly Highlight Reports, pinpointing significant new developments in clinical cancer research; and assists in database quality control.

Significance to Biomedical Research and Program of the Institute: The CIDAC serves as a valuable resource for the NCI and the worldwide cancer research community in the area of oncology research. The CANCERGRAMs collectively provide comprehensive coverage of this entire field, quickly alerting researchers to new findings with minimal expenditure of effort, and thereby allowing them more time for productive research. ONCOLOGY OVERVIEWs enable researchers to rapidly update their knowledge in emerging areas of research concentration.

Proposed Course: The contractor will continue production of CANCERGRAMs and ONCOLOGY OVERVIEWs and provision of information services.

Date Contract Initiated: June 24, 1976

Current Annual Level: $338,942

UNIVERSITY OF TEXAS SYSTEM CANCER CENTER (NO1-CO-85405)

Title: Cancer Information Dissemination and Analysis Center (CIDAC) for Cancer Diagnosis and Therapy

Contractor's Project Director: Dr. Eugene McKelvey

Project Officer (NCI): Dr. Dianne E. Tingley

Objectives: The CIDAC provided scientific input necessary to produce information products and services for cancer researchers, and provided guidance to the ICRDB Program, in the area of cancer diagnosis, therapy and rehabilitation.

Major Accomplishments: The CIDAC regularly produced 21 monthly CANCERGRAMs, current awareness bulletins containing abstracts of recently published literature. Twenty-six ONCOLOGY OVERVIEWs, retrospective bibliographies with abstracts concerning high interest topics in clinical cancer research were published. The CIDAC performed custom searches of the CANCERLINE data bases in response to requests for information; submitted monthly Highlight Reports, pinpointing significant new developments in clinical cancer research; and assisted in database quality control. CIDAC staff and consultants prepared a manuscript entitled "Basic Science Research of Imminent Impact on Clinical Oncology," which appeared in the 1981 Yearbook of Cancer and in the 1982 edition of the UICC Manual of Clinical Oncology.

Significance to Biomedical Research and Program of the Institute: The CIDAC served as a valuable resource for the NCI and the worldwide cancer research community in the area of oncology research.

Date Contract Expired: September 5, 1982 (These activities are being continued under contract No. NO1-CO-14347.)

Date Contract Initiated: June 24, 1976

Final Annual Level: $240,893

NCI-SPONSORED RESEARCH IN FOREIGN COUNTRIES

During 1982, the Office of the Director, NCI, and the Divisions of Cancer Treatment and Cancer Cause and Prevention maintained extensions of their programmatic objectives in foreign countries through 23 contract research activities, compared to 34 during the previous year and 53 during 1980. No contractual research was in effect to extend the research effort of the Division of Cancer Biology and Diagnosis.

The Division of Extramural Activities provided fiscal support, through 60 grants, to scientists in foreign institutions conducting basic and applied cancer research.

The Division of Cancer Treatment (DCT)

DCT research contracts have been awarded to investigators in nine institutions of five foreign countries for studies related to the characterization of anticancer agents, the search for potentially useful anticancer agents such as those of microbial origin, the screening and testing of such compounds, synthesis of radiation sensitizing agents, and clinical trials on specific cancers. One contract is specifically for the production and delivery of human lymphoblast interferon. Examples follow of this international collaborative effort.

In 1972, DCT established a "Cancer Chemotherapy Research Collaborative Office" at the Institut Jules Bordet in Brussels, Belgium. This facility provides an important service function to cancer researchers and clinicians in the USA and Europe as a center of reference for the vast amount of pertinent information on ongoing cancer research programs in both continents. Its "liaison function" has been invaluable in promoting cooperative studies in experimental and clinical pharmacology and in clinical trials. In this context, there is a direct association with the European Organization for Research on the Treatment of Cancer (EORTC) which, among other activities, collects and manages data on clinical trials for Europe and serves as the coordinating center for clinical cooperative groups. By this means, the EORTC facilitates data collection, at a much faster rate, on the clinical evaluation of new drugs and therapeutic results from a large number of patients. Currently, there are approximately 64 clinical studies in progress among the EORTC clinical cooperative groups. Two hundred and fifty-five institutions in 13 countries are involved in the trials and, currently, 6,500 European patients are monitored by the EORTC data center. Since 1972, more than 25,000 new compounds have been collected through the direct efforts of the Collaborative Office and several of these proved to be interesting enough for development toward clinical trial.

DCT's maintenance in Tokyo, Japan, of a "Collaborative Office for Cancer Chemotherapy Research" contributes significantly to NCI's cancer treatment program. On the order of 35 to 40 potentially useful drug materials are collected per month, including synthetic preparations and products of natural origin. During the period spanning June 1979 and June 1980, 390 synthetics and 67 natural products were collected from 34 Japanese institutions. Active new materials include synthetic cyanines; analogues of 5-fluorouracil, cytosine arabinoside, and imidazolyl carboxamide; and nitrosoureas. Among

the natural products are fatty acid esters of a crude nagilactone mixture, and anthracycline antibiotics.

There is a continuation of cooperative preclinical and clinical research associations between American cancer centers and those of the United Kingdom, stimulated largely through DCT efforts and its partial support. The Institute of Cancer Research in London is contributing significantly to the DCT mission through research encompassing: (1) drug development and screening; (2) preclinical toxicology; (3) clinical Phase I-II testing; (4) drug rescue strategies and scheduling; and (5) collaborative pharmacologic and clinical testing of new drugs.

In association with the Muhimbili Medical Center in Tanzania, DCT is engaged in a study of the use of oral 13-cis retinoic acid as a chemopreventive agent of skin cancer in albino Africans. These people, living in the equatorial zone, are subject to the most intense ultraviolet irradiation on the surface of the earth and are candidates, virtually, to a 100% increase of skin cancer.

Three years ago, DCT entered into a cooperative relationship with Latin American cancer institutes by virtue of the NCI-PAHO Collaborative Cancer Treatment Research Program (CCTRP). Clinical research activities are being pursued jointly by investigators in 12 Latin American cancer institutes/hospitals and 10 American cancer centers. Treatment protocols currently being evaluated include therapeutic concepts in hematologic malignancies, childhood malignancies, osteosarcomas, and testicular cancer. Multimodal concepts in solid tumors are being pursued in advanced breast and head and neck cancer. Systemic therapy of solid tumors is being evaluated in advanced breast cancer, advanced gastric cancer and adenocarcinoma, and in sarcomas. Since the inception of this multinational effort, 1,158 patients have been accrued into the program.

Personnel of DCT play key roles in the NCI Bilateral Agreements with Egypt, France, Italy, Japan and the USSR through participation in: clinical trials; the preclinical screening and testing of potentially useful anticancer agents; the evaluation of the activity of substances indicating properties for biologic response modification; and programs in experimental/developmental therapeutics.

The Division of Cancer Cause and Prevention (DCCP)

DCCP is very active in its associations with international organizations and agencies that have well-defined objectives in cancer research, especially its cause and prevention. As well, DCCP is engaged in collaborative contract research in seven institutions/agencies in six foreign nations. These foreign extensions of the DCCP program thrusts enable the division to support fundamental studies on normal and malignant cells in relation to such carcinogens as viruses and chemicals, as well as epidemiologic studies of human populations for the identification of risk factors predisposing to various cancers. These studies are primarily conducted under three major programs: Biologic Carcinogenesis; Chemical/Physical Carcinogenesis; and Epidemiology. Excellent model systems are available to scientists studying the effects of potentially carcinogenic factors in the environment.

Several investigations, under the Chemical Carcinogenesis Program, are designed to determine the mechanism of action of chemical and physical agents in the transformation and progression of a cell from the "normal" to the malignant state. These foreign studies are targeted toward the understanding of the interaction of the activated metabolites of carcinogens with nucleic acids, both RNA and DNA, of the cell. Thus, they are attempting to: (1) define the mechanism of alkylation of N-nitrosamines and their derivatives; and (2) determine the DNA adducts generalized by exposure to benzo(a)pyrene and other hydrocarbon carcinogens. Other studies have long-range objectives for developing models to analyze and understand further the steps in the carcinogenesis process through: (1) defining cellular preneoplastic changes in epithelial cells following exposure to liver carcinogens; and (2) developing short-term assays for the detection of chemical carcinogens.

The Epidemiology Program includes studies on the natural history of cancer in humans and on the incidence of cancers in different geographic locations so as to help identify causal associations of various intrinsic and extrinsic risk factors. As such, many surveys are conducted in countries throughout the world, thus permitting comparison with the incidence of various cancers in the United States. Excess thyroid nodular disease, for instance, was detected following low-level exposure of children receiving X-ray therapy for ringworm of the scalp. Studies on the risk of developing second cancers among former cervical cancer patients given low-level doses of radiation suggest excess risks to other cancers such as bladder, rectal, kidney, ovarian, etc.

A new study in the Epidemiology Program holds the promise for highly significant information. This is a pilot study to be initiated to determine the basis of cancers of the esophagus, nasopharynx and other organ sites occurring in populations within the People's Republic of China.

Among the notable activities in the Environmental Carcinogenesis Program are the IARC Monographs on the "Evaluation of the Carcinogenic Risk of Chemicals to Humans," exemplary of which is the 1980 compendium entitled "Chemicals and Industrial Processes Associated with Cancer in Humans." These volumes serve as an authoritative source, for example, of the list of chemicals being tested for carcinogenicity in laboratories throughout the world. They reflect the international consensus on these agents and have become indispensable reference sources to scientific pursuits on carcinogenesis.

Personnel of DCCP play key roles in the NCI efforts under Bilateral Agreements with the People's Republic of China, France, Germany, Italy, Japan and the Soviet Union.

The Division of Extramural Activities (DEA)

Grants by the DEA have been made available to 37 institutions/organizations in 13 countries. The scientific investigations include both basic and applied research and range over the spectrum of the thrusts and objectives of the NCI. Among these are assays for and studies of the action of carcinogens and "promoters" of carcinogenesis by personnel of the National Research Council of Canada. At the University of London a study is underway on the therapeutic response of human tumor xenografts. In the University of Helsinki in Finland studies are being pursued to determine glycoprotein

differences in normal and malignant human blood cells. Scientists of the Weizmann Institute in Israel are engaged in research on the immunobiology of tumor metastasis.

THE NIH VISITING PROGRAM

During 1982, personnel of the National Cancer Institute served as hosts for scientists from 35 countries who came to the United States to engage in collaborative cancer research activities. There was a total of 310 foreign visiting scientists, associates, and fellows. Four of the visitors were appointed as Experts and 48 came as Guest Workers, whose financial support comes from sources other than NCI. The activities of these scientists were pursued in the laboratories of the NCI Divisions of Cancer Treatment, Cancer Cause and Prevention, and Cancer Biology and Diagnosis.

These associations are mutually beneficial. The NCI host scientist is afforded opportunities to learn from his/her visitor about cancer problems in a given foreign country; about factors peculiar to that nation that might be related to morbidity and mortality of cancer; and about activities underway toward the management, treatment, and prevention of cancer. On the other hand, the foreign scientists are provided with unique opportunities to improve their mastery of the scientific method or to develop their potential for significant contributions to basic and/or clinical research. The value of such scientific interaction can be assessed, ultimately, on the knowledge that cancer patients throughout the world are benefiting from an improved quality of care.

SUMMARY

The highest possible level of health for all people of the United States and the world is a goal of international scope. Attaining such an objective can be achieved only through the control and prevention of those diseases, such as cancer, which are obstacles to such a pursuit. Contemporary management and ultimate eradication of cancer, thus, are dependent on continued research activities which represent cooperative endeavors involving the integrated talents and skills of an internationally wide variety of specialists encompassing all areas of basic and applied science related to unraveling and understanding the phenomenal complexities of cancer.

The international team effort in cancer research, promoted and sponsored in part by the National Cancer Institute, is indicative of a scientific outreach that spans the world. It represents a multitude of cooperative scientific activities accomplished through bilateral agreements for cancer research; contracts and grants to support foreign scientists with expertise in priority scientific areas; the exchange of junior and senior scientists and information; and a global network of communication of research information through mechanisms of the ICRDB Program, the IARC and UICC, the EORTC, and the WHO and PAHO.

Although this interaction with the world's scientific community has brought forth gains in the war against cancer, strongholds remain and continue to resist even this aggressive deployment of the skills of contemporary science. However, as our international struggle against cancer continues, additional knowledge will accrue on how normal cells become malignant. We should be able to determine

more precisely which compounds and other factors are carcinogens or pose a risk for cancer incidence.

As efforts are continued toward the rational design and development of more effective anticancer agents and cancer treatment procedures, we will benefit, as well, from an insight into possible chemoprevention by virtue of an awareness of specific biochemical and pharmacokinetic action of chemicals in the control of cell differentiation and other cellular activities related to neoplastic growth.

A significant input from this international effort will be the accrual and analysis of demographic and geographic information endemic to a given population or region of the world. This resource will contribute to our understanding of the risk factors associated with a given cancer and the development of measures for cancer control and/or prevention.

Most important, however, is that continuous communication be maintained for the exchange of scientific information on cancer for the benefit of the peoples of all nations.

ANNUAL REPORT
OFFICE OF THE DIRECTOR FOR PROGRAM PLANNING AND ANALYSIS (ODPPA)
NATIONAL CANCER INSTITUTE

OCTOBER 1, 1981 - SEPTEMBER 30, 1982

OFFICE OF THE DIRECTOR

The ODPPA provides leadership, consultation and direct participation in: program analysis, planning and evaluation, the design, development and support of management information systems and is responsible for the analysis of all legislation that could have an impact on the NCI and the conduct of appropriate liaison with the Congress. Organizationally, it is located in the Office of the Director (OD), NCI, to enable it more effectively to provide its services to all operating units of the NCI and, at the discretion of the Director, to non-Federal organizations participating in the National Cancer Program (NCP). Operationally, it carries out its responsibilities in close collaboration with NCI operating units, counterpart offices at the NIH and DHHS, and other Federal agencies as required.

The Office consists of two branches: the Program Analysis and Formulation Branch (PAFB) and the Systems Planning Branch (SPB) which includes the MIS Project Office, and the Legislative/Congressional Unit which is part of the immediate OD. The PAFB is typically staffed with M.D.'s and Ph.D.'s with broad laboratory and clinical research experiences in the major disciplines involved in cancer research. The SPB is staffed with professionals with extensive experience in general management, planning, operations research, systems analysis, and management and technical information-systems. The legislative/congressional activities are performed by a senior analyst with extensive knowledge and experience in the Federal legislative process, and congressional committees and staff operations. Although primary and continuing assignments are made to each branch or unit based on expertise required, the Office typically operates on a project matrix system whereby staff members are assigned to specific projects to provide the mix of scientific and managerial talents required by much of the work performed by the Office. Thus, rather than an accounting by organizational units, this annual report describes activities and accomplishments in terms of the major areas of performance: Analysis and Formulation, Planning and Evaluation, Management Information Systems, Legislative Analysis/Congressional Liaison.

Historically, the OPPA has worked closely with NCI operational units on an as requested basis to carry out its responsibilities. During this reporting period, management decided that a more formal link between the OPPA and the operating units was desirable. Thus, the NCI Large Planning Group was formed. The group consists of at least one professional, programmatic person from each NCI division, and the senior members of the OPPA staff. Regularly scheduled monthly meetings are held to plan work, exchange information and select planning areas for future targetting.

Also, during this reporting period, the NCI established the policy of appointing Chiefs of Project Officers for each division and the OD, NCI to provide general oversight of this important function. The Director, OPPA, serves in this capacity for the OD, NCI.

Dr. Mary C. Knipmeyer, formerly of the National Institute on Drug Abuse, was appointed the NCI Legislative Analyst/Congressional Liaison in May of this year.

ANALYSIS AND FORMULATION

The staff of PAFB continued its review and analysis of NCI-supported extramural research and prepared tabular summaries of data concerned with this research using the data files of the Scientific Content Analysis (SCAN) System. Analytic services were provided and surveys prepared based on the specific needs of NCI staff. Reports, correspondence and official documents referred to the staff by the Associate Director for Program Planning and Analysis were reviewed and critiqued as required.

The SCAN system was operated with the aid of staff from ORI, Inc. NCI-supported grants and contracts active in FY81 were processed, reviewed and incorporated into the SCAN system in readiness for the final analysis report for 1981. These data relate NCI-supported extramural research to the components of the National Cancer Program Plan (NCPP) and to varied aspects of research and development.

As the scientific and programmatic information systems operated by the divisions evolved to provide greater coverage of NCI programs, the use level for SCAN dropped significantly, and the continued operation of a centralized system could no longer be justified. Therefore, the decision was made to archive the SCAN system as of June 1982.

The staff of PAFB participated in or completed the following activities (random listing):

- review and analysis of NCI-supported extramural projects initiated or renewed in FY81 for entry into the data files of the SCAN system
- completion of annual report for SCAN system for FY81 including trend analysis of different areas of research covering several fiscal years
- development of a capability to access the data files of the SCAN system on a quarterly basis
- generation of responses to queries on data in the SCAN system for FY81, e.g., chemoprevention, carcinogenesis
- preparation of data comparing 1972 resource estimates and priorities with actual 1980 allocations in reference to objectives of the National Cancer Program Plan
- service as executive secretary for the NCI Program Structure Review Committee and the Chemoprevention Coordinating Group
- provision of technical, logistic and scientific support for developing a major program in chemoprevention in the Division of Research, Resources and Community Activities
- service as executive secretary and participant in the updating of the logic diagram and decision networks of the NCI Chemotherapy Program
- participation in the NIH subcommittee on the B/A/D analysis of research and development to update operational guidelines for the different institutes
- service as a reviewer of OD contracts.

- V.S. Waravdekar in collaboration with Drs. Herman, Witiak and Hellman prepared a review on biological properties of ICRF 159 and related bis (dioxopiperazine) compounds for Advances in Pharmacology and Chemotherapy, Volume 19.

PLANNING AND EVALUATION

Since its creation in 1965, the ODPPA has been primarily responsible for the development and application of system analysis, planning and evaluation techniques and operations research techniques to cancer research and control activities; providing direct support for National Cancer Program planning at the national and individual program levels, and NIH and Department level planning. The Office also provides general planning, operations, and general management consultative services to various program areas within the National Cancer Institute and other institutions and groups participating in the National Cancer Program. In carrying out these responsibilities, staff participate as members of planning teams organized to develop individual program plans, work directly with program and administrative personnel in the development of operational plans; maintain liaison with program personnel, provide periodic consultation and direct efforts, as requested by program leaders, to revise and update both program and operating plans; provide education and training to program staff in the use of systems techniques; and work closely with the financial management staff during the budget preparation cycle to correlate budget preparation with existing plans.

Specific planning activities engaged in during the past year are described in the paragraphs that follow:

A. Requests for planning programs were exceptionally heavy during this year, and all could not be accommodated at the same time. Emphasis was directed towards the high priority areas of chemoprevention, smoking and health, and the radiation research program. The Division of Cancer Treatment's linear array for the Drug Development Program is in the process of being updated. During program planning, considerable emphasis is placed on developing or refining evaluation criteria so that planning may be more thoroughly integrated with evaluation.

B. Coordinated the preparation of the National Cancer Program 1981 Director's Report/Annual Plan (DR/AP) for FY1983-1987 for submission to the President and Congress as required by law. This report describes National Cancer Program progress during 1981, current activities, and planned efforts for the five-year planning period, including budget projections. The 1981 Report also included an expanded chapter on non-NCI participation in the National Cancer Program. Through the continuing efforts of NCI staff to broaden the scope of the report, additional nonprofit, state, and industrial groups were identified and contacted for information about their cancer-related activities. A new separate section described organized labor's contribution to the National Cancer Program. This information, along with that from contacts in other Federal agencies, resulted in a more complete description of non-NCI activities. After extensive internal and external review (NCAB, NIH, OMB, OASH, etc.) and incorporation of review comments, the Report was submitted to the Secretary for transmittal to the President and the Congress and was distributed to research and educational institutions, voluntary organizations, and Federal, State, and local agencies involved in cancer-related activities.

Since the Director's Report/Annual Plan highlights accomplishments during the past year as well as forecasts future activities, it has proven to be a valuable reference tool throughout the year.

C. Coordinated the preparation of the NCI chapter of the NIH Forward (Research) Plan and the associated activities of: preparation for NCI participation in the Director's (NIH) Forward Planning Review Session, including preparation of a briefing book for NCI Director and staff, and development of agenda items; and coordinating and reporting NCI activity action items which resulted from review session discussions. In previous years, the focus of the Review Session was to discuss program priorities and changes presented in the Research Plan submission. In recent years, however, the focus has changed to that of preparing the Director, NIH, for the upcoming congressional appropriation hearings and items to be discussed at that time.

D. Further developed the evaluation strategy and coordinated all evaluation activities of the NCI. Prepared the NCI Evaluation Plan which included a strategy statement and a description of Institute evaluative efforts (set-aside and non set-aside).

Assistance was provided to NCI staff in the development, implementation, and administration of 1% set-aside evaluation projects, including the preparation of close-out documents when the project is completed. Close-out submissions include an executive summary, assessment of benefits, and an impact statement describing the importance and implications of the study for the program and any decisions that have been or will be made as a result of the study. Close-out material was prepared for four completed set-aside projects, three ongoing projects were monitored, and proposals for 14 additional projects (to be initiated in FY83) were prepared. The ongoing (FY82) and proposed (FY83) budgets for these projects totalled $208,000 and $1,687,000, respectively. Progress reports are prepared for multiphase or long duration projects.

Material was prepared for NCI participation in Evaluation Plan review sessions at OD, NIH and departmental levels. The Office also has responsibility for coordinating and reporting any NCI activity action items which result from review session discussions. Branch personnel attend and participate in all reviews.

E. Coordinated NCI's contributions to the PHS and DCRT/ADP Plans

- The systems included in the Directory of Automatic Data Processing Systems in the Public Health Service which identifies and classifies computerized data processing systems in PHS provide information necessary to support effective and efficient management of automatic data processing resources and operations.

- Information collected from the divisions for the Fiscal Year 1984 DCRT ADP Financial Plan (43A) showed that NCI's ADP expenses totalled $17,089,900 in FY1982. This cost is projected to be $18,848,900 in FY1983 and $19,775,400 in FY1984.

Cooperated with the Financial Management Branch on the preparation of the FY1984 Commitment Base for ADP expenses to ensure agreement with the ADP Financial Plan (43A). The NCI figures were divided into two categories: 1) intramural research and 2) direct operations and program management, to reflect separate decision units.

Coordinated NCI's contribution to PHS, Operations Management System (OMS) Initiative: Fiscal Year 1982 Automatic Data Processing and Data Communications Cost Savings Initiative. The Secretary directed that PHS establish cost savings initiatives in ADP and data communications operations. Information was collected from the divisions about any economies they expected in each quarter of the fiscal year.

F. Provided staff support to the Director, NCI, in preparation for congressional hearings.

G. Other staff activities included:

- Participation in the NCI/ADP Committee with special reference to planning for future office technology at NCI.
- Consultative services to divisions on information and evaluation, and especially on the monitoring of support service contracts.
- Service as Assistant Project Officer for the ORI contract to operate the SCAN system. As this contract was terminated during the fiscal year, a major effort was made to review all systems documentation.
- Participation in monitoring the data processing activities at Frederick Cancer Research Facility and acted as a technical resource during recompetition of the data processing and library support contracts.

MANAGEMENT INFORMATION SYSTEM (MIS)

The National Cancer Institute's Management Information System (MIS) Project Office is responsible for:

A. the development of a Management Information System which provides information on budget, personnel, space, travel, and other primarily administrative activities; and

B. the coordination of selected NCI-wide automated data processing (ADP) activities, such as ADP security.

The MIS is composed of a network of user oriented and managed systems which are designed and developed at the request of and with requirements supplied by the operating areas and the MIS Office. In general, these systems support individual operating areas but are designed so that the information from several of them may be combined to provide a more unified picture of NCI activities than that provided by a single system. Components of the MIS developed to date support areas within the OD and several of the divisions with primary emphasis on the Financial Management Branch (FMB) and administrative offices.

The primary responsibility of the MIS Project Office is to maintain the operational state of current systems, to enhance current modules and to assist in the design and development of new components. This activity includes reviewing proposed modifications to ensure that the changes will produce the expected improvement without having a negative impact on other components of the system, the users, or interfacing systems; testing and documenting all new and modified programs and procedures; training of users; and resolving operational problems. Specific activities of this type during the year included:

A. Enhancement of the Budget and Status Systems which simplified operations by reducing the number of tables required to produce the reports and identifying errors at an earlier stage in the production cycle.

B. Preparation of quarterly manual updates for the NIH Space Management System from the NCI Space Management System database. Automated reports to assist in the preparation of the NIH required manual updates were developed and tested by MIS staff so that this activity could be assumed by the operating areas with minimal effort. Additional queries and summary reports were also added to the system, based on user requirements.

C. Modification of the NCI Personnel Data System (PDSS) operating procedures, software and documentation in order to keep the system operational when the NIH ARMS personnel system, the primary data source for the PDSS, was discontinued and replaced by the HHS TAPS System. Several PDSS monthly reports were redesigned in order to consolidate reports and to satisfy additional reporting requirements.

D. Enhancement of the NCI Travel System which included the development of software to provide a report to the Fogarty International Center on planned travel for the next fiscal year. Procedures were implemented and users trained to allow the divisions to input their own planned data. OD domestic travel data was added to the system to combine foreign and domestic data for use by OD travel and administrative staff.

E. Expansion of the Biweekly Status Report System to include reporting of Stay-in-School personnel as a separate group.

F. Modification of several versions of the Financial Data Report System (FDRS). A subobject class report was added to the FDRS/NCI as well as reports by division and the projection of obligations through the end of the fiscal year. For FDRS/OD, changes were made for FY82 which included reporting of additional CANs and object class codes, rearrangement of selected subobject classes, reformatting of the travel reports, and changes in the program area names on the summaries. A new report page to provide travel information by subobject class within program area was also added. For FDRS/DCBD, changes were made to regroup selected subobject class codes.

G. Introduction of a series of modifications throughout the year to reflect system changes invoked by the central computer facility, DCRT. These changes in the operating system, JCL utility programs, and procedures for handling tapes and disk data sets affect all of the MIS systems. In general, the required modifications were implemented and documented, so that users were unaware of any alterations in operating procedures.

H. A complete revision of the Personal Services Forecasting System with primary emphasis on including the new types of special pay for Commissioned Officers, adding additional categories such as Visiting Fellows to the report, expanding the forecast by accepting accessions and separations for additional categories of employees, and streamlining operations.

I. Implementation of a program which will automatically prepare flow charts from parameters in a WYLBUR data set. This procedure, when used in conjunction with the WYLBUR documenting facilities, allows all documentation for a system to be archived along with the software.

Support of the ADP System Security Program continued in the following areas:

A. Sixteen ADP System Security reviews of NCI application systems were conducted by the MIS Project Office. Guidance was given, upon request, to NCI system managers to aid them in improving their compliance with the requirements of the security program. A survey of facility managers was conducted in order to update the ADP equipment inventory.

B. A system was developed which takes the complete NCI file of financial data obtained monthly from the Central Accounting System and creates user-specific subsets on a need-to-know basis.

MIS staff provided support for specific ADP activities in other organizations in the Institute, primarily within the Office of the Director (OD) in the following ways:

A. Assisted the Program Analysis and Formulation Branch in monitoring the technical aspects of the operational support contract for the SCAN system. This effort was intensified during the year since the support contract was terminated on June 8, 1982, and the SCAN system was discontinued and archived at that time. MIS Project Office assistance included monitoring of archive procedures, acceptance testing of the resulting archive tapes, and detailed review and editing of all SCAN system documentation.

B. Assisted the Management Analysis Branch in the development of procedures for using the WYLBUR mail facility. MIS Project Office Staff helped conduct training sessions for NCI employees who were learning to use communicating word processing equipment to send messages via the DCRT computer. This activity was part of a larger investigation of improved office automation capability for which the office also provided technical support.

C. In conjunction with the Management Analysis Branch and the Training Office, provided a pilot WYLBUR training course, "Introduction to WYLBUR for Data Processing Applications," for a group of NCI employees. MIS Project Office staff assisted in all aspects of planning, coordination and classroom instruction.

D. Participated in the activities of the NCI/ADP Review Committee. Procedures for developing the system descriptions and coordination of the input for these narratives for the automated inventory of NCI administrative ADP systems were provided to the Subcommittee on Administrative Systems.

NCI was permitted by the Department to proceed with MIS development under the condition that the project results could be transferred to other institutes at NIH and other agencies. This effort continued in the following areas:

A. Software and documentation for one of the versions of the FDRS were given to NIADDK; consultation was provided to the NIADDK system manager to bring the system into operational status.

B. The software for the NIADDK Staffing Chart System was modified in order to reflect the conversion from the NIH ARMS to the TAPS system. This effort parallelled changes made to the NCI staffing chart program and reflects continued NCI consultation support for a transferred system.

C. Software and documentation of the Personal Services Forecasting System were transferred to the National Institute on Aging (NIA). Consultation on adapting the system to the NIA environment was also provided.

The staff of the MIS Project Office was assisted by a programming support contract with System Science, Inc. Major activities of this contractor are reported in the contract narrative.

LEGISLATIVE ANALYSIS AND CONGRESSIONAL LIAISON

The categories of activities in this area of responsibility are described below followed by a brief summary of typical actions carried out by the NCI during the past year.

1. Monitored and analyzed all legislation with potential impact or significance for the NCI. During the past year, bills on a wide variety of subjects were tracked and analyzed, i.e., Small Business Innovation Research Acts, Radiation Exposure Compensation Act, Humane Care for Laboratory Animals Act, and House and Senate reauthorization acts.

2. Assisted in the preparation of congressional hearings where the Director of NCI was requested to testify. Prepared briefing materials for the Director, reviewed testimony, attended hearings and prepared responses to follow-up questions. During the past year the Director of NCI testified regarding reauthorization bills and appropriations for FY1983. Special oversight hearings were held by the Senate Labor and Human Resources Committee on the NCI drug development program and the FDA in which the Director also testified. In addition, NCI senior staff were called upon to testify on the Radiation Exposure Compensation Act and on the issue of Kaposi's Sarcoma, a rapidly spreading form of cancer with high rates in California and New York.

3. Responded to numerous telephone, written and personal inquiries made by members of Congress and their staffs about NCI programs. Coordinated, when appropriate, such responses with the Department of Health and Human Services, and the NIH.

4. Through written and verbal communication, kept the senior NCI staff briefed on current congressional and legislative activities. Also kept the National Cancer Advisory Board informed of relevant congressional and legislative

matters. Responded throughout the year to inquiries from the NCAB about pending bills, particularly as such bills could affect the operation of the NCAB and the by-pass budget.

5. Arranged for meetings between NCI senior staff and members of Congress and their staffs.

CONTRACT NARRATIVE
OFFICE OF THE DIRECTOR FOR PROGRAM
PLANNING AND ANALYSIS, NCI
FY 1982

CONTRACTOR: JRB Associates (Contract #NIH-NO1-CO-75390)

TITLE: Planning and Support Services for the National Cancer Program

CONTRACTOR'S PROJECT DIRECTOR: Mr. Charles Fricker

PROJECT OFFICER: Barbara R. Murray

OBJECTIVE: Provide the support services necessary to assist the Office of the Director, NCI, in meeting the expanded responsibilities established by the National Cancer Act of 1971 and subsequent amendments.

MAJOR ACCOMPLISHMENTS: The activities included support services for program planning, the preparation of briefing and presentation materials, administrative and logistical support to the Office of the Director for planning conferences and meetings, and assistance in the preparation of draft documents required to develop the National Cancer Institute's Director's Report/Annual Plan.

SIGNIFICANCE TO THE NATIONAL CANCER PROGRAM: The expanded scope and responsibilities of the National Cancer Program have imposed additional requirements for reporting, planning and analyzing alternative courses of action. This contract provides assistance in areas which could not be performed within NCI.

DATE CONTRACT INITIATED: September 30, 1977

TOTAL CONTRACT VALUE: $3,403,104 all of which has been obligated. The contract has been extended through November 1982.

CONTRACT NARRATIVE
OFFICE OF THE DIRECTOR FOR PROGRAM
PLANNING AND ANALYSIS, NCI
FY 1982

CONTRACTOR: System Sciences, Inc. (NO1-CO-95460)

TITLE: NCI Management Information System Support Services (Programming)

CONTRACTOR'S PROJECT DIRECTOR: Christopher Gordon

PROJECT OFFICER: Betty Ann Sullivan

OBJECTIVE: (1) To provide maintenance support which includes modification to computer programs, testing, installation, user training, and documentation updates for software and/or procedural changes approved by the MIS Configuration Control Board; (2) to provide operational support which is used primarily to initialize systems at the start of a new fiscal year, to operate test or prototype systems prior to release to the user, and for problem resolution; (3) to provide implementation support for development of software and related documentation based on specifications prepared by the MIS Project Office.

MAJOR ACCOMPLISHMENTS: Maintenance activities included report modifications for the NCI Personnel Data System to consolidate existing reports and provide additional information; addition of a separate file for Stay-in-School employees in the Biweekly Status Report System to allow separate tracking of these employees; integration of foreign, planned and domestic data in the NCI Travel System; and report format changes and restructuring of subobject class codes in various Financial Data Report Systems to support additional financial monitoring in administrative areas. Operational support included incorporating numerous DCRT imposed changes in all MIS systems, implementing an automated flow charting system to permit archiving of documentation with the software, and teaching an introductory course on WYLBUR to MIS system operators. Development activities included a major enhancement of the Operating Budget and Status Systems to simplify operations, additional queries for the NIH Space Management System as requested by users, a complete revision of the Personnel Services Forecasting System to expand the coverage of the system, and implementation of a program to prepare required subsets of central files to support the ADP System Security Program.

SIGNIFICANCE TO THE NATIONAL CANCER PROGRAM: The National Cancer Act of 1971 provided for improved information systems. This contract gives NCI the programming support required to maintain the operational components of its Management Information System and to implement new modules.

PROPOSED COURSE: To continue the current pattern of maintenance, operational support and development activities under the current contract until March 1983. Competition for a follow-on contract has been initiated.

DATE CONTRACT INITIATED: September 24, 1979

TOTAL VALUE OF CONTRACT: $499,679

CONTRACT NARRATIVE
OFFICE OF THE DIRECTOR FOR PROGRAM
PLANNING AND ANALYSIS, NCI
FY 1982

CONTRACTOR: ORI, Incorporated - Contract #NO1-CO-95427

TITLE: Science Content Analysis System (SCAN)

CONTRACTOR'S PROJECT DIRECTOR: Mr. Norman Shusterman

PROJECT OFFICER: Dr. Michael Klein

OBJECTIVE: To maintain an updated science data base for each fiscal year on NCI supported projects and to relate these to the scientific recommendations of the National Cancer Program Plan; to enhance system capabilities in light of new requirements; to provide tabular data on the relationship of NCI projects to the Plan and to different aspects of cancer research; to provide an ad hoc query capability.

MAJOR ACCOMPLISHMENTS:

1. PAFB staff prepared several reports based on the FY 1981 data base, e.g., different aspects of chemical and physical carcinogenesis, prevention, radiodiagnosis.

2. Using PAFB science content analyses, ORI, Inc. developed an updated data base for the SCAN system covering NCI extramural projects active in FY81.

3. Information retrieved from the SCAN system provided a basis for analysis of National Cancer Plan (NCP) priority and resource estimates made in 1972 as compared with actual 1980 allocations by NCP objectives. This is referred to as the "Decade Overview."

4. The SCAN system was employed to provide an assessment of NCI-supported extramural activities in nutritional-dietary aspects of chemoprevention.

5. Enhancements were incorporated in operations including the capability of determining on a quarterly basis, the level of effort in different fields of cancer supported extramurally by the NCI.

6. The SCAN system was archived in a form that lends itself to rapid reutilization whenever requested.

SIGNIFICANCE TO THE NATIONAL CANCER PROGRAM: Use of the SCAN system provides the NCI and other groups with an objective measure of the scientific coverage by NCI-funded extramural projects in relation to the NCPP. General and specific questions relating to elements of the National Cancer Plan or to research fields in cancer can be answered from information in the SCAN system.

PROPOSED COURSE: The SCAN system was archived as of June 8, 1982.

DATE CONTRACT INITIATED: May 15, 1979

TOTAL VALUE OF CONTRACT: $379,503. The NCI contract officer has been informed that the services of ORI, Inc. will no longer be needed after June 8, 1982.

NATIONAL CANCER INSTITUTE

DIVISION OF EXTRAMURAL ACTIVITIES

ANNUAL REPORT

October 1, 1981 through September 30, 1982

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OFFICE OF THE DIRECTOR

DIVISION OF EXTRAMURAL ACTIVITIES

Director: Ms. Barbara Bynum
Deputy Director: William A. Walter, Jr., M.D.
Acting Assistant Director: Vincent T. Oliverio, Ph.D.
Special Assistant for Special Projects: Mary A. Fink, Ph.D.
Administrative Officer: Ms. Jean Stein

OFFICE OF THE DIRECTOR

The Division of Extramural Activities is one of the five major components of the National Cancer Institute. The mission of this Division is to plan and direct coordination with the other Divisions of the National Cancer Institute, a program in support of national and international cancer research and training through a system of grants and contracts.

During this fiscal year, a number of changes have occurred. The Grants Administration Branch and the Grants Financial Data and Analysis Branch were transferred out of DEA into the Office of the Director. This change was made in order to place all business management functions in the Institute within a single organizational setting. Although these two Branches are no longer within the DEA structure, a close working relationship has been maintained. Another change occurred when the Cancer Clinical Education Review Committee was transferred from the Division of Resources, Centers, and Community Activities to DEA. Formerly, this Committee was part of the Clinical Education Program, but with the transfer to DEA, the peer review of grants in support of the program has been separated from the programmatic activities which remain in the DRCCA. Finally, in order to implement the DEA responsibility for developing and implementing the technical merit peer review of Institute-wide research, resource, and intramural contract proposals, three new Committees have been chartered. With the addition of these new Committees, the DEA now have five chartered review Committees for the purpose of providing peer review of contract proposals.

The DEA has responsibility for the Committee Management Office whose activities encompass the development and implementation of policies, guidelines, and procedures for nomination, clearance, invitation and appointment of members; and establishment, utilization and management of approximately 26 chartered NCI review and public advisory committees requiring the services of some 600 committee members. Committees are divided into two broad categories--scientific review groups and program advisory groups. The primary function of the scientific review groups is to determine the scientific merit of research grant applications and contract proposals. The program advisory groups provide the broad perspective on the research needs and scientific opportunities of the Institute and their social impact.

The Director of the Division of Extramural Activities also serves as the Executive Secretary of the National Cancer Advisory Board. The Board has the responsibility for the second phase of the grant dual review process and also advises the Director of the National Cancer Institute and Director of the National Institutes of Health on policy matters regarding cancer grant- and contract-supported research and training programs.

The Orientation Handbook for use of the NCAB has been revised. This handbook includes the history of the NIH and NCI and instructions on the methods of the peer review process employed by the Department of Health and Human Services and the National Institutes of Health. In addition, a booklet on the peer review of contract proposals at the National Cancer Institute has been published. This is a guide for reviewers of contract proposals.

Office of the Special Assistant for Special Projects

The major function of the Office of the Special Assistant for Special Projects is to coordinate various functions of the extramural arm of the Institute. The more important of these activities are in support of: (a) the National Cancer Advisory Board; (b) the Request for Application (RFA) and Program Announcement (PA) aspects of NCI divisions; and (c) NCI's support of conferences.

National Cancer Advisory Board

The office is responsible for or involved in several aspects of the NCAB. These include: (a) the Special Actions Subcommittee; (b) the Activities and Agenda Subcommittee; and (c) the Chiefs of Program Directors meetings.

The Special Actions Subcommittee is responsible for bringing to the NCAB's attention any problems cited by a DRG or NCI review group or by a Program Director in any NCI Division for any grant under review at a particular meeting. This includes ethical and human subject problems and biohazard problems as well as perceived errors in review. The Subcommittee chore this year to discuss three NCI programs by reviewing in-depth all grants for that round. These included the Biomedical Minority Program in DEA and the Tumor Biology and Immunology Programs in DCBD. An additional 24 large multifaceted research grants were also reviewed for program content and progress. DEA staff advised staff of all NCI divisions on policy and procedures for NCAB review and convened a pre-Board meeting for rehearsal of matters to be presented to the Board. The Special Assistant serves as Executive Secretary of this Subcommittee.

The Activities and Agenda Subcommittee serves to select items to be presented at the full NCAB meeting. Subcommittee members met four times with DEA and NCI/OD staff, followed by DEA's formal setting of the agenda. Suitable topics are suggested by interested NCI staff from all divisions. The Director, DEA, serves as Executive Secretary of this Subcommittee.

During this year; the Director, DEA, formalized the establishment of the "Chiefs of Program Directors" group. The group, with a representative from each Division, met with DEA staff biweekly to discuss grant problems and to report staff changes, information items, etc.

Requests for Applications (RFA) and Program Announcements (PA)

The various Divisions of NCI sometimes solicit applications in particular areas by use of the Request for Application (RFA) and the Program Announcement (PA). After Divisional and Executive Committee approvals are satisfied, these documents are sent to DEA for review before being forwarded for publication in the NIH Guide to Grants and Contracts. Since January 1, 1982, ten RFAs have been reviewed. To date, two have been published, one announcement of a pending RFA has been received, and four Program Announcements have been reviewed, resulting in three having been published, and one withdrawal.

Conference Program

The NCI Conference Program has sustained major changes in the recent past. Whereas it was a program with a given budget to support high-priority conferences, conferences are now selected for payment using a variety of criteria and are

approved for payment by the NCI Executive Committee. Almost all NCI conference support is now by the R13 grant. These applications are usually reviewed within NCI by mailing to four or five knowledgeable scientists outside NCI. A summary of conference-related activities follows:

Requests for Applications (RFAs)

"Epidemiologic Studies of Rare Tumors"
NIH-NCI-DCCP-SPB-82-1

Grant applications are invited for epidemiologic studies of rare tumors. Epidemiologic investigations have tended to emphasize the more prevalent forms of cancer. A number of tumors which occur with less frequency have lacked the research interest of investigators.

"The Role of Natural Inhibitors in the Prevention of Cancer"
NIH-NCI-DRCCA-82-2

Grant applications are invited for studies which are directed at examining the role of several natural inhibitors in the prevention of cancer. The proposed studies should seek to (1) elucidate further the protective effect of several natural inhibitors in reducing the incidence of various site specific cancers, and (2) lead to a greater understanding of the extent, or action, of several natural inhibitors in the possible cancer prevention processes in humans. Clinical and epidemiological studies are being requested to develop basic information which may be helpful at a later date in decision making with regard to the application of the compounds in clinical trials for chemoprevention.
Published in Vol. 11, No. 4, March 26, 1982.

"Non Invasive Approach for Detection of Lung Cancer"
NIH-NCI-DCBD-DB-82-3 (Withdrawn)

"Immunohistochemical Classification of Solid Tumors"
NIH-NCI-DCBD-DB-84-4 (Withdrawn)

"Specific Immunoassays for Cancer Associated Isoenzymes"
NIH-NCI-DCBD-82-5 (Withdrawn)

"Cancer Control Research Units for Defined Population Studies"
NIH-NCI-DRCCA-CCB-82-6

Grant applications are invited for the establishment of Cancer Control Research Units for Defined Populations. Cancer control research includes both prevention (primary and secondary) and management (diagnosis, pre-treatment evaluation, treatment, rehabilitation, and continuing care). It builds on the research and knowledge bases of epidemiology, biomedical, clinical, behavioral and other sciences. It requires carefully designed investigations, often including both study and control groups and/or defined denominator populations.
Published in Vol. 11, No. 2, January 29, 1982.

"Cancer Control Studies in Occupational Settings"
NIH-NCI-DRCCA-82-7

Grant applications are invited for evaluation studies of established worker education programs whose goals are to reduce or eliminate exposure to cancer hazards in occupational settings. The proposed studies should seek to: (1) measure the impact of the intervention of prevention education on workplace behavior change; (2) lead to greater understanding of those workplace organizational, administrative, and social factors which serve as reinforcements or deterrents to the cancer control goals of education interventions. Such evaluation studies are being requested to develop information on effective cancer control approaches and methods to reduce or eliminate exposure to cancer hazards which can be replicated in other occupational settings.

"NCI Shared Instrumentation Grants"
NIH-NCI-DCBD-82-8

Grant applications are invited for the purpose of acquiring new, or the updating of existing, major research instruments which cannot be justified for use on a single project but which can serve several projects on a shared basis. Access to the instruments provided will not be restricted to NCI grantees nor to investigators within a particular grantee institution. This is a one time announcement that will not be repeated or awarded in future years.

"Cryopreservation of Morris Hepatomas"
NIH-NCI-DCBD-82-9

Grant applications are invited from interested investigators to develop procedures to freeze Morris hepatomas that prevent loss of viability or properties characteristic of each individual tumor type, and to set up a test system that rigorously monitors the persistence of those characteristics. Applicants should concentrate on two of the fast-growing and two of the slow-growing tumors currently maintained by serial transplantation in live rats at Howard University. Investigators may include other Morris hepatomas in the study.

"Community Clinic Oncology Program (CCOP)"
NIH-NCI-DRCCA-82-10

Grant applications are invited to establish a large scale cancer control effort to involve practicing community oncologists in the NCI clinical trials program. The purpose of the program is to utilize as a resource the increasing number of highly trained oncologic specialists who have entered community practice in recent years. Coupling such a network of practicing oncologists with ongoing clinical research projects will result in a sustained entry of patients to clinical studies and should result in improvements in cancer management for all cancer patients.

Program Announcements (PA)

Preventive Oncology Academic Award (POAA) - Reissue
Published Vol. 11, No. 5, 4/23/82

This non-renewable award for a project period of five years is intended to stimulate high-quality research on which educational programs oriented toward cancer prevention could be based in schools which do not have such programs or to strengthen the research and education programs of schools in which high-quality research in preventive oncology already exists. It is expected that each program in cancer prevention will build upon the institution's demonstrable expertise and experience in epidemiology, human genetics, biostatistics, clinical oncology, nutrition and other pertinent basic cancer research.

Cancer Control Science Program - Published Vol. 11, No. 4, 3/26/82

Grant applications are invited from interested investigators for the support of Cancer Control Science Programs. These programs will provide a scientific focus within which investigators can conduct a variety of cancer control research studies. Cancer control research includes both prevention (primary and secondary) and management (diagnosis, pre-treatment, evaluation, treatment, rehabilitation, and continuing care). It builds on the research and knowledge bases of epidemiological, biomedical, clinical, behavioral and other sciences. It requires carefully designed investigations, often including both study and control groups and/or defined denominator populations.

Research Related to Genetic Susceptibility to Human Breast Cancer - Published Vol. 11, No. 2, 1/29/82

Grant applications are invited from interested investigators for investigations of genetic susceptibility to human breast cancer. The clustering of breast cancer in families is a well-known phenomenon, and recent studies have indicated that in some families the disease appears to be segregating as a Mendelian trait, suggesting that one or more human genes are responsible for the susceptibility.

Evaluation of Carcinogenic Risk of Chemicals to Humans - Withdrawn

Conference Program

The NCI conference program has sustained major changes in the recent past. Whereas it was a program with a given budget to support high-priority conferences, conferences are now selected for payment using a variety of criteria and are approved for payment by the NCI Executive Committee. Almost all NCI conference support is now by the R13 grant. These applications are usually reviewed within NCI by mailing to four or five knowledgable scientists outside NCI. A summary of conference related activities follows:

Table 1

Cancer Reviewed Conference (R13) Grants

	Number	Mean Priority Score	Direct Costs
REVIEWED:			
Approved	37	206	$1,069,893
Awarded*	22	182	217,113
Not Awarded	15	239	--
Disapproved	0	--	--
Type 5s Awarded	--	--	433,361
TOTAL AWARDED:			$ 650,474

Table 2

Multi B/I/D Reviewed Conference (R13) Grants - Cancer Related

	Number	Mean Priority Score	Direct Costs
REVIEWED:			
Approved	28	192	$ 957,492
Awarded by NCI*	11	167	42,666
Not Awarded by NCI	17	208	--
Disapproved	7	--	--
TOTAL AWARDED:			$ 42,666

*Based on 9 months FY 82 awards. 6 paid in FY 81 are not included in direct costs.

Ten R13s returned to DRG, not of priority interest to NCI.

Table 3

Conference Grants (R13) Reviewed by NCI by Cancer Activity

Cancer Activity	Review* Number	Review* Direct Costs	Awarded** Number	Awarded** Direct Costs
Breast Cancer	2	$ 47,005	--	--
Biological Carcinogenesis	3	90,714	3	$ 59,101
Biochemical Pharmacology	4	44,332	4	28,543
Biological Response	1	34,430	1	5,000
Cancer Control	2	61,324	--	--
Chemical Carcinogenesis	2	36,820	2	36,820
Clinical Treatment	7	175,917	2	6,000
Diagnostic Imaging	1	33,000	1	10,000
Diagnostic Research	2	69,400	1	10,000
Epidemiology	--	--	1	127,173
Immunology	2	44,595	3	171,545
Nutrition (DCCP)	3	46,000	1	8,200
Radiation Therapy	2	130,760	2	50,074
Tumor Biology	6	255,596	6	258,149
TOTALS	37	$1,069,893	27	$770,605

*Based on 12 months.
**Based on 9 months. 6 paid in FY 81 are not included in direct costs. Includes Type 5s.

Table 4

Conference Grants (R13s) Reviewed by Multi B/I/D by Cancer Activity

Cancer Activity	Reviewed* Number	Reviewed* Direct Costs	Awarded** Number	Awarded** Direct Costs
Breast Cancer	2	$ 46,111	--	$ --
Biological Carcinogenesis	4	139,446	--	--
Biological Response	1	29,090	--	--
Chemical Carcinogenesis	2	271,693	--	--
Clinical Treatment	1	9,202	--	--
Diagnostic Imaging	2	58,500	--	--
Epidemiology	2	37,850	--	--
Immunology	13	397,926	9	35,666
Nutrition (DCCP)	1	8,000	1	3,000
Tumor Biology	7	145,950	1	4,000
TOTALS	35	$1,143,768	11	$ 42,666

*Based on 12 months.
**Based on 9 months. 6 paid in FY 81 are not included in direct costs. Includes Type 5s.

R13s Reviewed by NCI - FY 82

GRANT TITLE	PRINCIPAL INVESTIGATOR CONFERENCE DATES CONFERENCE SITE
**Support for Cancer Research Center Workshops	Terri Grodzicker, Ph.D. Series Cold Spring Harbor, NY
Conference on Particle Accelerators in Radiation Therapy	Eric J. Hall, D.Sc. 3/28-31/82 Houston, TX
*Cell Proliferation, Cancer and Cancer Therapy	Renato L. Baserga, M.D. 2/17-19/82 New York City, NY
Image and Display Optimization for Cancer Detection	Charles A. Kelsey, Ph.D. 1982 Santa Fe, NM
Cancer Symposium of 1981	Joseph R. Castro, M.D. 11/13-14/81 San Francisco, CA
Wilside Meeting on Modern Trends in Human Leukemia V	Rolf Dietmar Neth, M.D. June, 1982 Hamburg, Germany
Modulation and Mediation of Cancer by Vitamins	Frank L. Meyskens, Jr., M.D. 2/23-26/82 Tuscon, AZ
*The Possible Role of Nitrosomines in Human Cancer	Victor King McElheny 2/28-3/3/82 Cold Spring Harbor, NY
**Conference of T and B Cell Tumors	C. Fred Fox, Ph.D. 4/11-16/82 Los Angeles, CA
Conference on Tumor Viruses and Differentiation	C. Fred Fox, Ph.D. 3/21-28/82 Los Angeles, CA
*First Conference on Radioprotectors and Anticarcinogens	Michael G. Simic, Ph.D. 6/21-24/82 Gaithersburg, MD

*Funded FY 81
**Funded FY 82

*The Therapeutic Application of Liposomes	Stephen Carter, M.D. 11/5-7/81 San Francisco, CA
*Biochemical and Biological Makers of Neoplastic Transformation	Prakash Chandra, D.Sc. 9/28 - 10/8/81 Corfu Island, Greece
*Meeting of the Reticuloendothelial Society	Robert Evans, Ph.D., D.Sc. 10/12-16/81 Milwaukee, WI
**Conference on Micronutrients: Vitamin A and Retinoids	George Wolf, Ph.D. 6/21-25/82 Saxtons River, VT
**Gordon Research Conference on Mutagenesis, 1982	Bea A. Singer, Ph.D. 7/5-9/82 New Hampton, NH
Western States Conference on Cancer Rehabilitation	Stephen K. Carter, M.D. 3/24-26/82 San Francisco, CA
Research Opportunities in Diet and Disease	Max Milner, Ph.D. 4/16-19/82 New Orleans, LA
**The Third World Conference on Lung Cancer	George A. Higgins, Jr., M.D. 5/17-20/82 Tokyo, Japan
**Fourth International Workshop on Chromosomes in Leukemia	Janet D. Rowley, M.D. 9/2-7/82 Chicago, IL
**Conference on Rational Basis for Chemotherapy	C. Fred Fox, Ph.D. 4/18-23/82 Los Angeles, CA
**International Symposium on Leukemia Cell Biology and Therapy	Alvin M. Mauer, M.D. 5/19-22/82 Memphis, TN
Meeting on Advances in Breast Cancer Research	Marvin A. Rich, Ph.D. June, 1982 Oakland, CA
**Conference on Chemistry and Biology of Interferons	C. Fred Fox, Ph.D. 3/7-12/82 Los Angeles, CA

*Funded FY 81
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Conference: Prevention of Hereditary Large Bowel Cancer	John F. Ingall, M.D. 6/3-4/82 Detroit, MI
Workshop on Approach to Management of Mesothelioma	W. Donald Weston, M.D. 9/16-17/82 East Lansing, MI
**Gordon Conference on Chemotherapy of Experimental and Clinical Cancer	Joseph R. Bertino, M.D. 7/26-30/82 New London, CT
**Ninth Conference on Analytical Cytology	L.S. Cram, Ph.D. 10/17-23/82 Bavaria, West Germany
Conference on Cellular Systems for Toxicity Testing	Gary M. Williams, M.D. 10/5-7/82 New York City, NY
**Fourth International Symposium on Nasopharyngeal Carcinoma	Gary R. Pearson, Ph.D. 9/27-29/82 Kuala Lumpar, Maylasia
**Symposium on Anticancer and Antiviral Agents	William Niedermeier, Ph.D. 11/3-5/82 Birmingham, AL
**International Conference on Papilloma Viruses	Thomas R. Broker, Ph.D. 9/15-19/82 Cold Spring Harbor, NY
Symposium on Chromosomes and Lymphoma	Avery A. Sandberg, M.D. 7/27-31/82 Brugge, Belgium
**Gordon Research Conference on Cancer, 1982	Paul H. Black, M.D. 8/23-27/82 New London, CT
First World Congress on Trophoblastic Neoplasms	Roland A. Patillo, M.D. 10/24-28/82 Lagos, Nigeria
Current Controversies in Breast Cancer: 1982 Annual Cancer Conference	Robert C. Hickey, M.D. 11/3-6/82 Houston, TX
**First Annual Conference: Magnetic Resonance Imaging Society	Alexander R. Margulis 8/16-18/82 Boston, MA

**Funded FY 82

R13s Reviewed by B/I/D - Cancer Related

GRANT TITLE	PRINCIPAL INVESTIGATOR CONFERENCE DATES CONFERENCE SITE
National Symposium: Hybridomas and Cellular Immortality	Baldwin H. Tom, Ph.D. 11/4-6/81 Houston, TX
**IgD Structure and Function	G. Jeanette Thorbecke, Ph.D. 1/13-15/82 New York City, NY
**Conference on Evolution of Hormone-Receptor Systems	C. Fred Fox, Ph.D. 3/14-20/82 Los Angeles, CA
Conference on Interferons	C. Fred Fox, Ph.D. 3/7-14/82 Los Angeles, CA
Conference on Gene Regulation	C. Fred Fox, Ph.D. 3/28 - 4/4/82 Los Angeles, CA
Genetic Toxocology: An Agriculture Perspective	Raymond A. Fleck, Ph.D. 11/1-5/81 Davis, CA
International Symposium: The Secretory Immune System	Jerry R. McGhee, Ph.D. 5/4-7/82 New York City, NY
Unresolved Research Problems in Otolaryngology	David J. Lim, M.D. 1/19-21/82 St. Petersburg Beach, FL
**Ninth International RES Congress	Sigurd J. Normann 2/8-12/82 Davos, Switzerland
In Vitro Mutagenesis Meeting	James D. Watson, Ph.D. May, 1982 Cold Spring Harbor, NY
AVMA Colloquium on Clinical Immunology	Joe S. Cloyd, DVM May, 1982 Palatine, IL

**Funded FY 82

**Workshop on Macrophage Activation	Dolph O. Adams, Ph.D. 5/82 Hilton Head, SC
Seventh Herpes Virus Workshop	James D. Watson, Ph.D. 8/31 - 9/5/82 Cold Spring Harbor, NY
Second International Symposium on Medical Virology	Luis M. de la Maza, Ph.D. 11/4-6/82 Anaheim, CA
**Third Conference on Hemoglobin Switching	George Stamatoyannopoulos, M.D. 6/82 Seattle, WA
Gordon Research Conference on Hormone Action	John D. Baxter, Ph.D. 8/9-13/82 Meridien, NH
Conference on Proteolytic Enzymes and their Inhibitors	Michael Laskowski, Jr., Ph.D. 6/28-7/2/82 Plymouth, NH
Workshop on Physics and Engineering in Medical Imaging	Orhan Nalcioglu, Ph.D. 5/82 Pacific Grove, CA
Gordon Research Conference on Fibronectin	John A. McDonald, M.D., Ph.D. 7/5-9/82 Tilton, NH
**1982 Gordon Research Conference: Food and Nutrition	James R. Kirk, Ph.D. 8/8-13/82 New London, NH
Human Immune Response to Viruses	John L. Sullivan 6/27-2/82 Creaton, England
**15th International Leucocyte Culture Conference	Richard L. O'Brien, M.D. 12/5-9/82 Pacific Grove, CA
Gordon Conference on Animal Cells and Viruses	Barbara A. Hamkalo, Ph.D. 6/21-25/82 Tilton, NH
Workshop on Rabbit Immuno-genetics and Immunobiology	Louise T. Adler, Ph.D. 4/7-9/83 Memphis, TN

**Funded FY 82

**Immune Network	Constantin Bona, M.D., Ph.D. 9/28 - 10/1/82 New York City, NY
Infections of Laboratory Rodents: Effect on Research	Pravin N. Bhatt, Ph.D. Btwn 11/82 - 5/83 Bethesda, MD
International Society for Experimental Hematology 11th Annual Meeting	Lyle L. Sensenbrenner, M.D. 8/11-15/82 Baltimore, MD
Third International Immunological Monitoring Symposium	Joshua Miller, M.D. 11/21-24/82 Key Biscayne, FL
**Fifth IR Gene Workshop	Carl W. Pierce, Ph.D. 9/82 St. Louis, MO
**Third International Lymphokine Workshop	Stanley Cohen, M.D. 8/1-5/82 Farmington, CT
ICPEMC-A Request for Support for its Second Phase	Frits H. Sobels Series Lausanne, Switzerland
**Conference on Molecular Cell and Antibody Networks	Alfred Nisonoff, Ph.D. 7/5-9/82 Saxtons River, VT
Eleventh International Biometric Conference	David L. Solomon, Ph.D. 9/6-11/82 Toulouse, France
Conference on Magnetic Resonance	Oleg Jardetzky, M.D., Ph.D. 8/29 - 9/3/82 Stanford, CA
Symposium: The Extracellular Matrix	Susan P. Hawkes, Ph.D. 6/28 - 7/2/82 Midland, MI

**Funded FY 82

RESEARCH ANALYSIS AND EVALUATION BRANCH

Chief: Mr. Harry Y. Canter

RESEARCH ANALYSIS AND EVALUATION BRANCH

Overview of Branch Activities

The Research Analysis and Evaluation Branch (RAEB) serves as the major centralized source of scientific information on NCI-supported research projects. Members of the Branch analyze and index the scientific content of all grants awarded by NCI, all NCI contracts, and all NCI intramural projects, and monitor published results supported by grants through a unique literature surveillance program. This information is widely disseminated throughout NCI--to the other Divisions, Office of the Director, Office of Cancer Communications, Financial Management Branch, Program Analysis and Formulation Branch, and the International Research Data Bank; to other NIH organizations such as the Research Documentation Section and the Research Analysis and Evaluation Branch of the Division of Research Grants; to other NIH Institutes; and to other Government and private organizations. Staff members also compare pending grants and contracts with existing NCI-supported projects at the same institution to assure that there is no project overlap or duplicated support.

Computer Information System: GENIUS

The heart of the operation of the Research Analysis and Evaluation Branch is the Grant Elements Network-Internal Users System (GENIUS), in use since 1975. The bulk of the data base consists of scientific data for NCI grants indexed according to fixed categories as well as specific key words or phrases taken by the indexer from the text of the grant application. Data can be retrieved in a variety of formats in order to respond to inquiries and prepare reports.

In addition to the scientific indexing prepared by the Branch, other data available from the system include administrative data from the IMPAC system of the Division of Research Grants (DRG) and abstracts of each grant. Until the end of FY 1981, these abstracts, written by the principal investigators, were prepared for the computer by the Smithsonian Science Information Exchange (SSIE). Since the SSIE is no longer being supported, DRG is now responsible for preparing the abstracts for input into the CRISP System.

In January 1982, the Director of NCI concluded that GENIUS "will be the official NCI programmatic information system and will be the reference system for program content and dollar information." He based this decision on the results of a study of NCI and NIH science information systems done by Enviro-Control, Inc., under contract to NCI. In this study, the contractor compared the content, quality, capabilities, and usage of all systems.

When completely operational, the Grant Elements Network-Internal Users System will include data from five separate computer information storage files: (1) active research grants and companion history file of terminated grants; (2) unfunded grants and history file, which includes a total of five previous years of data; (3) active contracts and history file; (4) intramural research projects and history file; and (5) training programs. All scientific and administrative data on the active and history files and the intramural research file are searchable on the computer. The current unfunded grants file consists of disapproved and approved-but-not funded grants for the past two years. This file contains only administrative data from IMPAC. The project title, program area, applicant department, and study section are the only points of access to scientific information on these projects.

The intramural research project file was added to the GENIUS system and became operational in 1978. The active contracts file became operational with all contracts active as of August 1, 1980. The contract data base is currently dependent on the IMPAC System for administrative items. Any data not available on the IMPAC System can be supplied by the Contracts Management System, recently acquired by the Grants Financial Data and Analysis Branch, Office of the Director, NCI. Once this Branch completes its policy statement on the use of the Contracts Management System, programming efforts will resume to augment data missing from IMPAC. After the GENIUS contract file is completed, the training file will be automated.

About 80 percent of the active grants, including new proposals and type 2 requests for continuing support, 5 percent of contracts, and 40 percent of the intramural research projects have been entered into the system. GENIUS is maintained and operated solely by the Branch, which is greatly indebted to the Division of Computer Research and Technology (DCRT) for help in developing and implementing the system. Other instititues at NIH have expressed interest in GENIUS and with the help of DCRT are using it as a model for their own systems.

Requests for Information

Requests to the Research Analysis and Evaluation Branch are made daily and vary in complexity. Most are now answered by using the GENIUS system, but other sources of information are maintained and used frequently by the Branch. These include copies of grant applications and contract proposals for active projects, progress reports, study section summary statements, reprints of published grant-supported papers, and documents concerning individual trainees and fellows. The Branch has also developed several unique files of information, including one that lists the names and backgrounds of principal investigators on all applications submitted to NCI, whether approved or not, and the names and backgrounds of all other professional personnel on awarded grants only. This file is used often by RAEB members and by staff of the Review and Referral Branch looking for and verifying the names of scientists with a particular expertise to send on site visits.

The number of requests for information increased to almost 700 in calendar year 1981, 17 percent more than the previous year. Almost half (46 percent) came from the Office of Cancer Communications (OCC), Office of the Director, NCI, and ranged from information to answer letters from the public to inquiries from members of Congress and the White House staff. This high percentage reflects increasing public awareness of NCI programs and the important role the RAEB plays in helping the OCC respond to a wide variety of requests.

The next largest number of requests came from the offices of the program directors in the various divisions of NCI--150 or 21 percent of the total. In large part, these requests deal with both grant-and contract-supported studies and reflect the increased number of scientists involved in the extramural programs, especially grants, as a result of the major NCI reorganization finalized in 1980.

The remainder of the requests came from the NCI Budget Office, Office of the Director (11 percent), other NIH organizations (5 percent), and non-NIH organizations and individuals (17 percent). Because of the continued high rate and

complexity of requests, much more time and effort had to be spent this year in the information retrieval process, resulting in fewer staff-hours available for scientific indexing of information for input into GENIUS.

This year the requests, as well as an index of the requests, have been entered into the computer and put on microfiche. Data include the date, requester and subject. This information makes for an efficient way of avoiding repetition, keeping track of past requests, and analyzing the ways in which the GENIUS system is used and by whom.

Requests cover a wide range of topics from a wide variety of sources. Some examples are given in the following table.

Information Requests to the RAEB, FY 1982

Request	Source
1. NCI grants related to studies of Vitamin C, 1973-80	Division of Extramural Activities, NCI
2. NCI grants, contracts and intramural projects on tuberous sclerosis, FY 1979-81	Office of Cancer Communications, NCI
3. R01 & P01 grants with major emphasis on colon/rectum, bladder, prostate, or pancreas cancer	Division of Extramural Activities, NCI, for NCAB Subcommittee on Organ Sites
4. FY 1981 NCI dollars for recombinant DNA research	Financial Management Branch, NCI, for Dr. DeVita/Congressional hearings
5. Total amount awarded for expired contract CB64010	National Heart, Lung and Blood Institute
6. NCI-funded project on leukemia and thyroid disease in relation to nuclear fallout in Utah	Office of the Director, NIH
7. NCI-supported projects from 1937 to present related to asbestos hazards; estimated number of pages of materials related to these projects	Office of the Director, Division of Cancer Cause and Prevention, NCI, for Secretary, DHHS
8. FY 1980 grants, contracts, and intramural projects related to environment, nutrition, or epidemiology with percentage relevance	Office of Cancer Communications, NCI, for NYC Public TV
9. Current grants and contracts on thermography	Washington, D.C., Council of Medicine and Health
10. NCI support to detect mutagenic halogenated hydrocarbons	NIH Patent Office

Special Projects

Branch staff continued to devote much time to requests to retrieve and analyze information for special programs and activities. Mr. Harry Canter, Chief of RAEB, and Ms. Rosemary Cuddy, Deputy Chief, along with other members of the staff, were directly involved in providing the necessary information.

Diet, Nutrition and Cancer Program

This is the fourth year that Branch staff has assisted the Diet, Nutrition and Cancer Program (DNCP), established to coordinate all nutrition research supported by the various NCI programs. The function of the Nutrition Program is to collect, analyze, and disseminate information on the interrelationships between diet, nutrition, and the etiology of cancer and the therapy and rehabilitation of the cancer patient.

Branch members played a significant role in helping DNCP implement their information function. They identified all fiscal year 1981 NCI grants, contracts, intramural, and training projects, estimated the percentage of dollars spent on each award for nutrition research relevant to the Program, and entered these data on a special file, which they provided in machine-readable form to the NIH Nutrition Coordinating Committee. Branch members used these data to help compile the DNCP status report and answer inquiries on NCI support of nutrition activities.

Bellrad Research Projects Analysis Subcommittee

The RAEB is providing information expertise to aid NCI and NIH in their role on the PHS Subcommittee to Coordinate Radiation Activities. Mr. Canter and Ms. Cuddy are members of the Biological Effects of Low Level Radiation (Bellrad) Research Projects Analysis Subcommittee, formed at NCI to concentrate on this topic of major concern to the PHS Subcommittee. Branch members have developed a separate file of information on low level ionizing radiation and incorporated into the GENIUS system a special series of radiation-related categories developed by the Bellrad Subcommittee. In this way, the RAEB can store, search, and retrieve information on NCI-supported grant, contract, and intramural research projects according to criteria determined by the Subcommittee, and will continually update the data set. They also incorporate similar information on projects supported by other NIH Institutes, provided by the Division of Research Grants, NIH.

Radiation Program

In FY 1982, the RAEB agreed to modify its GENIUS System to incorporate terms suggested by the Director of the Radiation Program, Division of Cancer Treatment, and to maintain a subsystem for the Radiation Program.

Other NIH Institutes

At the request of several of the other NIH Institutes, the RAEB prepared a list of grants, contracts, and intramural projects supported by NCI in an area of mutual interest. Included were the following requests:

1. Digestive diseases, NIAMDD
2. Diabetes, NIAMDD
3. Arthritis, NIAMDD
4. Blood research, NHLBI
5. Heart, vascular, and lung research, NHLBI
6. Population research, NICHD

Literature Surveillance

Published results are monitored through the Branch's unique literature surveillance program. Ann Whiteman, a member of the Branch, scans 325 major medical and scientific journals and other periodicals to identify those reports resulting from NCI grant-supported or combined grant and contract-supported research. These references and additional references obtained from reprints submitted by grantees are entered into the computer system which generates an alphabetical keyword in context (KWIC) index of the terms in the titles plus additional augmented terms.

In augmenting these terms, staff enters related or hierarchical terms which do not appear in a given title but which are pertinent to the topic and are necessary for efficient retrieval. Terms are assigned by generic and specific categories as well as by their conceptual relationship to cancer and other research areas. Library and investigator file data are used to verify information and ensure accuracy and subject relevance. This comprehensive augmentation incorporates the terminology of all scientific disciplines encompassed by cancer research.

The references are arranged according to NCI cancer activities and published monthly with a subject and author index as the NCI-Grant-Supported Literature Index. The index is the most complete record available within NCI of accomplishments of the total NCI extramural research grants program. As a computer-searchable system, it is used for yearly and monthly listings of current literature and for responding to requests from staff and other members of the scientific community. In calendar year 1981, about 9,464 articles, representing the work of 12,782 authors, appeared in the Index.

In FY 1982, WYLBUR, the computer system used for the literature index, was streamlined by the DCRT. The modified programs and procedures, adopted by all users of WYLBUR, make the system more efficient and easier to use.

CONTRACTS REVIEW BRANCH

Chief: David L. Joftes, Ph.D.
Executive Secretaries: Kendal G. Powers, Ph.D.
Richard A. Rhoden, Ph.D.
Wilna A. Woods, Ph.D.

CONTRACTS REVIEW BRANCH

During the past year, two Executive Secretaries left this Branch, reducing the professional staff to two persons. It was several months before new staff could be recruited, but the Branch was able to meet its obligations and accomplish the many contract proposal reviews which were necessary. Due to the efforts of the one remaining Executive Secretary and devoted support personnel, no reviews were unduly delayed. The three newly recruited Executive Secretaries have since taken hold quickly and are dealing with the growing workload effectively. The Branch still requires two additional Executive Secretaries and three support personnel. Recruitments for these positions are proceeding.

During this year, the Branch added a person who serves as an Assignment Officer and Program Analyst. Receipt and assignment of RFPs and their proposals to the appropriate Executive Secretary and the capture, maintenance, and analysis of many types of data related to the operations of the Branch are the responsibility of this person. Using capabilities of our word processing equipment, this person is able to maintain accurate, up-to-date meeting calendars and track the status of all proposals received, or expected, on a weekly basis. This information makes possible effective control of the workload and ensures efficient planning and timely completion of our tasks. This is significant because timely award of contracts is dependent partially upon prompt execution of the technical review function. By monitoring the concept review and approval process, we are able to anticipate workloads and plan personnel assignments realistically. While the system became operational at the end of May and still requires some adjustment, it is already clear that it is a most valuable, yet simple, management tool.

As reported last year, interpersonal contacts continue to develop, and communications among program, contracting, and review personnel continue to improve. There have been several meetings of the staffs of the Research Contracts and Contracts Review Branches which have proved mutually beneficial. A number of specific suggestions from Contracting Officers and Specialists have been incorporated into our procedures, such as modification of our standardized rating scale and the format of the Summary Reports of technical review which have eliminated problems with the scale and made the Summary Report easier for the Contracting personnel to use. At the suggestion of a Contracting Officer, a policy regarding waivers of technical review has been developed for use in controlled, appropriate circumstances. This has slightly lightened the load for project officers, contracting officers, and contracts review Executive Secretaries.

A significant achievement of the Branch staff last year was the completion of a booklet titled "Peer Review of Contract Proposals at NCI." This is a handbook for peer reviewers on the standing committees and for ad hoc consultants. It explains the negotiated procurement process and the procedures used by NCI for the peer review of contract proposals. The process arises from laws and regulations designed to insure fairness of competition, avoidance of conflict of interest, and selection for award of those proposals best suited to fulfill the needs of the Institute. Over six hundred copies of the booklet have been distributed to reviewers, NCI and NIH staff, the NCAB, and the various Division Boards of Scientific Counselors. Reaction to this publication has been very positive. Many consultants, NCI staff, and others, have commented that the guidance offered by the booklet is very helpful. A revised and expanded edition based on our experience with this booklet is planned for next year. CRB staff

are currently involved in developing an Executive Secretary's Handbook for training new Executive Secretaries and for reference purposes.

The Contracts Review Committees

Biometry and Epidemiology Contract Review Committee. This Committee advises the Director, NCI, as well as the Directors of the operating divisions, especially those of the Division of Cancer Cause and Prevention and the Division of Extramural Activities, on the technical merit of contract proposals responsive to RFPs relating to cancer epidemiology and biometry. In addition to the usual reasons for collaborative studies using contracts, staff of the Division of Cancer Cause and Prevention use contracts to obtain large amounts of data which might otherwise be unavailable to them. The Committee members must be experts in the various aspects of epidemiology and biometry. They must also understand the problems and opportunities inherent in epidemiological studies. The consequences and implications of the committee's recommendations affect a substantial part of the epidemiological research effort in cancer in the United States as well as other countries.

This Committee was very active during this reporting period. In addition to its regular meetings, members participated in a number of ad hoc meetings because of a temporary delay in clearances for appointments of new members. For a period, it was not possible to convene a regular meeting of this Committee because there were not enough duly appointed members to constitute a quorum. This problem has abated with the receipt of clearance to appoint new members.

Cancer Control Intervention Programs Review Committee. This Committee advises the Director, NCI, and the Directors of the Division of Cancer Control and Rehabilitation and the Division of Extramural Activities on the technical merit of contract proposals in the fields of cancer prevention and detection, diagnosis, pretreatment evaluation, treatment, rehabilitation, and continuing care. Programs of a more applied nature than the research grant programs reviewed by the Control Grant Review Committee are stimulated and implemented through RFPs. Committee members must understand not only the underlying science and clinical medicine involved but also the implications for cancer control of the activities of significance in the prevention of cancer and the reduction of its morbidity and mortality. Because of the reorganization of the existing Division into the new Division of Resources, Centers, and Community Activities (DRCCA), there had previously been little work for this Committee. This year the major activity was the review of 23 proposals for the Community Hospital Oncology Program. Current indications are that there will be substantial activity in this area in the future. Therefore, the charter has been retained and the membership is being brought up to full strength. An Executive Secretary and a clerical support person are being recruited for this Committee.

Cause and Prevention Scientific Review Committee. This Committee advised the Director, NCI, and the Directors of the operating divisions, especially the Division of Cancer Cause and Prevention and the Division of Extramural Activities, of the technical merit of contract proposals for research into chemical, physical, and viral carcinogenesis. The workload of this Committee diminished to the point where it was no longer sensible to maintain the charter and therefore it was not renewed. The review responsibilities of the Committee will be met by assignment of proposals in this area to ad hoc review or to other standing Committees if they contain members with the appropriate expertise.

Clinical Trials Committee. This Committee advises the Director, NCI, as well as the Directors of the Division of Cancer Treatment and the Division of Extramural Activities on the scientific and technical merit of contract proposals involving clinical trials and related studies. The Division of Cancer Treatment uses such contracts when it wishes to stimulate clinical trials in which it will exercise some or substantial control on the design, conduct, and statistical analysis of the research. The Committee reviews contract proposals from the other divisions if they are clinical in nature.

It is expected that this Committee will continue to be active. A new Executive Secretary, to replace the one who left, has been recruited and assigned to this Committee and its membership is being brought to full strength as rapidly as possible.

Developmental Therapeutics Contract Review Committee. This Committee advised the Director, NCI, as well as the Directors of the Division of Cancer Treatment (DCT) and the Division of Extramural Activities on the scientific merit of contract proposals for development of therapeutically useful anticancer agents through research in radiobiology, molecular biology, biochemistry, and pharmacology. The charter of this Committee had been allowed to lapse previously. However, the new initiatives of DCT in the clinical aspects of biological response modifiers has and will continue to, stimulate many proposals. Therefore, a request for a new charter for a similar committee constituted of experts in drug development as well as biological response modifiers research was requested and has been approved. An Executive Secretary has been recruited and assigned and the process of bringing the membership to full strength is well advanced. By the end of this reporting period, a regular meeting of this Committee will have been held. An ad hoc meeting involving some of the proposed members has already taken place.

Resources and Repositories Contract Proposals Review Committee. In past years, it became obvious that all of the NCI Divisions operate contracts involving blood and/or cell banks, maintenance of tumor lines and/or special animals, information storage and retrieval, distribution of cells, compounds or animals and other, less common, resources. The number of RFPs and proposals related to these activities is substantial. Therefore, on the theory that a specialized, experienced and indoctrinated Committee would serve the review purpose best, a charter was requested and approved for a Committee to deal with the technical reviews required. An Executive Secretary has been recruited and assigned and the membership appointment process is well advanced. A considerable number of proposals will have been reviewed by this Committee in June 1982.

Intramural and Administrative Support Contract Proposals Review Committee. During FY 1981, it was determined that it was in the best interest of NCI to separate review of intramural support contract proposals from program in the same way as extramural contracts review had been. The responsibility for review of the intramural laboratory support and administrative support contract proposals was assigned to this Branch. In repsonse to the thought that the review of intramural and administrative contract proposals would be best understood and accomplished by uninvolved Federal employees familiar with the activities requiring support, a committee composed of two subcommittees was authorized by the Director, NCI, for one year as an experiment. Subcommittee A contains twenty members recruited from the senior scientific personnel of NCI Branches which use support contracts. Members do not attend meetings when proposals for contracts for their own Branches

are to be reviewed. Subcommittee B is composed of ten NCI and NIH personnel with administrative or information analysis competence and serves to review contract proposals in support of the administrative activities of the respective Office of the Director, NCI, and the Division Directors. Both Subcommittees have met twice and while there are some problems associated with obtaining appropriate expertise yet avoiding conflict of interest, the system seems to be working reasonably well. Therefore, a four-year authorization will be sought and existing and/or new members will be recruited for the usual four-year, overlapping terms. An Executive Secretary is being recruited for this Committee, but meanwhile plans for reappointment and additional appointments of members are proceeding.

Summary of Activities

Table I presents the number of meetings held and the number of reviewers and ad hoc consultants used. The Table is divided into actual data covering the period up to the end of June 1982 and projected totals for the whole fiscal year. The actual data are reliable and we have sufficient advance information to consider the estimates for the whole year to be quite firm. The disparity between ad hoc meetings (28) and chartered Committee meetings (4) is explained by the long period during the year when clearances for appointments to membership were delayed and the fact that for a considerable period there were too few Executive Secretaries available to spend time on the appointment process. This situation is rapidly ameliorating. However, even when CRB is fully staffed we expect to utilize a number of ad hoc groups to obtain optimum expertise for review and/or to avoid conflict of interest situations.

Table II displays the numbers of RFPs and the number of proposals responding to them, as well as the numbers of non-competative renewal contract proposals reviewed. Based on known contracts direct cost data only, the estimated cost of operating the Contracts Review Branch (including staff annual salaries, postage, consultant travel, per diem and honoraria, etc.) in FY 82 represents 0.35% of the direct costs requested. Because direct costs usually account for approximately half of the total cost of a contract award, the actual percentage may be fairly estimated to be less than 0.2% of the total costs requested.

Table I

Meetings Held and Reviewers Used in FY 82
CONTRACT REVIEW BRANCH, DEA, NCI

	Actual thru June 1982	Total Projected for FY 82
Number of Proposed or Officially Appointed Committee Members	117	117
Number of Ad Hoc Consultants	138	172
Total Number of Meetings		
Ad Hoc	28	34
Chartered Committees	4	5
Number of Site Visits	2	4

Table II

CONTRACTS REVIEW ACTIVITY: OCT. 1, 1981 THROUGH JUNE 30, 1982*
CONTRACTS REVIEW BRANCH, DEA, NCI

REVIEW GROUPS	NO. OF COMPETITIVE RFPs	NO. OF PROPOSALS IN RESPONSE	TOTAL $ REQUESTED: COMPETITIVE DIRECT COSTS	NO. OF NON-COMPETITIVE PROPOSALS	TOTAL $ NON-COMP. PROPOSALS DIRECT COSTS	TOTAL NO. PROPOSALS	TOTAL $ ** REQUESTED DIRECT COSTS
Ad Hoc	39	249	$138,339,084	6	$2,867,144	255	$141,202,228
Biometry and Epidemiology				8	6,553,914		6,553,914
Intramural	6	12	6,670,518				
GRAND TOTAL	45	261	$145,009,602	14	$9,421,058	275	$154,430,668

* As of June 2, 1982 there are 9 additional competitive RFPs and 1 extension due to be reviewed in FY 1982. A reliable projection as to the number of responses and total direct costs regarding these can not be made at this time. These RFPs are excluded from the table.

** Total $ = Total Direct Costs reported for the entire proposed contract period.

GRANTS REVIEW BRANCH

Chief: Dennis F. Cain, Ph.D.

Executive Secretaries:
John W. Abrell, Ph.D.
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GRANTS REVIEW BRANCH

The Grants Review Branch is responsible for: (1) internal NCI program assignment of all grant applications referred to the NCI from the Division of Research Grants, NIH; (2) assignment of grant applications for program projects, cancer center core support, construction, training, and other special-purpose grant applications to appropriate NCI review committees; (3) scientific merit review of the applications noted under (2) above; and (4) preparation of summary reports of the evaluations and recommendations of each committee review and of each site visit. The Branch also serves as liaison between the Division of Extramural Activities, NCI, and the Division of Research Grants, NIH, in matters related to grant review and referral.

Most investigator-initiated research grant applications (R01, R23, K04) and fellowship applications (F32, F33) are reviewed in the Division of Research Grants. However, a number of special grant mechanisms have been developed to meet the particular programmatic needs of the separate NIH institutes. In the NCI, the Grants Review Branch provides for the initial peer review of these special grant instruments: P01 (program project grant); P30 (center core support grant); C06 (construction grant); R18 (cancer control grant); R25 (clinical education grant); T32 (training grant); and U10 (cooperative clinical trials cooperative agreement).

During the period of this report, there were a number of changes in the committee structure of the Branch. The final phases of the reorganization of the NCI resulted in the transfer of the Clinical Cancer Education Committee from the Division of Resources, Centers, and Community Activities to the Grants Review Branch, DEA. The assignment pattern of program project grant applications to the two existing program project review committees (the Clinical Cancer Program Project Review Committee and the Cancer Special Program Advisory Committee) was examined with the intent of developing a more equitable and homogeneous review pattern in these committees. This has resulted in a redistribution of certain applications from these committees to a newly formed committee, the Cancer Therapeutics Program Project Review Committee (Ad Hoc). These three committees now receive a more coherent series of applications for review, and the workload is now more evenly distributed. The NCI has initiated a program to promote regional cooperative clinical trials. A new committee, the Cancer Regional Studies Review Committee (Ad Hoc) was established to review applications received in response to a Request for Applications (RFA). This new committee will continue to review applications received for both regional and organ-specific cooperative clinical trials.

Occasionally, applications are received for ongoing NCI programs or in response to an RFA which cannot be reviewed by the chartered review committees due to workload or to the lack of appropriate scientific expertise. In this circumstance, ad hoc committees are formed to review these applications. During the period of this report, ad hoc committees met to review multiple applications for construction grants, planning grants in surgical oncology, and a series of cancer control applications. Special Review Committees (SRC) are formed to review single applications which cannot be reviewed by a chartered committee due to conflict of interest considerations or the lack of appropriate expertise.

The appropriate balance and expertise of each committee are assured by the selection of members who are active investigators and are nationally and internationally recognized leaders in the disciplines relevant to the cancer problem. The breadth of expertise of each committee is determined by the speciality area of the applications that it reviews. Committee recommendations are reviewed by the National Cancer Advisory Board as required by the National Cancer Act.

Review Committees

The Cancer Center Support (Core) Review Committee (CCS) provides merit review of of cancer center support grant applications submitted by comprehensive cancer centers, laboratory cancer centers and clinical cancer centers, as well as applications for the construction or renovation of related cancer facilities. The peer review activities of the CCS require that the Committee members have a broad knowledge of the basic sciences that contribute new information about the cause and prevention of cancer and of the clinical sciences involved in prevention, diagnosis, and treatment of cancer. In addition, a thorough understanding of the administration and organization of medical schools, universities, and free-standing cancer research organizations is essential. Sensitivity to an institution's organizational and administrative strengths and deficiencies is important. Reviewers must be able to recognize those management practices that promote good research.

During the period of this report, the review of cancer center support grants has been substantially modified in accord with the newly adopted program and review guidelines. This committee was formerly merged with the Cancer Clinical Program Project Review Committee, but was reestablished as an independently chartered committee in 1982. The charter provides that the Committee consist of 20 members who are appointed by the Director, NCI.

The Cancer Clinical Investigation Review Committee (CCI) was reassigned to the Grants Review Branch in 1978. Its major function is to review applications in support of cooperative clinical trials and related areas of cancer research. The review of cooperative clinical trials requires that the reviewers be sensitive not only to the usual issues of scientific merit of clinical research, but to the special problems involved in cooperative research where the standardization and effective management of clinical research efforts at multiple institutions, sometimes distributed over wide geographic distances, are also important factors. Review by this Committee provides the NCAB and the Director, NCI, with recommendations concerning the opportunities and problems regarding the testing of chemotherapeutic agents and multimodality approaches to therapy. The Committee consists of 24 members selected primarily from the areas of medical oncology, pediatric oncology, surgical oncology, gynecologic oncology, radiation therapy, pathology, and biostatistics.

The Cancer Control Grant Review Committee (CCG) reviews applications for grants involving the demonstration and dissemination of methods to reduce the incidence, morbidity, and mortality of cancer. The methods proposed involve one or more of the full range of possible interventions--prevention, detection, diagnosis, pre-treatment evaluation, treatment, rehabilitation, and continuing care. The Committee also reviews applications for projects involving basic research in cancer rehabilitation. The Committee is composed of 20 members,

experienced in implementing cancer control programs, who represent specific disciplines in the clinical, behavioral, educational, analytical, and organizational aspects of cancer control. The Committee advises the NCAB and the Director, NCI, on the scientific merit of cancer control grant applications.

The Cancer Research Manpower Review Committee (CT) was assigned to the Grants Review Branch in December 1980. It provides advice to the Director, NCI, and the NCAB concerning the technical merit of National Research Service Awards which are institutional, multidisciplinary cancer research training grant applications. The Committee has 20 members with expertise in the basic and clinical sciences relating to cancer etiology, prevention, detection, diagnosis, and treatment.

The Cancer Special Program Advisory Committee (CSPAC) reviews applications requesting support of cancer-related program projects in the basic sciences or for the construction of related facilities. The Committee has 16 members with expertise in the basic sciences related to the cause, treatment, and prevention of cancer. The review activities of this Committee also require a thorough understanding of medical school and university organization, administration of large research programs, and a sensitivity to the effect on the applicant institution associated with the initiation, continuation, or termination of large-scale programs. The group advises the NCAB and the Director, NCI, regarding the scientific merit of the basic science program project grant applications submitted to the NCI.

The Clinical Cancer Education Committee (CEC) was transferred to the Grants Review Branch in February 1982. This Committee reviews applications for grants to stimulate and expand multidisciplinary efforts in cancer education at various educational levels so that physicians and dentists deal more effectively with the clinical aspects of cancer. The Committee consists of 15 members with special expertise in cancer education programs, and it provides advice to the Director, NCI, and the NCAB regarding the quality of the proposed education programs.

The Clinical Cancer Program Project Review Committee (CCP) provides merit review of applications requesting support of clinical program projects as well as applications for construction of cancer related facilities. The review of large clinical research grant applications requires special expertise in cancer clinical trials; understanding of the special demands of research with human subjects, of hospital and medical school organization, and of the administration of program projects; and, most importantly, detailed expert knowledge of the diagnosis and treatment of all types of cancer.

During the period of this report, the workload of both program project grant review committees was modified such that applications concerned with developmental therapeutics, clinical trials of new drugs and diagnostic and prognostic markers are being transferred to a new committee, Cancer Therapeutics Program Project Review Committee (Ad Hoc). Consequently, most of the applications reviewed by this chartered committee are concerned with radiation biology and therapy, cancer clinical immunology, and surgical oncology. This Committee was formerly merged with the Cancer Center Support Review Committee and was reestablished as an independently chartered committee in 1982. The Committee consists of 20 members who are appointed by the Director, NCI.

The Cancer Construction Grant Review Committee (Ad Hoc) was formed to review applications for construction or renovation of facilities for cancer-related research. These applications are routinely received for review at the May NCAB meeting and differ substantially from the other applications reviewed by the committees to which they were previously assigned. The ad hoc review process appears to be more satisfactory and it is likely to be continued in the future.

The Cancer Regional Studies Review Committee (CRSRC) (Ad Hoc) was established in 1982 to review cooperative agreement applications for regional and organ-specific cooperative clinical trials. The Committee is to have an eight member core group supplemented by ad hoc reviewers to provide appropriate expertise for the applications under review. A charter for this Committee is pending.

The Cancer Therapeutic Program Project Review Committee (CTR) (Ad Hoc) was formed in 1982 to review program project grant applications concerned with drug development and testing, prognostic and diagnostic markers, and clinical studies of cancers. These applications were reassigned from the other program project review committees in the Branch to reduce excessive workload and to provide a more contiguous review activity in each of the Committees. A charter for this Committee is pending.

Grants Referral Office: The Grants Review Branch is responsible for the assignment of all NCI research grant applications to the most appropriate program of the 18 program areas in NCI. During the past year, over 3,800 research grant applications (R01, R13, and R23)were so assigned in addition to 93 program project grants (P01), 23 cancer center core support grants (P30), 28 surgical oncology grants (P20), 1 specialized cancer center grant (P50), 103 cooperative clinical trial grants (R10 & U10), 83 cancer control grants (R18), 31 clinical cancer education grants (R25), 35 training grants (T32), and 7 construction grants (C06). Grant assignment information is maintained in a computer file and is distributed regularly to all NCI program, review, and grants administration staff.

Summary

During the year, the Referral Office in the Grants Review Branch received and assigned approximately 4,200 grant and cooperative agreement applications. The chartered, ad hoc, or special review committees of the Branch reviewed 404 grant applications requesting a total of $781,311,000. Seventy-five percent or 299 applications were recommended for approval with recommended budgets totaling $310,463,000 or 40 percent of the total requested in all of the applications reviewed. The recommended budgets amount to 45 percent of the total requested for all the applications approved. A total of $385,361,000 was disallowed in the approved grants. The grants review activity of the Grants Review Branch is presented in detail in Tables I, Ia, Ib, Ic, and II.

TABLE IA

GRANTS REVIEW ACTIVITY BY CHARTERED COMMITTEES - OCTOBER 1, 1981 through SEPTEMBER 30, 1982

(Dollars in Thousands - Direct Costs Only)

Review * Group	Applications Reviewed			Applications Approved				Approved Rate Overall	
	No.	$Requested	PSV	No.	$Recommended	$Deleted	$%	No.	$
CAK (P01)	26	$ 96,040	24	26	$ 46,031	$ 49,006	48%	100%	48%
CCG (R18)	71	40,198	6	21	7,570	2,304	77%	30%	19%
CCI (U10 & R10)	80	47,669	7	67	15,886	28,996	35%	84%	33%
CCP (P01)	34	173,885	34	33	70,166	94,103	43%	97%	40%
CCS (P30)	19	92,772	19	19	50,083	42,689	54%	100%	54%
CEC (R25)	31	3,843	31	31	1,797	2,046	47%	100%	47%
CT (T32)	35	34,763	3	25	13,601	10,487	56%	71%	39%
TOTAL	296	489,170	124	222	205,134	229,631	47%	75%	42%

* CAK - Cancer Special Program Advisory Committee
CCG - Cancer Control Grant Review Committee
CCI - Cancer Clinical Investigation Review Committee
CCP - Clinical Cancer Program Project Review Committee
CCS - Cancer Center Support Grant Review Subcommittee
CEC - Clinical Cancer Education Review Committee
CT - Cancer Research Manpower Review Committee

TABLE IB

GRANTS REVIEW ACTIVITY BY Ad HOC COMMITTEES - OCTOBER 1, 1981 through SEPTEMBER 30, 1982

(Dollars in Thousands - Direct Costs Only)

Ad Hoc Committee	Applications Reviewed			Applications Approved				Approved Rate Overall	
	No.	$Requested	PSV	No.	$Recommended	$Deleted	$%	No.	$
Construction (C06)	7	5,644	7	7	$ 4,646	$ 998	82%	100%	82%
Control (R18)	12	10,632	5	8	4,661	3,826	55%	67%	44%
CRSRC * (U10)	17	30,293	0	7	10,978	4,830	69%	41%	36%
CTR ** (P01)	5	20,435	5	5	8,242	12,193	40%	100%	40%
Surgical Oncology (P20)	28	8,621	0	14	1,704	2,715	39%	50%	20%
TOTAL	69	75,625	17	41	30,231	24,562	55%	59%	40%

* Cancer Regional Studies Review Committee
** Cancer Therapeutics Program Project Review Committee

TABLE IC

GRANTS REVIEW BY SPECIAL REVIEW COMMITTEE - OCTOBER 1, 1981 through SEPTEMBER 30, 1982

(Dollars in Thousands - Direct Costs Only)

	Applications Reviewed			Applications Approved				Approved Rate Overall	
SRC	No.	$Requested	PSV	No.	$Recommended	$Deleted	$%	No.	$
P01	28	$170,336	28	25	$ 57,304	$102,782	36%	89%	34%
P30	4	23,486	4	4	12,954	10,532	55%	100%	55%
P50	1	14,634	1	1	3,368	11,266	23%	100%	23%
R10	5	7,489	1	5	1,007	6,482	13%	100%	13%
U10	1	571	1	1	465	106	82%	100%	82%
TOTAL	39	216,516	35	36	75,098	131,168	36%	92%	35%

TABLE II

GRANTS REVIEW ACTIVITY BY MECHANISM - OCTOBER 1, 1981 through SEPTEMBER 30, 1982

(Dollars in Thousands - Direct Costs Only)

	Applications Reviewed			Applications Approved				Approved Rate Overall	
Mechanism	No.	$Requested	PSV	No.	$Recommended	$Deleted	$%	No.	$
C06	7	$ 5,644	7	7	$ 4,646	$ 998	82%	100%	82%
P01	93	460,696	91	89	181,743	258,084	41%	96%	39%
P20	28	8,621	0	14	1,704	2,715	39%	50%	20%
P30	23	116,258	23	23	63,037	53,221	54%	100%	54%
P50	1	14,634	1	1	3,368	11,266	23%	100%	23%
R10	5	7,489	1	5	1,007	6,482	13%	100%	13%
R18	83	50,830	11	29	12,231	6,130	67%	35%	24%
R25	31	3,843	31	31	1,797	2,046	47%	100%	47%
T32	35	34,763	3	25	13,601	10,487	56%	71%	39%
U10	98	78,533	8	75	27,329	33,932	45%	76%	35%
TOTALS	404	$ 781,311	176	299	$ 310,463	$ 385,361	45%	74%	42%

TABLE I

GRANTS REVIEW ACTIVITY - OCTOBER 1, 1981 through SEPTEMBER 30, 1982

(Dollars in Thousands - Direct Costs Only)

Committees	Applications Reviewed			Applications Approved				Approved Rate Overall	
	No.	$Requested	PSV	No.	$Recommended	$Deleted	$%	No.	$
CHARTERED COMMITTEES	296	$489,170	124	222	$205,134	$229,631	47%	75%	42%
AD HOC COMMITTEES	69	75,625	17	41	30,231	24,562	55%	59%	40%
SRC**	39	216,516	35	36	75,098	131,168	36%	92%	35%
TOTAL	404	781,311	176	299	310,463	385,361	45%	75%	40%

* Project Site Visits
** Special Review Committees

COOPERATIVE MINORITY BIOMEDICAL PROGRAM

Ms. Nola J. Whitfield

COOPERATIVE MINORITY BIOMEDICAL PROGRAM

The Cooperative Minority Biomedical Program (CMBP) within the National Cancer Institute (NCI) is an effort to increase NCI's participation in cancer research and training activities at minority institutions. Each year the Division of Extramural Activities staff makes consolidated efforts to broaden the scope of activities in support of the National Cancer Program mission.

In earlier years, the NCI entered into an Intra-Agency Agreement with DRR to support certain MBS Projects. In 1981, this process was eliminated and replaced by a "co-funding assistance award." The arrangement is more clearly defined as a multiple funding activity method and reflects the projects that are of mutual interest to two or more institutions.

The CMBP operates through two Cooperative Agreements: (1) between the National Cancer Institute and the Division of Research Resources; and (2) between NCI and the National Institute of General Medical Sciences (NIGMS). These agreements provide collaboration in the funding of grants in research, training, fellowships, visiting scientists, young investigator awards, and honors undergraduate research training awards and symposiums. The DRR goal is to provide support to strengthen the institutional health-related research capabilities of four-year colleges, universities, health professional schools, and other eligible institutions with significant enrollments of ethnic minority persons. The MARC goal is to foster research and research training in basic medical, biological, preclinical, clinical, and related natural and behavioral sciences. The uniqueness of the MARC program includes five-year institutional awards; all other awards range from one to three years.

To augment these activities, the National Cancer Institute conducts staff visits and programmatic advice to support meritorious research and training that have an impact on the overall mission of the National Cancer Program in either the MBS or MARC programs.

All initial scientific merit reviews are conducted by the General Research Support Review Committee (GRSRC) for DRR grants, and the National Advisory General Medical Sciences Council of the NIGMS for the MARC grants. Program relevance determinations are made by the NCI Special Advisory Group for minority research and training activities and are approved by the National Cancer Advisory Board.

While the CMBP is limited in its authority to initiate grants, significant progress has been made in influencing a greater number of institutions to engage in cancer research and research training activities.

Approximately 97 minority institutions of higher education (including Hawaii and Puerto Rico) are eligible to compete for awards in this program. Each year the growth of the program is represented by new awards made to minority institutions as a result of their competing capabilities.

In fiscal year 1982, the NCI provided $2.1 million dollars to fund in whole or in part numerous applications in the MBS and MARC programs. A modest increase in funding is projected for fiscal year 1983. These awards represent NCI's involvement with 25 minority institutions.

☆ U.S. GOVERNMENT PRINTING OFFICE: 1982-361-132:662

Division of

RESOURCES, CENTERS & COMMUNITY ACTIVITIES

1982 Annual Report
October 1, 1981-September 30, 1982

U.S. DEPARTMENT
OF HEALTH
AND HUMAN SERVICES

National
Institutes of
Health

National
Cancer
Institute

Bethesda,
Maryland 20205

National Cancer Institute

TABLE OF CONTENTS

DIVISION OF RESOURCES, CENTERS, AND COMMUNITY ACTIVITIES
NATIONAL CANCER INSTITUTE

ANNUAL REPORT - FISCAL YEAR 1982
(October 1, 1981 - September 30, 1982)

* TREATMENT, CONTINUING CARE, AND REHABILITATION PROGRAM

I.

OFFICE OF THE DIRECTOR

DIRECTOR'S REPORT

The Division of Resources, Centers, and Community Activities (DRCCA) is emphasizing a dynamic new course which links cancer control and prevention research with program activities. A system of classifying cancer control research into phases will help focus and monitor progress. Developing or testing specific actions or interventions aimed at having population impacts on important cancer problems are the major priority. This new quantitative approach will assist in translating the major strides in clinical and basic laboratory research into a measurable decline of cancer incidence and mortality in coming years.

DRCCA is one of five Divisions within the National Cancer Institute (NCI) and is comprised of three principal areas-(1) preventive medicine (2) centers and community oncology, and (3) cancer control applications. The Division has the principal Federal responsibility for assuring--

- research and development for applied cancer prevention and control, including chemoprevention, diet and cancer, occupational cancer, early detection, behavioral medicine/smoking and cancer, and other aspects of cancer prevention and control,

- the rapid and effective utilization of cancer research findings in prevention, detection, diagnosis, and treatment of cancer,

- the development of a national system of cancer centers and community oncology programs,

- the management of research programs focused on developing new knowledge concerning cancers of particular organs,

- the development of educational research and the evaluation of its relevance to cancer and the management of training programs for clinical oncologists and cancer research scientists, and

- the development of plans for necessary construction of laboratory and clinical research facilities.

Highlights of DRCCA activities include:

- Initiating management procedures to assure DRCCA Board of Scientific Counselors review of all major existing and proposed programs.

- Bringing on key new staff who have a wide range of research and management experience in clinical oncology, cancer control, and preventive medicine.

- Developing a new chemoprevention research program to determine whether selected micronutrients or synthetic compounds can be shown in human trials to reduce cancer incidence.

- Planning for a more extensive control effort in relation to smoking, nutrition, and occupation.

- Establishing a community clinical oncology program to promote cooperation among community physicians, cancer centers, and other research bases.

- Conducting cooperative efforts with cancer centers to maintain excellence in research, control, and education remain a priority for DRCCA. The Cancer Centers Program continues as a focal point for the National Cancer Program

- Fostering interdisciplinary research directed toward increased understanding of the etiology, detection, diagnosis, prevention, or treatment of cancer at specific sites where levels of research activity have not been commensurate with the morbidity and mortality caused by the diseases.

- Sponsoring a joint working conference between the National Cancer Institute and the National Institute on Aging (NIA) on issues in the prevention and treatment of cancer in the elderly.

- Creating Cancer Control Research Units and Science Projects to encourage study of how best to apply new knowledge in the prevention and treatment of cancer in such a way as to achieve measurable population impacts.

- Designing a new classification system of phases of cancer control research which provides an orderly sequence from basic or clinical research through cancer control research to widespread population benefits.

The Chemoprevention Research Program rationale stems from advances in laboratory research on carcinogenesis inhibition and complementary data from epidemiology. This is one of our most promising areas for cancer prevention research. Potential chemopreventive agents include several naturally occurring substances found in many foods, such as vitamin A and its precursor beta-carotene, vitamins C, E, and the trace metal selenium. These will be the first compounds studied in human trials. Synthetic analogs of vitamin A and other cancer inhibitors such as phenolic antioxidants, protease inhibitors, prostaglandin synthesis inhibitors and indoles are a current laboratory focus. Tracking of consumption and cancer incidence patterns related to chemoprevention hypotheses also is important to the chemoprevention program.

Complementary to the chemoprevention research thrust, the diet and cancer program shall emphasize methods of nutritional assessment for population studies. This shall allow better testing of current hypotheses related to fat, fiber, vegetables, and other components of our diet. The National Cancer Advisory Board and the DRCCA Board of Scientific Counselors have stressed the need for a greater diet and cancer research effort. In a DRCCA sponsored study, the National Academy of Sciences has reviewed current evidence, made interim recommendations to the public, and is in the process of considering future research needs.

The Community Clinical Oncology Program (CCOP) has now begun, after extensive consultation during program development with community physicians. This cancer control effort shall bring advantages of clinical research to cancer patients

in their own communities. Practicing physicians and their patients will have the opportunity to participate in clinical research protocols thus fostering a dynamic interaction between community physicians and those at research centers to the benefit of cancer control. CCOP shall provide a basis for studying the diffusion of cancer therapy throughout medical practice. The networks established should serve as an excellent resource for future NCI-sponsored cancer control and prevention research activities.

The principal purpose of cancer centers is to extend knowledge and understanding of the causes, mechanisms, diagnosis, and treatment of the multiple forms of cancer through the development of either specialized or broad multidisciplinary programs in basic clinical cancer research. They constitute a national resource providing a critical core of: (1) highly trained laboratory and clinical research personnel; (2) physical facilities and equipment; and (3) administrative support structures. These three important elements facilitate the generation of new knowledge about cancer and accelerate transfer of new information about cancer prevention, diagnosis, treatment, rehabilitation, and continuing care to health professionals in their surrounding communities and to the general public.

The Organ Sites Program consists of grant supported projects of targeted and coordinated cancer research encompassing the epidemiologic, laboratory, and clinical modes. Currently, there are organ site projects concerned with cancer of the urinary bladder, large bowel, pancreas, and prostate. Each site represents a major public health problem and yet there has been comparatively little research, particularly at the preclinical level. The breast cancer program will be transferred to this division. It will continue its multidisciplinary research activities in the laboratory and the clinic with the aim of increasing our understanding and improving methods regarding the etiology, epidemiology, diagnosis, prognosis, treatment, or prevention of breast cancer.

The collaborative working conference between NCI and NIA was a significant first step to develop information that could be used to improve treatment and control of cancer for older Americans. This activity represented a DRCCA cancer control effort to extend the national commitment to cancer research to include the growing national concern for the older segment of our population.

With the new knowledge learned within the past decade, it is now more realistic than ever to build a cancer control program that will lead to a measurable decline in cancer incidence and mortality. We are enthusiastic about being able to work together with our advisory bodies and with physicians and scientists throughout the country toward this end. Our aim is to assure that the new DRCCA programs shall be key contributors to the success of the Nation's cancer effort as a whole.

STAFF

Immediate Office of the Director

Director:	Peter Greenwald, M.D., Dr.P.H.
Deputy Director:	Joseph W. Cullen, Ph.D.
Special Assistant:	Rosemary Yancik, Ph.D.
Secretarial Support:	Joyce A. Heinonen A. Elizabeth Mugge Judith Binstock Gertrude P. Anthony (Detailed)

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Deputy Administrative Officer:	Debra A. Donnelly
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Secretarial Support:	Evelyn Fine Linda Chandler
Machine Operator/Messenger:	Marvin Brown
Executive Secretary:	Robert G. Burnight, Ph.D.
Secretarial Support:	Nola Alpert Amparo Carpio

Purpose and Objectives

Cancer chemoprevention, a priority research area in the Division of Resources, Centers and Community Activities (DRCCA), is aimed at testing the concept that certain natural or synthetic agents may lower cancer incidence. Potential chemopreventive agents include several naturally occurring substances already in public use, such as vitamin A and its precursor beta-carotene, ascorbic acid (vitamin C), alpha-tocopherol (vitamin E) and the trace metal, selenium (Se), as well as others still in the realm of the laboratory such as phenolic and prostaglandin synthesis inhibitors.

Current research data, collected largely from laboratory studies, suggest that chemopreventive agents have the capacity to inhibit the neoplastic effects of chemical carcinogens and may prevent, inhibit, retard or reverse one or more of the stages of carcinogenesis. For example, laboratory studies indicate that chemopreventive agents (e.g. retinoids) can inhibit the expression of the transformed cell state in a number of in vitro cell culture systems as well as prevent the development of cancers (including skin, bladder, trachea and mammary gland) in a number of in vivo animal systems.

Although still few in number, epidemiological studies related to chemoprevention, suggest that humans may have lower risks of cancer associated with the consumption of these chemopreventive substances. Several studies, for example, suggest a reduced risk of lung cancer for male smokers with higher intakes of vitamin A in their diets. Other epidemiological studies suggest that ascorbic acid may have a beneficial effect in preventing upper gastrointestinal tract cancers.

The Chemoprevention Program is committed to support studies in two major research areas:

- o epidemiological investigations involving consumption and usage of micronutrients and chemopreventive agents and clinical trials of selected agents in risk populations, and

- o investigations directed at examining the safety and toxicity of various substances and their application both prior to initiating human intervention studies and during their course.

Background and History of the Chemoprevention Program

At the first meeting of DRCCA's Board of Scientific Counselors on September 18-19, 1980, a Chemoprevention Task Force was established as a subcommittee to the Board. The purpose of this Task Force was to recommend to the Director, NCI, through the Director, DRCCA, whether the chemoprevention research endeavors should exist as a separate program. The Task Force convened January 28, 1981, and conducted three subsequent workshops (May, June and September) with invited speakers to assess the state-of-the-art of chemoprevention by reviewing hypotheses and data from both laboratory and human studies.

The May 1981 workshop focused on those agents which are potentially available for immediate use in clinical studies and included beta-carotene, ascorbic acid

alpha-tocopherol and selenium. Data from studies using synthetic retinoids, phenolic inhibitors, protease inhibitors and prostaglandin synthesis inhibitors were discussed at a June 1981 workshop. At the September meeting, protocols from eleven chemoprevention clinical studies were reviewed. The recommendations resulting from these workshops were that intervention trials using chemoprevention should be initiated, but with care to see that toxicity and safety issues were adequately addressed. It was also recognized that additional research was needed in all areas including laboratory, epidemiological and clinical investigation.

With the appointment of Dr. Peter Greenwald as Director, DRCCA, the Chemoprevention Program was initiated. A core of staff members meet with the Director on a regular basis to coordinate and provide direction to the Chemoprevention Program until the permanent staff are recruited. Both short and long-range planning activities have begun and a number of research activities have been initiated. Staff recruitment and hiring is underway.

Program Accomplishments

During this initial year extramural accomplishments have included:

- o Chemoprevention Referral Guidelines

  Referral guidelines which are used to assign appropriate grant applications to DRCCA (prepared for the Division of Research Grants) were presented to the Board of Scientific Counselors, January 1982, for comments and suggestions. These referral guidelines include all categories of chemoprevention agents--those currently available to the public such as ascorbic acid, and alpha-tocopherol, and those still in the laboratory such as protease and prostaglandin synthesis inhibitors. Research areas include epidemiological and clinical studies, as well as those studies concerning toxicity and agent application. Some appropriate research topics for DRCCA are to:

  identify populations at risk of developing cancer to study the effect that chemopreventives have on cancer incidence

  design and conduct clinical trials to test for efficacy of agents in inhibiting the onset of or retardation of the progress of pre-neoplastic changes, and

  examine the long term toxicity of dosing with various agents in appropriate models (animal and human).

  Grant applications which fulfill these guidelines are presently referred to the Chemoprevention Program. A mechanism is in place to have the applications reassigned if not appropriate for DRCCA.

- o Request for Application (RFA): The Role of Natural Inhibitors in the Prevention of Cancer

  Approximately $2 million has been allocated to support studies in response to the above RFA which will examine the role of several natural inhibitors including beta-carotene, ascorbic acid, alpha-tocopherol

and the trace metal selenium in the prevention of cancer. This RFA was issued in March 1982 with a June 15 deadline for grant application submission. Proposed studies under this RFA should:

- o elucidate the protective effect of natural inhibitors in reducing the incidence of various site specific cancers, and
- o lead to a greater understanding of the extent or action of several natural inhibitors in the possible cancer prevention process in humans.

These studies may include case-control studies as well as cohort studies and risk reduction clinical trials. Safety and adverse health effects are to be studied also.

A favorable response to this RFA by the scientific community was evidenced by the receipt of approximately 70 Letters of Intent. Potential grant applications include intervention studies, cohort studies and case-control studies. At the end of year three of these grants, answers are expected on the possible benefits of naturally occurring micronutrients and on the potential toxicity from megavitamin use depending on studies proposed. Also expected at this time are early results from human trials with synthetic analogs in preventing the recurrence of primary skin cancers or the progression of precursor lesions to cancer.

- o A Randomized Trial of Aspirin and Mortality in U.S. Physicians - Dr. Charles Hennekens

The National Cancer Institute and the National Heart, Lung, and Blood Institute are jointly sponsoring a five-year clinical trial to determine the usefulness of beta-carotene and aspirin in the primary prevention of cancer and cardiovascular disease, respectively. Approximately 22,000 healthy U.S. physicians, 40-75 years of age, are being invited to participate in the trial. The principal investigator is Dr. Charles Hennekens of Harvard Medical School.

Each participant will take one pill daily. On even days the tablet will contain either aspirin or a placebo; on odd days the preparation will contain either beta-carotene or a placebo. For convenience the pills will be supplied in calendar packs. Every six months each participant will be sent a new supply of pills together with a follow-up questionnaire on which to report compliance with the regimen and current health status. Randomization of the physicians to study subgroups is expected to begin in the Fall of 1982.

- o Program Planning

Chemoprevention staff and members of NCI's Office of Program Planning and Evaluation have developed an operational plan for a comprehensive NCI Chemoprevention Program. This is a systematic approach to program development through identification of program objectives and decision criteria, with "sub-flows" to achieve the desired objectives. Each sub-flow identifies a logical arrangement of major research elements followed by a decision point before proceeding to the next stage. Finalization of the plan is expected by October, 1982.

Program Projections

Following are extramural and intramural program plans projected for 1982 and 1983.

- o National Health and Nutrition Examination Survey (NHANES) Epidemiologic Follow-up Survey

  From 1971-1975, 14,407 persons were interviewed by the National Center for Health Statistics about their health and nutritional status. They also received a battery of medical and laboratory examinations including an assay for serum vitamin A levels. These individuals, whose ages range from 25-74, comprise a representative sample of the U.S. population.

  The Division will enter into an Intraagency Agreement with the National Center for Health Statistics which is conducting a follow-up survey of these individuals, in collaboration with NIH components, to investigate the relationships between nutritional factors and the incidence and mortality of cancer. This follow-up survey has advantages not found in other cohort studies. The sample is large and geographically heterogenous; it is diverse in terms of social and economic characteristics. Epidemiological findings of the follow-up will be more representative of the U.S. population compared to other studies which are usually considerably smaller in size and scope. On May 7, 1982, DRCCA's Board of Scientific Counselors approved the concept of this study which will begin in the latter part of 1982.

- o Clinical Chemistry Laboratory and Quality Assurance Center

  The Chemoprevention Program will undertake a number of studies to examine the role of natural and synthetic inhibitors, including but not limited to beta-carotene, vitamin A and its analogs, vitamins C and E and selenium, in reducing the incidence of site specific cancers.

  The above Center will be initiated under contract to support the Division's analytical requirements. A major role of the contract will also be to facilitate the quality of these chemopreventive substances since they are not routine analyses carried out by prospective grantees. The contractor will provide a quality control and assurance program, assist in standardizing analytical methodology for contractors and grantees participating in the program, and provide advice and consultation to program participants concerning sampling, storage, and analytical results from various participating laboratories.

  This concept was presented to and approved by the Board of Scientific Counselors on May 7, 1982. It is expected that one or more contracts will be awarded for a three-year period beginning in the latter part of 1982.

- o Cancer Among Aspirin Myocardial Infarction Study Subjects

  Sera collected from participants in the Aspirin Myocardial Infarction Study (AMIS) will be analyzed to determine whether pre-disease levels of beta-carotene, retinol, retinol-binding protein, alpha-tocopherol

and selenium are related to the subsequent development of cancer. Among the 4,524 men and women who enrolled in AMIS, 107 reported the occurrence of cancer during their participation in the trial. The initial study was sponsored by the National Heart, Blood, and Lung Institute. Through an Interagency Agreement, the Center for Disease Control will collaborate with DRCCA in analyzing these samples. As part of the study, the effect of thawing and refreezing sera will be assessed by comparing baseline retinol levels in the random half of patients whose sera were invaded for other analyses with those whose sera remained frozen since baseline.

The concept for this study was reviewed and approved by the Board of Scientific Counselors on May 7, 1982.

o DRCCA Intramural Studies

The ultimate goals of the Chemoprevention Program is to test the efficacy of various agents, either natural or synthetic, in reducing cancer incidence. Several controlled human intervention trials of selected chemopreventive agents are planned. Populations to be examined will be selected on the basis of their cancer risks, environmental exposures and the extent of knowledge indicating a potential for inhibiting cancer at specific sites by specific agents. Important aspects of the program involve the assessment of the current consumption of micronutrients, consideration of human study subjects in this type of trial, and efficiency of study design.

Timetable For Progress

The Chemoprevention Program aims at the end of the second year to have results from the retrospective studies using sera banks; by the third year to have clear results on the possible benefits of naturally occurring micronutrients, including vitamins, and on potential toxicity from megavitamin use. Early results of human trials with the synthetic analogs might also be expected by year 3; in years 4-6 we expect results of human trials involving the synthetic agents which will include studies of high risk groups and major cancer sites.

Staff Publications

Sestili, M.A., Norris, J.S., Lipshultz, L.I., and Smith, R. G.: Dunning adenocarcinoma in tissue culture: isolation of a cloned cell line, R3327H-G8-A1. Journal of Urology. 127:823-825, 1982.

La Rosa, J.H., Feinleib, M., Hoops, D., Schreiber, G.B.: Training in Epidemiology for the Occupational Physician. Journal of Occupational Medicine. 24:3, 237, 1982.

Ward, G.W., Morrison, W., Schreiber, G.: Pilot study of health professionals' awareness and opinions of the hypertension information in the mass media they use. Public Health Reports. 92:2, 113, 1982.

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Nutrition Coordinating Activities

Nutrition and nutrition-related research have been an important part of the National Cancer Institute's (NCI) activities for many years. In response to the 1974 amendments to the National Cancer Act, the Diet, Nutrition and Cancer Program (DNCP) was established within the NCI to develop and disseminate information related to the role of diet and nutrition in the etiology and prevention of cancer and in the treatment, long-term management, and rehabilitation of the cancer patient. The DNCP coordinates NCI activities with those of non-NCI organizations and encompasses all phases of nutrition and cancer activities: research, education, training, resource development, and demonstration projects.

From 1975 to 1978, the DNCP was administered by the Division of Cancer Cause and Prevention. In 1978, the program was reorganized and through 1980 was provided with central coordination through the Office of the Director, NCI. In 1981 responsibility for DNCP coordination was transferred to the Division of Resources, Centers and Community Activities (DRCCA). Although the program has historically been centrally coordinated, the actual direction of nutrition activities, including research, comes from the operating NCI divisions and offices. Each division retains responsibility for the programming, funding, and day-to-day management of specific nutrition projects. Representatives from the divisions serve on an Institute-wide working group to plan and coordinate program activities.

Guidance in program planning and conceptual review of program areas is the responsibility of the Advisory Committees or Boards of Scientific Counselors of each of the divisions or offices involved. Overall direction of the program is provided by the National Cancer Advisory Board.

The DNCP includes both extramural and intramural activities. The extramural projects are supported through grants and contracts. Research in etiology and prevention, cancer biology, treatment, and rehabilitation is managed by the division of Cancer Cause and Prevention, the Division of Cancer Biology and Diagnosis, the Division of Cancer Treatment, and the Division of Resources, Centers and Community Activities. Research training and activities in resource development, communications, and central program coordination are managed by the DRCCA. Future plans for DRCCA include nutrition and chemoprevention programs which will be implemented within new organizational settings within the Division. These programs will deal with research and applied aspects including epidemiologic and intervention studies.

Smoking, Cancer, and Health Program (SCHP)

The SCHP represents a number of organizational units within the NCI. The Program supports grants, contracts and intramural projects with central coordination provided by the Deputy Director of the Division of Resources, Centers, and Community Activities (DRCCA). The Program is concerned with research and demonstration activities in toxicology, epidemiology, prevention, behavior, pharmacology, education, information training and other areas appropriate to tobacco use, cancer and health.

The aim of the SCHP is to identify cancer risks associated with smoking and tobacco use and to develop strategies for prevention and cessation of tobacco-use behavior. Current activities include studies aimed at understanding the bio-behavioral dependence on smoking and tobacco use; epidemiological studies to assess health effects due to changing smoking and tobacco habits; toxicological studies to determine promoting and carcinogenic effects of constituents in both the particulate and gaseous phases of cigarettes; and biological studies to identify individuals at unusually high risk for the development of cancer. Also included are community demonstration and education programs aimed at deterring smoking behavior in children and adolescents, as well as the development of cessation programs targeted toward high risk subgroups that are not decreasing usage.

Future research attention will be given to evaluation of smoking prevention/cessation methods among blue collar workers in industries where exposure to carcinogens is likely to occur; studies monitoring changes in smoking prevalence and preference; epidemiologic and behavioral studies on smokeless tobacco use as a means of recruitment to regular tobacco smoking; and educational/media based prevention/cessation efforts with an emphasis on mass communications.

The NCI supports approximately 12 million dollars of smoking and tobacco related research through the mechanism of grants, contracts, and interagency and intramural agreements.

DRCCA Smoking and Health Activities

The Division is responsible for bio-behavioral, psychological, social, and educational research related to smoking and health. These activities cut across several branches and represent an approximate $4 million annual commitment to research and demonstration projects. These efforts include development and delivery of training courses for physicians and allied health professionals; smoking and tobacco components of the 21 Cancer Information Services; projects concerned with the cancer control implications of informal self-help approaches to smoking cessation; and projects directed at preventing the uptake of smoking by children and adolescents. Special emphasis has been placed on projects aimed at reducing the incidence of smoking among subgroups at higher than average risk for the development of cancer.

National Cancer Institute (NCI) and National Institute On Aging (NIA) Working Conference: "Perspectives On Prevention And Treatment Of Cancer In The Elderly," September 21 to 23, 1981

Under the auspices of its Cancer Control Program, DRCCA convened a working conference on problems and needs unique to the elderly for prevention, early detection, diagnosis, and management of cancer. This clinically-focused meeting was jointly sponsored by NCI and NIA and held at the Lister Hill Center, NIH campus, September 21 to 23, 1981.

The conference provided a forum for exploring ways in which geriatric physicians and oncologists can make contributions toward resolving problems of the older aged population. The conference grew out of a concern that use be made of accumulated knowledge existing at the interface of the clinical areas of cancer and aging. The 38 participants in the conference represented the fields of aging, oncology, epidemiology, and the social sciences. Speakers prepared manuscripts for a proceedings to be disseminated to community physicians and other health care professionals. This will help them to know about the important medical and social considerations involved in dealing with older persons regarding cancer prevention and treatment.

The rationale for the conference was that older citizens require special attention because of their vulnerability to cancer. Cancer affects older persons disproportionately. Also, our older population is increasing steadily, and particular attention is needed in view of the greater numbers of people of 75 years and older. This growth in the older age groups within the context of the United States health care system clearly indicates that there will be more old people who will require cancer treatment and continuing care.

The Conference Goals were to:

1) Identify, organize, and synthesize information from oncology, geriatrics, gerontology, and relevant fields concerned with improving prevention, early detection, and diagnosis of cancer in older persons; and the treatment, care, and recovery processes of elderly cancer patients

2) Disseminate the useful information

3) Recommend research efforts in selected areas where knowledge is unavailable or ambiguous, and intervention techniques which merit additional exploration and development.

Four common kinds of cancer--breast, colorectal, prostate, and skin--were addressed in the meeting. The discussion centered on (1) health behavior, illness behavior, and early detection of cancer in the elderly; (2) influence of old age on cancer patients to conventional forms of diagnosis and treatment; (4) balance between the treatment and care priorities; and (5) social, emotional, and economic consequences of cancer for the older person. Prevention topics included nutrition problems concomitant with both the process of aging and the disease condition of cancer, and monitoring and screening issues.

The conference highlighted the vast range of issues that exist in both fields of cancer and aging. Current patterns of care for elderly cancer patients were discussed. A dearth of data on the clinical interface of cancer and aging was noted. The jointly-sponsored conference served to (1) bring together a great deal of information which is continually being generated in both geriatric medicine and oncology and (2) identify the research gaps (e.g., in epidemiological studies, in clinical trials; on tumor behavior as related to age; on pharmacokinetics and pharmacology, etc.). The conference proceedings will be available in early 1983.

II.

PREVENTION PROGRAM

The prevention area focuses on primary cancer prevention, cancer screening which utilizes techniques known to be safe, effective, and ready for demonstration and implementation in the community, and applied research in cancer prevention. The primary prevention activities emphasize efforts on populations at risk to cancer due to exposure to carcinogens in the workplace, lifestyle habits, genetic and familial background and general environmental exposures. Studies are also included on screening, cancer diagnosis, refinement of diagnostic guidelines, and the promotion of improved approaches and techniques.

Primary Prevention

Radiation Quality Assurance and Risk Reduction Program

The use of radiation in medicine is recognized as the largest man-made component of radiation exposure to the United States population. Diagnostic radiologic procedures have continually become more varied and useful in medical practice. Radiation therapy has become a recognized modality for the treatment of cancer. Greater than half of all cancer patients will receive radiotherapy at some time in the course of treatment. The emphasis of the Preventive Medicine Branch has been not only on improvements in these diagnostic and therapeutic technologies, but also attention has been devoted to protection and on avoidance of unnecessary and, therefore, undesired radiation.

The Regional Centers for Radiological Physics (CRP), provide quality assurance and risk reduction activities in therapy as well as diagnostic radiology. The CRP's review physics support at all facilities in the DRCCA affiliated clinical programs, and serve as a resource for quality assurance, technology transfer, and education of the radiological community.

The CRP coordination program, conducted by the American Association of Physicists in Medicine, ensures national uniformity in the nature and quality of activities performed by the consensus development, and evaluates the impact of the centers on the cancer control effort.

As of February 1982, the CRP's have carried out 862 reviews of 500 different radiation generators at 344 different facilities. These include reviews of 441 cobalt machines, 409 accelerators, and 12 betatrons. The current number of radiotherapy facilities at which the CRP's carry out reviews is 260. The percent of facilities meeting the 5% tumor dose delivery criteria on the first review was 78%; at the time of the second review, 89% met the criteria.

The CRP's continue to interact with the presently funded DRCCA projects. They are beginning to implement reviews of clinical facilities associated with the Community Hospital Oncology Projects (CHOPS). With the implementation of the Community Clinical Oncology Program (CCOP) and the expansion of the affiliates of the Clinical Cooperative Groups, it can be anticipated that between 100-200 additional facilities will be added to the review program during the coming fiscal year.

The CRP's continue to measure mammographic exposures at 11 mammographic centers under the Community Based Cancer Control Program and CHOPS. Three CRP's have helped review fluoroscopy techniques in the screening of colorectal cancer. A protocol for performance evaluation of computerized tomography equipment has been developed and a pilot survey of 36 facilities conducted. A pilot survey of chest radiography equipment was also initiated in June.

Under an interagency agreement with the Food and Drug Administration (Bureau of Radiological Health) the CRP's have performed a field study of the effectiveness of mammography phantoms on various x-ray units. Physical parameters and phantom images were evaluated from 36 units. The finding of this study suggests that the "random" phantom had advantages over others available for film screen systems.

The CRP's participated in and/or conducted 12 workshops in their regions during the past year. Among the topics considered were radiotherapy safety, thermoluminescent dosimetry, digital radiography, advances in medical imaging, quality assurance in diagnostic radiology, calibration of brachytherapy sources, and treatment planning in radiotherapy.

The agreement with the Bureau of Radiological Health provides for conduct and support of activities that will result in reducing unnecessary radiation to patients and improving image quality by better diagnosis. The BRH continues to provide assistance to states in the mammography program known as Breast Exposure: Nationwide Trends (BENT). To date, approximately 3500 mammography units have been surveyed. This represents more than 80% of the units in the United States. Comparison of data from the initial evaluation and the re-evaluation demonstrates a 27 percent reduction in average exposure. The American College of Radiology is also producing training material for radiation therapists and a protocol for calibration of electron beam energies has been developed and is presently being evaluated.

During this fiscal year a project was implemented with the National Council on Radiation Protection and Measurements (NCRP) to develop a report on mammography and basic radiation criteria. Much information has accumulated on parameters for optimum utilization of mammography including dose reduction and image quality. This information will be incorporated into a handbook which will be made available to practitioners, physicists and public health professionals.

A study at the Peter Bent Brigham Hospital in Boston, Massachusetts (grant 28847) will determine the feasibility of a restricted set of indications for the upper gastrointestinal series (UGI) and the intravenous pyelogram (IVP). An optimal strategy for clinical use of the UGI and IVP examinations will be designed so as to minimize cost and radiation exposure with the least possible loss of important diagnostic information. A series of forms will be prospectively completed by the referring physician, the examining radiologist, and the research physician in three different health care settings. Data will be accrued for the first two years of the project and analyzed during the third.

The overall objective of the American Health Foundation's Primary Prevention of Cancer in Childhood grant program (25521) is to identify major cancer risk factors in school age populations (fifth graders); to reduce the elevated risk

status and to provide continuous reinforcement of health behavior. The program is currently in its second year. The school curriculum was revised to comply with the requirements of the inner-city district of New York. Biomedical screenings were conducted in the study and control groups. The data were collected and stored for analysis at the conclusion of the program.

Secondary Prevention
Screening

Breast Cancer

Active screening in the Breast Cancer Detection Demonstration Project ended in March of 1981 upon completion of the planned period which provided the opportunity for up to five annual screening visits for approximately 280,000 women. A descriptive paper on the data base generated by that program was published in July 1982. Data correction, validation, and analysis will continue until September of 1983. Several publications are anticipated from the analyses of that data during the next year.

A long-term follow-up was designed, approved in 1978, and implemented in January of 1980 to gather health status information on approximately 65,000 women who had participated in the breast cancer screening program. The follow-up was planned for five years with annual contact by mail and telephone of a population which included 1) 4274 breast cancer cases, 2) 25,072 cases having benign breast disease determined by biopsy or aspiration, 3) 25,169 normal controls matched to the benign cases by age, date of entry in the program, geographic location of the project where screening was done and race, and 4) 9685 women for whom a surgical referral was made by the screening project but biopsy was not performed. Twenty-eight interview projects have been established along with a central Data Management and Analysis Center. The earliest projects established are in their third year and the latest ones established are early in their second year. To date a response rate of 98% has been maintained on interviews. In the fourth year of the follow-up, an extensive analysis will be made to determine if the five-year period of follow-up will be sufficient to obtain optional information from the cohorts. This follow-up will provide an excellent opportunity to determine estimates of risk to breast cancer and provide detailed information on the biology and natural history of breast disease for specific defined groups within a screened population.

A study to determine the predictive value of the Wolfe classification of mammograms is in its third year. Preliminary reports indicate that reliability, validity, consistency, and reproducibility can be achieved among radiologists to classify mammograms into the various patterns. An atlas of Wolfe's classification patterns has also been developed. Continuation of the study would seek to apply this training among community radiologists and to explore a possible relationship between estrogen use and the presence of calcifications in mammograms.

To implement part of the cancer control program by demonstrating for the public and medical practitioners the value of earlier detection to decrease cancer morbidity and mortality, a contract with Vanderbilt University, Establishment and Operation of the Pathology Control System for the Breast Cancer Detection and Demonstration Project (PQCS and BCDDP), was awarded for

five years (06/30/76-08/31/81). That contract has been extended for one year for the sole purpose of maintaining a repository of slides as a study resource. The pathology review program began three years later than screenings for the BCDDP. The basic objective was to provide hierarchical review and standardization of procedures, criteria and terminology of the diagnoses of lesions which were biopsied or excised to validate the BCDDP detection process, to permit comparability and analyses of results among projects.

Of 19,036 cases reviewed during the period of active screening, which ended in March, 1981, and submitted for central review to the PQCS principal investigator, 16,189 were reaffirmed as benign, 2,775 as carcinoma (533 in situ and 2,242 invasive), and 72 cases were incomplete when the review contract ended.

Colorectal Cancer

The National Polyp Study, supported by grant 26852 is a project to determine the benefits, risks and costs of a surveillance program for patients who have had polyps removed. Based on seven study groups coordinated by the Memorial Sloan-Kettering Cancer Center, the overall objectives are to determine the best method and interval of follow-up for patients who have had polypectomy utilizing a randomized design. The results of examination by barium enema air contrast x-rays (pneumocolon) and colonoscopy will be compared. The role of the fecal occult blood test will also be evaluated. The overall benefit, costs and risks in the two modality arms of the study will be compared. In the present state-of-the-art, medical practice varies in the recommendation of frequency and method of follow-up examination. This study will attempt to answer the following questions:

1. Should an annual examination be performed routinely after polypectomy or should it be done every three years?
2. Should both one and three-year searches be done?
3. If either x-ray or endoscopy is to be performed as the primary follow-up examination method, which should it be, or should both be done at each contact?
4. What is the value of the fecal occult blood test on an interval examination?

In addition to recommendations on the best methods of follow-up, data will be gathered prospectively on the natural history of adenomatous polyps. The natural history will be correlated with age, family history, and number and histology of adenomas. Detailed uniform pathology is being obtained on all adenomas. Patients have been enrolled in this study for approximately one year. One of the most significant problems has been an unexpectedly low enrollment level to date. Methods of increasing the enrollment are being addressed in the seven study groups.

Before mass screening programs using stool occult blood testing are initiated, improved survival rates in screened individuals should be demonstrated. More information is also needed about the net margin of benefit to health in comparison with the costs and risks entailed in the further study of positive occult blood reactions by barium enema and endoscopy. Many of these screened individuals are found to have benign polyps in the colon.

A major controlled clinical research trial to evaluate survival rates in screened individuals using occult blood testing is being conducted in a study group as a part of the patient examination at the Preventive Medicine Institute Strang Clinic in collaboration with the Memorial Sloan-Kettering Cancer Center. Supported by grant 15529 this project was initiated in the organ site program before the initiation of the cancer control program. Since the primary thrust is to demonstrate the feasibility of screening, it has been transferred to the Preventive Medicine Branch. A detailed description of accomplishments under this grant can be found in the description of the organ site program.

Gynecologic Cancer

The program for gynecologic cancer has supported projects for the study of cervical and endometrial cancers, cancers related to trophoblastic disease, and cancer associated with in utero diethylstilbestrol (DES) exposure. The largest of the above studies was the State/Territorial Health Department Cervical Cancer Screening Program (CCSP). The next largest effort were the studies on the anomalies found in females exposed to DES in utero. Next in order was the trophoblastic disease program in which the goal was to enhance the availability of quality care for women with malignant trophoblastic disease in two regions of assessment of various techniques and the efficacy in detecting endometrial cancers and precursors in asymptomatic women.

The outcomes of the above studies have been varied in terms of definitive answers and quantitative findings. The study for the assessment of techniques for detecting endometrial cancer provided data which recommended endometrial aspiration as a method of choice. It also provided answers on the most effective fixative(s) for the collected tissue samples. The trophoblastic disease programs have provided tangible services to physicians in two U.S. regions in the form of hormone assays for the monitoring of patients with trophoblastic disease. The laboratory studies also undertook the identification of unique macromolecules whose presence might serve as predictive markers. The positive impact has been based on the willingness of the local physicians to avail themselves of the clinical and laboratory expertise provided by the two centers, and their interest in participation as a whole. During the final year of study, more information on the program's effectiveness should become available.

The DES study is directed toward an understanding of the abnormal lesions seen in females who were exposed to the hormone in utero. Four study centers, the Baylor College of Medicine, The Massachusetts General Hospital, the Mayo Foundation, and the University of Southern California have collected data on more than 5000 women through yearly physical examinations. Two publications describe the major findings as vaginal epithelial changes and other pathologic lesions. The first paper dealt mainly with the frequency and duration of vaginal lesions. The second major paper discussed the pathologic findings which ranged from adenosis to clear-cell cancer based on a survey of several thousand biopsy specimens. At this time in the analysis, the relation of adenosis to clear-cell cancer remains tentative. In the concluding months of the DESAD program, greater emphasis will be given to the analysis of collected data. These analyses might permit more definitive statements about vaginal epithelial changes (adenosis), pathologic findings, and perhaps disease natural history.

The largest effort in the area of gynecologic cancer has been the screening program for cervix cancer. The program will be concluded during July 1982 and will have screened more than 1.2 million women. The design of the study was not constituted for a direct analysis along the lines of prevalence, incidence, and relative risk. Accordingly, an indirect or modeling approach was used with the data in lieu of a more conventional analysis. The computer-assisted model was used to estimate the probability for any given disease state among precursors and invasive cancer.

Grant Programs were supported to study the relationship between endometrial cancer and estrogen replacement therapy in postmenopausal women. One project entitled Cancer in Women Receiving Exogenous Estrogen (29543) by the University of Denver, confirmed that the changes in the cancer incidence rates are inversely related to the rate of estrogen prescriptions. An annotated bibliography was completed and disseminated to obstetricians/gynecologists, family and general practitioners, internists, doctors of osteopathy and general surgeons in the Denver metropolitan area. The other project entitled, The Educational Approaches to Endeometrial Cancer (25280) being performed by the New York State Health Department is a demonstration education program, but includes a retrospective study of the causes of the sharp decline in estrogen prescriptions since 1977, and a population survey of the symptoms of perimenopausal women. The study will be completed in FY 83.

Lung Cancer

A collaborative study involving three institutions, Memorial Sloan-Kettering, Johns Hopkins University, and Mayo Foundation, currently is in progress to evaluate possible effectiveness of diagnostic procedures in early diagnosis, and hence earlier treatment, of lung cancer in males at high risk for developing lung cancer.

The goal of the study is: to test new methods for diagnosis of early lung cancer and to assess survival of patients with lung cancer detected by these methods. The three studies are operated independently but with frequent interchange of information and several meetings per year.

Recruitment for the Memorial Sloan-Kettering Cancer Center National Lung Program was completed in January 1978. Total enrollment is 10,040. Participants were randomly assigned to the Study Group (4,969), receiving annual chest x-rays and 4 monthly sputum exams; and to the Control Group (5,071), receiving annual x-rays only. There have been a total of 188 confirmed lung cancers identified so far, 94 in the Study Group and 94 in the Control Group. The principal mode of detection in the Study Group was by cytology in 19 cases, x-ray in 48 cases and both techniques in 7 cases. Of the 19 cases detected by cytology, 12 were Stage 0 or I; of the 55 cases detected by radiology in the Control Group, a total of 118 cases, there were 57 in Stage I. There were 51 interval cancers diagnosed following symptoms or signs, and 19 were oat cell cancers.

Among the 94 lung cancers appearing in the Study Group, 31 were prevalence cancers for a prevalence rate of 6.2/1000 and 63 were incidence cancers for an incidence rate of 3.0/1000/year. In the Control Group the 94 lung cancers included 22 prevalence for a prevalence rate of 4.3/1000 and 72 incidence cases, for an incidence rate of 3.4/1000/year. Survival rates so far have

been excellent for the cases detected early (Stage 0, I), with 5-year survival estimated at better than 90%.

A total of 10,828 men have been enrolled in the Johns Hopkins project, of which 5,407 were randomized into the Control Group and 5,421 into the Study Group. To date, 609 have died, while 1,316 have withdrawn from the study or moved from the area. Currently, 8,463 remain as active participants; 4,289 in the Control Group and 4,174 in the Study Group. At the initial screening 74 cancers were detected (39 in the Control Group and 35 in the Study Group) for a detected prevalence of 7.1 per 1,000. Following an initial negative screening, a total of 169 cancers have developed (89 in the Control Group and 80 in the Study Group) for an incidence of 4.6 per 1,000. In the Study Group there were 12 cases detected (15%) in Stage 0 and 28 (35%) in Stage I; thirty-three additional cases occurred in that group between screening procedures. In the Control Group no cases were detected in Stage 0 and 33 (37%) were in Stage I; 33 additional cases occurred in the group between screenings. Among the 80 incidence cases detected in the Study Group, 40 (50%) were resected; 40 (45%) of the 89 incidence cases detected in the Control Group were resected. Two hundred forty-three total lung cancers have appeared in the screened population, 128 in the Control Group and 115 in the Study group. Among the 128 cases of lung cancer found in the Control Group 76 (59%) have died; 49 (43%) of the 115 lung cancer cases in the Study Group have died. The observed rates of lung cancer mortality are 42 per 10,000 person-years in the Control Group and 25 per 10,000 person-years in the Study Group.

At the Mayo Foundation both the Study Group and the Control Group have been observed more than 23,000 man-years, and 243 new ("incidence") cases of cancer of the respiratory tract had been detected, 55 involving the upper airway and 188 the lungs. In the Study Group there were 110 new lung cancers (12 of which were detected by cytology only) and 51 lung cancer deaths. Early survival data in this group are encouraging. In the control Group there were 78 new lung cancers and 54 lung cancer deaths. Thus, once lung cancer has been detected, survival in the Study Group appears better than among the Control Group. However, further observation and prolonged follow-up are essential before final conclusions and specific recommendations will be possible. As "incidence" cases continue to accrue, more detailed analyses of data are becoming feasible. Particular attention is currently being directed towards evaluation of the results of screening by cell type of tumor and by modality of detection. The post-surgical American Joint Commission Stage I lung cancer study indicates that 69% of those with no-small cell cancer survive 5 years. The Hematoporphyrin Derivative study has detected several squamous cancers that were both radiographically and endoscopically occult. Cryotherapy continues to be used in selected cases.

Pathology

Under the cancer control technology transfer dimension of continuing professional education, two three-year contracts were awarded on Professional Education in Cytology Related to Bladder, Lung, Colorectal and Cervical Cancer, for the period 09/30/79-09/29/82, one to the University of Washington (#95435) and one to the St. Louis University (#95485), both having experienced cytopathologists as principal investigators (P.I.). The goals of these contracts were to reduce morbidity and mortality from cancer, by helping to assure the widest possible awareness and use of the latest advances in

concepts, knowledge and practical procedures of earlier detection and presumptive diagnosis of cancer using cytology. The goals were emphasized, especially in the more frequent and difficult cancer sites, such as colon/rectum and lung, which are examined by practicing cytopathologists, cytotechnologists and cytology laboratories. Each contractor was expected to provide special continuing education to at least 250 cytotechnologists (CT) and 50 cytopathologists (CP) during the three years; continuing education units or credit hours are given for completing the course.

St. Louis University was the site of several two-week courses and the University of Washington sent workshop teams to cost-effective sites in the Western States, mostly in Washington and Oregon. A Steering Committee consisting of Principal Investigators and the Project Officer met during the contact period to compare curriculum and problems. Although both programs had more difficulties than anticipated with recruitment and retention (30% no-shows), related to shortage of personnel for laboratory coverage during trainee absences, the St. Louis contractor completed 13 courses and the Seattle contractor 25 workshops. Updating of knowledge, new laboratory expertise, test and follow-up materials have been provided to 394 cytotechnologist and 338 cytopathology enrollees. During the past two years Dr. John Berg (grant 31802) has developed and tested computer programs designed to scan newly-acquired cancer registry data and to isolate cancers of specific histological types such as angiosarcoma or those occurring in anatomical subsites such as the pleura that have shown a significant increase in relative frequency. A major part of the work consisted of grouping cancers together that were known to be alike on the basis of past knowledge or simple examinations of the test data. Two problems have emerged which indicate that further work is required. First, the new coding scheme, WHO's International Classification of Disease for Oncology, 1976, (ICD-O), has far more categories than those used in the past. Hence, the identification of synonyms becomes much more important if the analyses are not to be confounded by a plethora of misclassifications for the same entity. Second, and perhaps more important, while the programs are designed to precede but not replace formal calculation of incidence rates, such calculations for specific histologies and for many anatomical subsites appear difficult or impossible with present reparting. Much more must be learned of the special characteristics of patients with unconfirmed cancers and of the cases given only histologic site designations. The continuation of this work is expected to resolve many of the difficulties encountered by the lack of uniformity in coding.

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OCCUPATIONAL CANCER BRANCH

The Occupational Cancer Branch (OCB) was established in July 1980 to create a focus at the NCI for applied research and other activities aimed at prevention and control of occupational cancer.

At the time of its formation, the Branch was given responsibility for several occupational cancer programs begun under other auspices. These consisted mainly of efforts to inform or educate workers about the risks of occupational cancer and to organize community support for medical surveillance and follow-up for workers known to be at high risk of occupational cancer or who had experienced an apparently increased incidence of cancers of certain sites suspected to be of occupational origin.

Planning in Occupational Cancer

The Branch has devoted most of its efforts during the current year to a systematic review of the problems of occupational cancer, with a view to drawing up a program designed to produce demonstrable benefits (in terms of reduced risk of exposure or disease) for workers whose occupations put them at elevated risk of cancer.

These efforts suffered a significant handicap with the untimely death in December 1981 of the Acting Branch Chief, Dr. Margaret H. Sloan, and the later death of Dr. Andrew Hegyeli in June 1982.

The staff has been assisted in its planning by an advisory committee of the DRCCA Board of Scientific Counselors. The result of these deliberations, to date, is that a general framework for a program has been worked out. The principal elements of the plan include support for efforts to identify, monitor, and control occupational cancer risks in defined groups; to intervene to prevent occupational cancer through education and training; and to monitor progress in efforts to reduce the risk of occupational cancer. In order to centralize the currently fragmented basic information on occupational cancer and to provide a clearinghouse and source of data for research workers, it is also proposed that the idea of establishing a data center for occupational cancer be considered. Such a data center would, of course, require the collaboration of the many other agencies and organizations with interests in the field.

Community Based Occupational Cancer Intervention Program

The Western Institute for Occupational and Environmental Sciences (WIOES) has been supported by contract (95450) to establish the Bay Area Asbestos Awareness Project. The main objective of this project is to inform workers, their families and the public about the hazards of exposure to asbestos and other occupational and environmental carcinogens.

The Workers Institute for Safety and Health (WISH), through a grant (27582) is supporting community-based cancer intervention programs at the Ford and General Motors companies for 15,000 pattern-makers believed to be at high risk of developing colon/rectal cancer. The etiological agents are not known, but the higher rate of cancer observed by NIOSH in these groups might be associated with exposure to wood dust, solvents, adhesives and other chemicals. Medical surveillance for these groups is provided by the employers. A similar program was established by WISH for about 1,000 workers in Augusta, Georgia, known to have been exposed to beta-naphthylamine. The medical follow-up for this group is conducted in collaboration with NIOSH, and the medical surveillance of the workers is provided by the Medical College of Georgia. A third group followed under this grant is an asbestos-exposed cohort of about 12,000 workers in Port Allegany, Pennsylvania. The medical surveillance in this group is paid for by the company and is conducted in collaboration with the Mt. Sinai School of Medicine in New York.

Education of Workers

Through an Interagency Agreement with the Occupational Safety and Health Administration (OSHA), the Branch has supported cancer-related portions of the Institutional Competency Building Program (New Directions) grants for the education and training of workers about occupational health hazards. As a consequence of the decentralization of the management and evaluation of these grants by OSHA, the Branch has been exploring methods by which the cancer-related New Directions grants could be brought under direct NCI administration. The concept of continued support of these grants, with direct review and management by NCI, was approved by the DRCCA Board of Scientific Counselors. The staff has issued a request for grant applications (RFA) to provide the means for funding and to ensure appropriate peer review.

The Resource Center of WIOES (95450) published a "Workers Guide to Radiation" and developed fact sheets on health hazards in shipyards and in the electroplating industry. The "Asbestos Newsline," a semiannual news letter, and an article entitled "Legal and Ethical Dilemmas of Worker Notification," edited by F. S. Lee and W. N. Room, Legal and Ethical Dilemmas in Occupational Health, Ann Arbor Science, 1982, provided much needed information to the public.

Under the grant entitled Environmental Cancer Prevention and Labor Health Education (27557) the Johns Hopkins University, in collaboration with the Center for Labor Studies in New York, has developed and field tested several model occupational cancer health education programs. The final version of the cancer education curriculum for workers is being prepared for field test and evaluation.

Education of Health Professionals

The Resource Center of the Bay Area Asbestos Awareness project 95450) conducted 21 professional education workshops for physicians and other health care providers on asbestos and other occupational cancer agents. A forum was held for health professionals, and the staff members of the Speakers Bureau provided speakers for

professional and community information programs on the harmful effects of asbestos and other carcinogens. The Center cosponsored the continuing education conference, "Hidden Health Hazards in the Environment." WIOES developed the course material and served as faculty.

A National Correspondence Course on Lung Cancer and Asbestos-Related Pulmonary Disease, by the American College of Chest Physicians (95455), was completed and published. To date, about 40,000 copies have been distributed to physicians specializing in pulmonary diseases, occupational medicine and internal medicine, and for use in medical schools, cancer centers and special training courses. This course, which is based on intensive review of the world literature, is believed to be unique in its field and has been very well received.

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The Behavioral Medicine Branch has responsibility for planning, conducting, and directing a program of biobehavioral research related to cancer prevention, early detection, and treatment. The scope of current research programs extends from health promotion/disease prevention issues through behavioral contributions to the course and treatment of cancer and its aftermath to the broader social impact of the disease (Cullen, Fox, and Isom, 1976; Levy, in press). The ultimate aim for research across all of these areas is the translation of study findings into community practice in order to control cancer in the population at large.

The table below displays FY 1982 expenditures for behavioral medicine extramural research across these three program areas.

Fiscal Year 1982 Funds by
Extramural Program Area Within the

Behavioral Medicine Branch
(Dollars in Thousands)

	Primary Prevention	Secondary Prevention	Treatment
Grants	1,249	659	1,886
Contracts	500	---	90
TOTAL	1,749	659	1,976
GRAND TOTAL	4,384		

Extramural Programs

Primary Prevention Research

Research within this category is concerned with health promotion/disease prevention efforts, including identifying environmental and developmental factors associated with at-risk status for the future development of cancer, as well as altering unhealthy lifestyles (for example, smoking or excessive alcohol consumption in order to prevent the carcinogenic effects of known risk factors. This is a major program area targeted for future growth; current funded projects involve the estimation of environmental and behavioral contributions to morbidity and mortality (28163 and Y01-CN-00711), the identification of early childhood experience contributing to future cancer risk (24416), and a number of research activities in smoking prevention and cessation. This latter program area is of particular importance to the Institute as well as this Division, and more will be said below about future program plans in this area.

The Behavioral Medicine Branch supports research aimed at understanding the nature of bio-behavioral dependence on smoking and tobacco use and its

development in high-risk subgroups that are not decreasing usage (e.g., adolescents, females, minorities and workers exposed to known or suspected carcinogens). Special attention has been given to evaluation of smoking prevention and cessation interventions with a special emphasis on self-help techniques.

Projects supported by the BMB have contributed to a nationwide effort to reduce the incidence of cancer and related morbidity and mortality due to cigarette smoking and tobacco use. Data concerning bio-behavioral antecedents and correlates in subgroups (29558 - Smoking Prevention in Youth, 29640 - and Smoking Prevention Training for Youth, 30237 - Adolescent Antecedents of Cigarette Smoking Behavior in Special At-Risk Populations); endocrine functioning and central nervous system correlates (29231 - Environment, "Need for Stimulation", and Smoking , 29320 - Gonadal, Behavioral and EEG Correlates of Smoking); and identification of factors which may assist the "resistant" smoker (27821 & 29479 - Informal Self-Help Approaches to Smoking Cessation, 27092 - Factors in Self-Help Smoking Cessation Attempts, 27332 - The Self-Help Process in Smoking Cessation) are to be translated into prevention and cessation strategies with the aim of reducing cigarette smoking and tobacco use. There is suggestive evidence that application of these strategies is likely to have the impact of reducing cancer related mortality through a decline in incidence rates.

Secondary Prevention Research

D'Onofrio (1982) described two major purposes of behavioral research related to cancer screening and early detection. One purpose is to advance the effective application of currently approved screening methods (e.g., pap test or mammography for women over 50), as well as to identify factors associated with non-compliance which could then expedite the application of other screening methods as these become perfected. The second purpose of behavioral research related to early detection of cancer is to contribute to the evaluation of screening tests on the technical criteria of yield, cost, and acceptability. Recent research has shown that there are still population subgroups (e.g., the socially and economically disadvantaged) that underutilize screening and detection tests, and fail to follow through with early diagnostic referrals (Berg, J, Ross, R., and LaTourette, N., 1977; Devesa and Diamond, 1980). Future research and demonstration efforts should be aimed at recruiting such subgroups into cancer detection and early treatment activities. There are two major categories of secondary prevention research currently being supported within the Branch program area: Health behavior related to health care utilization and the practice of breast self-exam (BSE) as a patient-oriented cancer detection strategy. As an example of research within the first category, Francis (27281) is examining factors related to delay in diagnosis--symptom, patient, physician, and health care system characteristics--as well as to examine access, continuity, and satisfaction with care received.

Breast Self Exam (BSE) is a particularly unique detection activity, in that it relies wholely upon the behavioral initiation and accomplishment of the lay person, herself. In this sense, it is a "patient-centric technology" (Levy, and Howard, in press). Although still under investigation, the weight of the evidence suggests that BSE may facilitate the earlier diagnosis of breast cancer and thereby reduce morbidity and mortality from this disease. The Behavioral Medicine Branch supports research efforts relevant to testing the screening value of BSE (26363), as well as the utilization of the technique (18451, 28269, and 26216). In Foster's (26363) study, data are being collected in the state

of Vermont to determine the relationship between BSE performance, the clinical and pathologic stages of breast cancer at diagnosis, and survival outcome. In this study, a retrospective analysis of tumor registry data through 1979 revealed a significant association between increased frequency of BSE performance and more favorable (TNM) clinical stage of disease at diagnosis. This investigator is currently continuing with a prospective study, examining women who were taught BSE during implementation of a breast cancer network demonstration project in Vermont, and were subsequently (1979-1984) diagnosed with breast cancer. These investigators will then examine whether trends found in the retrospective data favoring women who practice BSE frequently will hold up in the prospective data. They will also attempt to analyze survival curves for women diagnosed between 1975-1979, to see if BSE performance is related to decreased mortality.

The Branch is also reviewing the spectrum of research evidence related to the efficacy of BSE as a detection strategy, and this activity will be discussed below.

Treatment and Continuing Care Research

The treatment and continuing care projects can be grouped into those related to the behavioral management of adult cancer patients, those related to symptom control, and those related to disease and treatment sequelae in pediatric populations. Since behavioral medicine is an interdisciplinary research approach to understanding disease processes, research in the treatment area is not (or should not be) primarily concerned with mental health or behavioral dysfunction variables as ends in themselves. These factors are important only as they influence the course of the disease, its symptomatic expression, or its outcome. This effect can be direct (for example, stress effects on hormonally dependent tumors) or indirect (for example, non-compliance compromising treatment effectiveness). Although not all of the treatment projects currently supported within the BMB directly address the course of the disease and its associated symptoms, ultimately these are the fundamental questions that should be pursued. During Fiscal Year 1982, there were 20 treatment and continuing care projects supported. Only a sample of these will be discussed here.

The Psychosocial Collaborative Group (PSYCOG, 19681) is in its sixth year of investigation into the nature and frequency of emotional and behavioral sequelae in patients receiving chemotherapy and/or radiation therapy. This consortium of investigators from Memorial Sloan-Kettering Cancer Center, The Johns Hopkins Medical Center, and the University of Rochester Medical Center has also examined such issues as the process of informed consent to investigational protocols and the effectiveness of certain psychopharmacological interventions in the amelioration of pain and distress. A recently completed study by PSYCOG revealed significant undertreated levels of clinical depression among cancer patients. PSYCOG is currently initiating a clinical trial, examining the efficacy of a tricyclic antidepressant (nortriptyline) in the amelioration of depression and pain.

There are three additional studies supported through the BMB. They are related to the control of emotional distress and adverse side-effects in chemotherapy patients (26235, 25516, and 26832). Preliminary findings from one of these studies indicated that a behavioral intervention (systematic desensitization) produced a significantly greater reduction in anticipatory side-effects than either counseling or non-intervention. If these findings are reliable, these behavioral techniques could be valuable for symptom control in community settings.

A research program that spans detection, diagnosis, and treatment activities relates to patient compliance. An RFA entitled "Cancer Patient Compliance with Therapeutic Regimens" was released in FY 80. Three R01 grants have been funded: two of them (31151 and 31157) concerned with compliance and toxicity in adult chemotherapy patients, and the third (31167) concerned with dental compliance in head and neck patients receiving curative doses of radiotherapy. Findings from these studies should enable those treating cancer patients to predict subgroups at risk for non-compliance, and to intervene in order to achieve optimal treatment outcome.

In the pediatric area, there are three behavioral projects (26292, 27376, and 33340) related to the management of pain and distress in children with cancer. Kellerman's (26292) and Zeltzer's (27376) work have utilized hypnosis and the training of self-hypnosis in children undergoing bone marrow aspiration and chemotherapy, supporting the effectiveness of hypnosis as an intervention to reduce anxiety and discomfort for adolescents undergoing chemotherapy.

In general, the cognitive, behavioral, and emotional sequelae of disease and its treatment in long surviving pediatric patients is an important area of investigation in secondary prevention. That is, these children may be at risk not only for recurrence of disease, but also for developmental defects arising directly from the treatment of their primary disease.

BMB Staff Collaboration

In addition to scientific program areas within the Branch, branch staff--because of particular expertise in the behavioral sciences--also consult and collaborate with other branches in the Division. An example is staff collaboration in the development of chemoprevention trials, where questions of behavioral compliance related to "drop-ins" and "drop-outs," and issues concerned with trial ethics must be considered in sample size calculations and trial methods development.

Staff Research

Emotional Response to Breast Cancer and its Treatment: NCI Protocol No. 80-C-49 (Dr. Sandra M. Levy)

There have been studies in the U.S. and England with breast cancer patients suggesting a link between emotional expression, "fighting spirit", and better disease outcome. The objective of this study is to investigate whether outward emotional expression, as compared to passivity, is significantly associated with an increased survival in metastatic breast cancer patients. Cognitive and behavioral components of the patient's response to her illness are being analyzed to identify responses associated with better disease outcome. Preliminary findings showed that when the first 22 patients were divided at one-year follow-up into three groups of stable, progressing, or dead, the stable group had expressed significantly more emotional distress at baseline than the other two groups ($P<.05$). This psychological response appeared to be independent of any biological difference between the outcome groups at baseline testing.

If the association between emotionality and survival is reliable, an intervention study will be developed to attempt to build in a psychological response of the character found to be associated with survival in this present work. A second aim will be to measure biological correlates of these response patterns.

Breast Cancer Diagnosis in Minority Groups (Dr. Jan Howard)

A collaborative investigation with the staff of the Epidemiology Branch (DCCP) is in progress to examine the interactive effects of race, socioeconomic status, age, and marital status on the stage of breast cancer at diagnosis in 22,000 female cases recorded by the California Tumor Registry. Dr. Howard has also reviewed the health care literature relevant to the unequal burden of cancer endured by certain disadvantaged groups in American society, such as the poor and blacks (see below).

Breast Cancer Laterality: Effects on Survival (Dr. Jan Howard)

In cooperation with scientists in the Biometry Branch of DCCP, the investigator is exploring the relationship between the side of female breast cancer and relative survival rates at 5 to 10 years after diagnosis. Several stratification criteria are being utilized: stage of disease at diagnosis (localized, regional, and remote); age (younger and older than 55 years); and data source (End Results data from 1967 forward and Seer data from 1973 forward). Relationships between laterality and stage of disease are also being investigated. A published paper from Israel showed no association between laterality and survival over a 15-year period, but preliminary findings from the NCI study suggest that women with cancer of the left breast may have a poorer prognosis than those with cancer of the right breast.

Health Beliefs Related to Cancer in Minority Subgroups: A Pilot Study (Dr. John Friedl)

A descriptive pilot study is underway in Washington, D.C., with the aim of developing a survey instrument that can then be applied to a larger population sample. The objective of the survey is to describe and analyze health beliefs associated with early diagnosis and treatment of cancer in Hispanics and black population subgroups.

Scientific Seminars and Working Groups

The BMB has sponsored one scientific working group related to BSE, and three seminars related to the topic of smoking and cancer. A fourth seminar was co-sponsored with the NIH Working Group on Health and Behavior relating to health beliefs and health care utilization.

Future Plans and Projects

Future program areas are in various stages of development. These range from primary prevention through rehabilitation and terminal care. Emphasis, however, will be placed on primary and secondary prevention issues.

Primary prevention areas of major importance to the Branch will be concerned with the alteration of lifestyle factors associated with cancer risk. These include investigations into the nature of nicotine dependence, its development as well as its cessation; the modification of nutritional intake as epidemiological evidence suggests a link between diet and cancer risk; and the modification of other forms of addictive behavior such as excessive alcohol consumption in population subgroups. In addition, the alteration of the behavior of those exposed to other environmental carcinogens (such as those found in the workplace), and the development of effective risk counseling techniques are areas of future program interest.

Two specific initiatives in the area of tobacco use and cancer risk have recently been initiated in the form of Program Announcements. One of these is concerned with the prevention and cessation of smoking in blue collar workers; the other is concerned with behavioral, epidemiological and biobehavioral studies related to the use of smokeless tobacco in adolescents. The latter practice has been found to be associated with a higher incidence of oral cancer in population subgroups, and current media efforts aimed at recruitment of the young to smokeless tobacco use makes this an area of programmatic concern to the Institute and the Division. It is hoped that research responding to these two initiatives will ultimately lead to reduction in lung and oral cancer in the U.S. population.

In terms of secondary prevention program areas, the major focus of concern will be on what has been referred to as "patient-centric technologies" (Levy and Howard, 1981). That is, the Behavioral Medicine Program will be particularly concerned with understanding and fostering patient-initiated behaviors in the area of screening and early detection. An important future program area will be the health beliefs/behavior of the disadvantaged in order to isolate factors that can be modified, thus improving prognosis in these subgroups. Along these lines, an RFP in the area of black/white differences in treatment outcome is being initiated by the BMB, DRCCA, in collaboration with scientists in DCCP. The aim of research supported under this funding mechanism will be to isolate factors that significantly contribute to differential survival between blacks and whites in the U.S., including genetic, histological, immunological, and behavioral contributors to outcome.

Program priorities in the area of treatment and continuing care will involve the application of behavioral techniques that lend themselves to systematic, quantifiable research on problems associated with cancer patient care (pain control, nutritional deficits, anticipatory nausea and vomiting, etc.). And certainly the area of terminal care (particularly in pediatric patients), including the systematic analysis of environmental variables affecting the course and nature of dying, remains an important area for future work.

Across all of the above program areas, fundamental research needs to be carried out concerned with the biological correlates of behavioral patterns--from smoking initiation to non-compliance with chemotherapy. In addition, the fundamental search for mediating mechanisms between behavior and disease needs to be pursued at every level. And ultimately, this new knowledge must be generalized and applied to population subgroups at risk in order to achieve reduction in cancer incidence, morbidity, and mortality in the population at large.

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III.

CENTERS AND COMMUNITY ONCOLOGY PROGRAM *

* TREATMENT, CONTINUING CARE, AND REHABILITATION PROGRAM

TREATMENT, CONTINUING CARE, AND REHABILITATION PROGRAM

Program Scope and Strategies

The activities supported by the Treatment, Continuing Care, and Rehabilitation Program focus on applying successful research advances and practical cancer control interventions in the community. By implementing proven technology and successful methods of cancer patient management in various settings, increasing the involvement of community health care professionals in cancer care, and facilitating the dissemination of the vast therapeutic experience in cancer control, this program attempts to reduce the impact and effects of cancer for the nation's population.

The Treatment, Continuing Care, and Rehabilitation Program addresses extramural research programmatic efforts under four organizational components which include the: (1) Community Outreach and Rehabilitation Branch; (2) Cancer Centers Branch; (3) Organ Site Branch; and (4) Research Facilities Branch. Each Branch emphasizes and develops programs which foster multidisciplinary cancer management at the community level and encourages the demonstration of effective application of successful approaches in cancer control.

A primary emphasis in this past year has been on establishing a large-scale cancer control effort involving practicing community oncologists in NCI clinical trials programs. This program initiative, known as the Community Clinical Oncology Program (CCOP), is discussed under the Community Outreach and Rehabilitation Branch Program. Community physicians will work with regional cancer centers and/or national cooperative cancer research groups to place cancer Patients on protocol protocol studies. Another recently initiated long-range program, Cancer Control Research Units for Defined Population Studies, is discussed under the Cancer Centers Branch section. This new programmatic effort will support specialized research units to conduct studies on the impact of cancer control activities on the incidence, morbidity, and/or mortality of the general population.

The Treatment, Continuing Care, and Rehabilitation Program is the NCI focal point for several areas of special interest in Cancer Control. Among the more prominent research and demonstration activities supported are (1) rehabilitation, both physical and psychosocial; (2) pain control; (3) improved approaches to the care of patients with advanced cancer and the support of their families; (4) organizational research, and (5) studies of the education, attitudes, and behavior of physicians, nurses, and other health professionals. The investigations are designed to address cancer control issues relevant to patients, families, the public in general, volunteers providing care, health professionals, and those persons organizing to deliver cancer care.

Cancer control projects which come under the Treatment, Continuing Care, and Rehabilitation Program will continue to emphasize (1) participation of physicians in the community who are experienced oncologists to reduce the time that important advances in treatment research may be applied to cancer patients in the community; (2) inter-hospital relationships linking community hospitals with cancer center resources; and (3) support of efforts to expand and extend the cancer care knowledge base. As a new thrust, the program is encouraging cancer control research which develops or tests actions or interventions aimed at specific high risk population groups. It is also anticipated that new directions will include examining the social, economic,

and emotional burdens which cancer creates for patients and families. Relationships shift with the reordering of priorities of daily living. Rigorous study of areas of beneficial manipulation is needed. Single and combinations of interventions to reduce or eliminate these burdens represent fertile areas for future exploration. Branch activities currently being conducted follow.

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CANCER CENTERS BRANCH

Since the early 1960's, the National Cancer Institute (NCI) has conducted a Cancer Centers Program to provide grants for the support of programs in cancer research, education, and cancer control at educational and research institutions in the United States.

The primary objective of the Cancer Centers Branch is to promote and support the development of both specialized and multidisciplinary programs in laboratory and clinical cancer research and applied research in prevention and treatment.

This description of the Cancer Centers Branch will focus upon the principal instruments that serve its primary objective: Cancer Centers Support (Core) Grants, the Centralized Cancer Patient Data System, and the Cancer Control Outreach Program.

Cancer Centers

Purpose

The principal purpose of cancer centers is to extend knowledge and understanding of the causes, mechanisms, diagnosis, and treatment of the multiple forms of cancer through the development of either specialized or broad multidisciplinary programs in basic and clinical cancer research.

The rationale for centers is that the increasingly complex and costly demands of modern cancer research can be effectively and efficiently advanced by creating environments conducive to interdisciplinary coordination and collaboration.

General Characteristics

Cancer centers are unique and flexible entities and are not patterned after rigid models. They have developed from areas of existing strength to encompass a variety of activities ranging from highly specialized and narrowly focused programs to broad, coordinated, multifaceted programs. Cancer centers provide a national resource for the conduct of the full spectrum of activities necessary to achieve the objectives of the National Cancer Program.

As a national resource, cancer centers provide a critical core of: (1) highly trained laboratory and clinical research personnel; (2) physical facilities and equipment; and (3) administrative support structures. These three elements facilitate the generation of new knowledge about cancer and accelerate transfer of new information about cancer prevention, diagnosis, treatment, rehabilitation, and continuing care to health professionals in their surrounding communities and to the general public.

Types of Cancer Centers

Cancer centers have developed in a number of different organizational settings. Some are independent, free-standing institutional entities; others are under the auspices of universities; still others are consortia or multi-institutional in nature. Although any cancer center needs a certain minimum number of research programs for a "critical mass," centers vary greatly in size and breadth of programs from rather small specialized centers to large complex comprehensive centers. They may be classified as follows: (1) Laboratory Cancer Research Centers (LCRC)--centers engaged only in laboratory research; and (2) Clinical Cancer Research Centers (CCRC)--centers engaged in both laboratory and clinical research.

In addition, a Clinical Cancer Research Center (CCRC) with a funded Cancer Center Support (Core) Grant may apply to the National Cancer Institute for recognition as a Comprehensive Cancer Center. Such recognition may be granted by the Director of the National Cancer Institute if evaluation of the center demonstrates compliance with the guidelines for comprehensiveness established by the National Cancer Advisory Board and revised by the Board in 1979.

In FY 1982, a total of 62 cancer centers had active core grants, of which 16 are Laboratory Cancer Research Centers. Of the remaining 46 centers which are either clinical centers or which combine both basic and clinical research programs, 20 have been designated as Comprehensive Cancer Centers. Appendix I lists centers by type.

National Cancer Institute Support for Cancer Centers

Although cancer centers' activities are funded by both Federal and non-Federal funds, more than 66 percent of their total financial support is drawn from the NCI. An important funding mechanism is the Cancer Center Support (Core) Grant (CCSG) available through the Cancer Centers Branch, NCI. All types of cancer centers are eligible for a core grant. Applications undergo competitive scientific and technical review according to the prescribed peer-review procedure of the NIH.

The purpose of a CCSG is to provide a mechanism for support of those elements of a cancer center required for the planning, development, evaluation, administration, and maintenance of an active and unified cancer center in order to consolidate and focus cancer-related activities in a single administrative and programmatic structure. The CCSG may support salaries for key professional and administrative personnel, shared equipment, special facilities and services, alteration and renovation, and developmental research activities. A unique and important feature of the core grant is its provision of funds for major equipment and shared resources and services for which funds would not be possible or appropriate from individual grants or other grant programs. By virtue of being shared, such resources may result in a cost saving to the center and, therefore, to the National Cancer Program. Specific examples of shared resources include media preparation, glassware washing, animal colony central services, clinical research bed units, etc. For these shared resources and services, only costs for centralized services may be charged to the CCSG. Costs directly related to individual research projects must be charged to the applicable project.

It is important to emphasize that research itself is not supported by the core grant except for developmental projects. Despite its importance, the core grant provides only a minor portion of total support for the centers. Recent analyses have shown that core grants account for an average of 12 to 13 percent of total cancer center funds. The major portion of cancer center research is funded by combinations of individual research grants, clinical and basic program project grants, cancer control grants, clinical education and training grants, fellowships, contracts, and various funds received by the centers themselves from other Federal, non-Federal, and local sources. As a support structure for laboratory and clinical cancer research, the core grant makes no provision for funding cancer control or education and training activities. These important cancer-related activities are eligible for funds from other NCI sources.

Core Grant Awards

Decisions concerning final approval and award of funds are based upon review recommendations, priority scores, and the availability of funds. Continued support through this mechanism requires submission of a renewal application which is reviewed in the same sequence of steps as an initial application.

If a cancer center's renewal application is disapproved or fails to achieve a priority score which permits funding, the center enters a "phase-out" period during which it may receive a specified fraction of its current funding level for up to 1 year after initiation of the action. During this interim period, centers may resubmit a competitive renewal application. Loss of a CCSG grant by a comprehensive center automatically requires re-evaluation of the comprehensive designation.

The Growth of Centers--Consequences and Implications

Enactment of the National Cancer Act of 1971 marked the beginning of a period of rapid growth of the Cancer Centers Program. In addition to an increased number of centers, there has been a concomitant growth in their size and complexity, expansion of their research programs and activities, and augmentation of their professional staffs. These elements of growth coupled with the rising costs of research have been reflected in steadily mounting financial needs and requests.

Cancer centers depend heavily upon the NCI for research and operational support funds. The NCI contributes an average of 66 percent of total external support funds; other NIH programs provide an additional 20 percent. The total NIH contribution is, therefore, 86 percent of all external financial support. The remaining 14 percent derives from other Federal, public, and private sources. Any changes in the NCI budget appropriation and its apportionment can be expected to have a significant impact upon the research and operational stability of the cancer centers.

Current Problems

With the recent leveling of NCI and NIH appropriations, centers' rising costs have become a source of concern for both centers and the NCI. The limited growth of the NCI and NIH budgets have made research grants increasingly competitive and less certain as sources of funds for investigators. As a result, the core grant support program has received increased attention. Although the core grant constitutes an average of 12 to 13 percent of total cancer center funds, it is a critically important element of support which is not available from other grant programs.

Adoption of Revised Core Grant Guidelines

In order to control sharp increases in requested levels of support and, at the same time, preserve the intended purposes of the core grant, revisions of the 1976 Core Grant Guidelines were approved by the NCAB and the DRCCA Board of Scientific Counselors in the early part of 1981. The revised guidelines became effective October 1, 1981.

The Centralized Cancer Patient Data System (CCPDS) Grants

Objectives

CCPDS is a standard system for registering persons with reportable malignant neoplasms who are patients at Comprehensive Cancer Centers. Eligible patients were those first admitted to a center on or after July 1, 1977. All cases meeting certain requirements are reported to the Statistical Analysis and Quality Control Center (SAQC) in Seattle, Washington. SAQC is responsible for maintaining the system, analyzing the data, and acting as the coordinator for research activities.

Thirty-eight items of information are collected on each patient, including demographic characteristics, diagnosis, therapy, and survival. Standardized definitions of data items have been documented in the "CCPDS Data Acquisition Manual" (DAM). This manual also includes recommended procedures for abstracting, coding, submitting data to SAQC, and quality control.

Initially, standard definitions and codes were established for reportable patients and tumors, as well as for each of the 38 items. Criteria for quality control were set up to assess accuracy, completeness, and timeliness of reporting. There is a continuing effort to maintain inter-center comparability and compatibility with other national and international cancer reporting systems. CCPDS data are disseminated according to policies and procedures developed by a Policy Advisory Committee for that purpose.

Accomplishments

The CCPDS grants have resulted in a computerized patient data system in each of the centers. This system plus the quality control activities developed by SAQC have resulted in a higher quality, more efficient patient data system for the centers. In addition, these grants have supported statistical activities within the center to ensure better research uses of the system.

These grants were originally funded in 1977. To date, 20 cancer centers have been funded. Approximately 50,000 new cases are registered each year at SAQC.

Future Plans

At the May 7, 1982, meeting, the Board of Scientific Counselors, DRCCA, decided that funding of institutional CCPDS grants should be discontinued as of July 31, 1983. Institutional participation is expected with NCI support continuing for the SAQC headquarters.

Plans for future submissions of patient data to the SAQC center have not been developed. This program may be discontinued.

Cancer Centers Outreach Program

The Cancer Centers Outreach Program emphasizes planning, evaluation, pilot project development, and general cancer control program support. This requires a core of scientific and administrative staff that can develop detailed knowledge of the regional population patient loads, different and unusual demographic factors and disease characteristics in the region; develop broad program areas of emphasis; plan for the evaluation of control activities; and develop spin-off projects that can compete for separate funding on the basis of scientific merit and community support. In the past year, the outreach programs have stimulated development of a wide range of support for community hospitals, including multidisciplinary, multi-institutional consultative services for cancer diagnosis and treatment.

The Cancer Centers Outreach Program supports 24 comprehensive, clinical, or community cancer centers in the planning, development, and implementation of applied research in prevention and treatment programs. The Outreach Program will be succeeded by two new programs in FY 1983: the Cancer Control Research Units and the Cancer Center Science Program.

Cancer Control Research Units

The NCI's Division of Resources, Centers, and Community Activities has initiated two new directions for its cancer control effort with a combination of research programs intended to replace the Cancer Centers Outreach Program. The new programs are designed to meet the critical need for more cancer control research in both prevention (primary and secondary) and management (diagnosis, pretreatment evaluation, treatment, rehabilitation, and continuing care). A maximum of $7.5 million will be available for these programs in FY 1983.

In March, a request for applications (RFA) was issued for the first new program, entitled Cancer Control Research Units for Defined Population Studies (CCRUs). Successful applications will be awarded in FY 1983.

In defined populations, three types of activities may be supported using the CCRU grant mechanism:

1. Research to determine how, whether, and to what extent actions proposed for a particular cancer are effective for defined populations. These populations should be defined in such a way as to allow generalization to large segments of the U.S. population for purposes of cancer control program development.

2. Research to determine the optimal strategies for reducing incidence, mortality, or morbidity for a particular cancer(s) in a measurable way, and research on methods for efficiently implementing these strategies.

3. Selective implementation of strategies proven efficacious for particular cancer(s) and assessment of the efficacy and practicality of such strategies for large populations.

The CCRUs will be specialized research units and will require long-term support, involve multidisciplinary participation, and will need to have access to defined populations in order to measure the population impact of any cancer control activities. It is believed that a number of institutions or organizations in the United States have the "critical mass" of resources and qualified personnel to become research units of this type. This RFA is not intended to create a CCRU in a location where such a critical mass does not already exist.

A CCRU will be organized around a core group of highly competent investigators, each capable of obtaining peer-reviewed project support. Under a CCRU Director, investigators will receive project support for research using defined populations, for other approved studies, or for developmental research projects, or will seek other peer-reviewed funding support. A minimum of three defined population studies (a chemoprevention study may substitute for one of these studies) must successfully pass peer review and be approved before the CCRU application will be considered for funding. Highest priority for awards is being given to research involving: (1) cancers causing the greatest mortality/morbidity in the United States; (2) those cancers for which substantial risk has been associated with common exposures; and (3) those cancers for which apparently effective actions are available.

Cancer Control Science Program

The CCSP encourages development throughout the United States of core groups of researchers who will perform cancer control research studies (a minimum of three cancer control research projects that can successfully undergo review for scientific merit). Development funds for pilot projects of high scientific merit and with future promise of being supported as individual peer-reviewed research projects could be included. This program will be for a period of 5 years, and applications may be made at three different times in a year. Grant applications are due by August 15, 1982, for funding in FY 1983.

A second new program announcement, the Cancer Control Science Program (CCSP), was published in the March 1982 issue of the NIH Guide for Grants and Contracts.

Appendix I

Comprehensive Cancer Centers

1. Comprehensive Cancer Center, University of Alabama
   in Birmingham
   Birmingham, Alabama

2. Kenneth Norris, Jr., Cancer Research Institute
   University of Southern California
   Los Angeles, California

3. UCLA Jonsson Comprehensive Cancer Center
   UCLA School of Medicine
   Los Angeles, California

4. Yale University Comprehensive Cancer Center
   New Haven, Connecticut

5. Georgetown University/Howard University
   Comprehensive Cancer Center
   Vincent T. Lombardi Cancer Research Center
   Georgetown University Medical Center
   Washington, D.C.

   Howard University Cancer Research Center
   College of Medicine
   Washington, D.C.

6. Comprehensive Cancer Center for the State of Florida
   University of Miami School of Medicine
   Jackson Memorial Medical Center
   Miami, Florida

7. Illinois Cancer Council
   Chicago, Illinois

   Northwestern University Cancer
   Center
   Chicago, Illinois

   University of Chicago Cancer
   Research Center
   Chicago, Illinois

8. Johns Hopkins Oncology Center
   Baltimore, Maryland

9. Sidney Farber Cancer Institute
   Boston, Massachusetts

Comprehensive Cancer Centers (Cont.)

10. Comprehensive Cancer Center of Metropolitan Detroit
Detroit, Michigan

11. Mayo Comprehensive Cancer Center
Rochester, Minnesota

12. Columbia University Cancer Research Center
College of Physicians and Surgeons
New York, New York

13. Memorial Sloan-Kettering Cancer Center
Sloan-Kettering Institute for Cancer
Research/Memorial Sloan-Kettering Cancer Center
New York, New York

14. Roswell Park Memorial Institute
Buffalo, New York

15. Comprehensive Cancer Center
Duke University Medical Center
Durham, North Carolina

16. The Ohio State University Comprehensive Cancer Center
Columbus, Ohio

17. Fox Chase/University of Pennsylvania
Comprehensive Cancer Center

The Fox Chase Cancer Center
Philadelphia, Pennsylvania

University of Pennsylvania Cancer Center
Philadelphia, Pennsylvania

18. The University of Texas System Cancer Center
M.D. Anderson Hospital and Tumor Institute
Houston, Texas

19. Fred Hutchinson Cancer Research Center
Seattle, Washington

20. The University of Wisconsin Clinical Cancer Center
Madison, Wisconsin

Clinical Cancer Research Centers

1. University of Arizona Cancer Center
   Tucson, Arizona

2. City of Hope Research Institute
   Duarte, California

3. Northern California Cancer Program
   Palo Alto, California

4. University of California at San Diego
   La Jolla, California

5. Cancer Center of Hawaii
   University of Hawaii at Manoa
   Honolulu, Hawaii

6. University of Iowa Cancer Center
   Iowa City, Iowa

7. Ephraim McDowell Community Cancer Network, Inc.
   Lexington, Kentucky

8. Cancer Center, Tufts-New England Medical Center
   Boston, Massachusetts

9. Norris Cotton Cancer Center
   Dartmouth-Hitchcock Medical Center
   Hanover, New Hampshire

10. Cancer Research Center
    Albert Einstein College of Medicine
    Bronx, New York

11. Mount Sinai School of Medicine
    New York, New York

12. New York University Medical Center
    New York, New York

13. University of Rochester Cancer Center
    Rochester, New York

14. Cancer Research Center, University of North Carolina
    Chapel Hill, North Carolina

Clinical Cancer Research Centers (Cont.)

15. Oncology Research Center
    Bowman Gray School of Medicine
    Winston-Salem, North Carolina

16. University of Puerto Rico, Medical Sciences Campus
    San Juan, Puerto Rico

17. Roger Williams General Hospital
    Providence, Rhode Island

18. Memphis Regional Cancer Center
    Memphis, Tennessee

19. St. Jude Children's Research Hospital
    Memphis, Tennessee

20. The University of Texas Medical Branch Hospitals
    Galveston, Texas

21. MCV/VCU Cancer Center, Medical College of Virginia
    Richmond, Virginia

22. Vermont Regional Cancer Center, University of Vermont
    Burlington, Vermont

Laboratory Cancer Research Centers

1. Stanford University Medical Center
   Stanford, California

2. Scripps Clinic and Research Foundation
   La Jolla, California

3 La Jolla Cancer Research Foundation
   La Jolla, California

4. Armand Hammer Center for Cancer Biology
   The Salk Institute
   San Diego, California

5. Purdue University
   West Lafayette, Indiana

6. Worcester Foundation for Experimental Biology, Inc.
   Shrewsbury, Massachusetts

7. Massachusetts Institute of Technology
   Cambridge, Massachusetts

8. Center for Basic Cancer Research, Washington University
   School of Medicine
   St. Louis, Missouri

9. New York University Medical Center
   New York, New York

10. American Health Foundation
    New York, New York

11. Grace Cancer Drug Center
    Buffalo, New York

12. Case Western Reserve University
    Cleveland, Ohio

13. The Pennsylvania State University, College of Medicine
    Hershey, Pennsylvania

14. The Wistar Institute of Anatomy and Biology
    Philadelphia, Pennsylvania

15. Fels Research Institute
    Temple University Medical School
    Philadelphia, Pennsylvania

16. The University of Wisconsin, McArdle Laboratories
    Madison, Wisconsin

Cancer Centers Branch Publications Available

1. Guidelines for the Cancer Center Support Grant of the National Cancer Institute (January 1982).

2. RFA-NCI-DRCCA-CCB-82-6: "Cancer Control Research Units for Defined Population Studies," announced in NIH Guide for Grants and Contracts, Vol. II, No. 2., January 29, 1982, pages 15-18.

3. Cancer Control Science Program: Guidelines, April 1982, announced in the NIH Guide for Grants and Contracts, Vol. II, No. 2, March 26, 1982, p. 28-34.

4. Cancer Centers Administrative Profile Summary Report, April 1982.

5. Caban, C.E.: Progress in Cancer Control: The NCI Assessment Mettlin, C. (Ed.): Progress in Cancer Control, New York: Alan Liss, 1981, pp. 65-84.

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COMMUNITY OUTREACH AND REHABILITATION BRANCH

The Community Outreach and Rehabilitation Branch supports programs designed to:

A. Increase the transfer of cancer control activities from research centers to the community;

B. Develop effective cancer management capabilities within the community;

C. Use community research resources to increase knowledge in cancer control leading to a decrease in morbidity and mortality for patients;

D. Continue the development of rehabilitation devices and strategies;

E. Develop new approaches to the management of pain associated with cancer; and

F. Study the problem of optimal care for the terminally ill cancer patient.

Clinical Cooperative Group Programs

The reduction of cancer morbidity and mortality in the community setting is the goal of the Cooperative Group Outreach Programs. The objectives of these programs are to upgrade the skills of community physicians and other health professionals in the management of cancer patients and to increase the number of these patients receiving the best available care.

The mechanisms for achieving this goal are:

1. Strengthening and enlarging the affiliated hospital programs of the Cooperative Group to increase the number of community health professionals linked with the resources of the Cooperative Groups to participate in well-defined and monitored protocols for the management of cancer patients.
2. Providing support services to community physicians to maintain a high standard of patient care and data collection.
3. Instituting quality controls of patient management by the analyses of treatment data to assure high standards of care for patients entered on treatment protocols.
4. Providing continuing educational activities for community health professionals.

This program currently funds six Clinical Cooperative Groups (5 contracts and 1 grant) with a total annual budget of approximately 5 million dollars. These groups are:

1. Childrens Cancer Study Group (Contract No. NO1-CN-65374)
2. Eastern Cooperative Oncology Group (Contract No. NO1-CN-75348)

3. Northern California Oncology Group (Grant No. CA-24751)
4. National Surgical Adjuvant Breast Project (Contract No. NO1-CN-85335)
5. Radiation Therapy Oncology Group (Contract No. NO1-CN-75335)
6. Southwest Oncology Group (Contract No. NO1-CN-65285)

This program has accomplished the technology transfer of optimal patient management techniques from the research community to the community-at-large. To date, more than 2000 community physicians in more than 700 hospitals have participated in this program and more than 4000 community patients have been enrolled into Group Protocol studies. As a "demonstration project," this program was originally intended to be completed in three years and was subsequently extended for an additional two years ending in 1982.

Projects Publication

Begg, Colin B., Ph.D., Paul P. Carbone, M.D., Paul J. Elson, M.S., and Marvin Zelen, Ph.D., Participation of community hospitals in clinical trials: Analysis of five years of experience in the Eastern Cooperative Oncology Group. The New England Journal of Medicine. pp. 1076-1080, May 6, 1982.

Community Hospital Oncology Programs (CHOPS)

This program field tested, in multiple settings, a model approach to the development of community hospital cancer programs. The CHOP Model was derived from the experiences of seven pilot Clinical Oncology Programs supported through FY 1980. The purpose of these community hospital oncology programs is to provide evidence that implementation of the CHOP model in a community will improve the scope and quality of care for cancer patients over that received prior to development of the program.

In the development and implementation of each program, the cooperating hospitals and health care professionals will:

1. Define criteria for cancer patient care through the development of management guidelines;

2. Implement a program to encourage community cancer care practices in accordance with these criteria for care;

3. Use a data management system (e.g., through upgraded tumor registries) to assess the extent to which community cancer care practices correspond to the recommended criteria; and

4. Use the information obtained to correct, modify, and improve the clinical oncology program and document effective changes in community cancer care.

Twenty-three CHOP contractors are completing 18 month planning contracts. Participating communities range from large metropolitan settings to more remote urban and rural settings and involve single institutions and multi-institutional programs involving as many as 10 hospitals.

COMMUNITY HOSPITAL ONCOLOGY PROGRAM

Contract Number	Institution	Principal Investigator
SINGLE HOSPITAL		
CN-00526	Georgia Baptist Medical Center Atlanta, Georgia	Mario Ravry, M.D.
CN-05527	Deaconess Hospital Evansville, Indiana	Thomas G. Lutz, M.D.
CN-05529	Our Lady of Lourdes Memorial Hosp. Binghamton, New York	Robert E. Enck, M.D.
CN-05530	Marshfield Medical Foundation Marshfield, Wisconsin	Robert H. Greenlaw, M.D.
CN-15547	California Medical Center Los Angeles, California	Joseph F. McKernan, M.D.
CN-15549	Hackensack Hospital Hackensack, New Jersey	Charles Vialotti, M.D.
CN-15550	Memorial Medical Center Savannah, Georgia	Ronald F. Goldberg, M.D.
CN-15551	Mercy Hospital Scranton, Pennsylvania	William S. Heim, M.D.
CN-15553	Riverside Methodist Hospital Columbus, Ohio	Joseph A. Bonta, M.D.
CN-15557	St. Luke's Hospital of Bethlehem Bethlehem, Pennsylvania	Richard J. Torpie, M.D.
CN-15558	St. Paul Hospital Dallas, Texas	Ronald F. Garvey, M.D.
CN-15560	St. Vincent Medical Center Los Angeles, California	S. Barry Sakulsky, M.D.
CN-15561	South Fulton Hospital Tri-City East Point, Georgia	John Warner Ray, M.D.
SMALL COMMUNITY		
CN-05525	Southwest Washington Hospital Vancouver, Washington	Robert W. Olwine, M.D. Eugene B. Blizzard, M.D.
MULTI HOSPITAL	(*Number of institutions participating)	
CN-05528	Penrose Hospital (4*) Colorado Springs, Colorado	Paul N Anderson, M.D.
CN-15546	Borgess Medical Center (2*) Kalamazoo, Michigan	Leo Zelkowitz, M.D.
CN-15548	Christ Hospital (10*) Cincinnati, Ohio	Richard Meyer, M.D.
CN-15552	Methodist Hospital (3*) Brooklyn, New York	Sameer Rafla, M.D.
CN-15554	Roanoke Memorial Hospital (4*) Roanoke, Virginia	Charles L. Crockett, M.D.
CN-15555	St. Francis Hospital of Wichita (4*) Wichita, Kansas	Harry E. Hynes, M.D.
CN-15556	St. Louis Park Med. Res. Found. (7*) Minneapolis, Minnesota	J. Michael Ryan, M.D.
CN-15559	St. Peter's Hospital (4*) Albany, New York	Robert W. Sponzo, M.D.
CN-15562	Toledo Hospital (9*) Toledo, Ohio	Charles D. Cobau, M.D.

Pain Programs

DRCCA supports projects in pain research ranging from the neurophysiology of pain to structured complex approaches to the study and management of pain of cancer patients. Pain is one of the most feared consequences of cancer. Severe pain generally occurs in advancing and terminal disease, and pain may also be an early manifestation of cancer or its presenting symptom. Cancer pain has been the focus of considerable attention and concern for clinicians, patients, their friends and families, the general public, and the Government. However, it is now the consensus that no adequate data base exists from which to determine the true magnitude of the cancer pain problem. DRCCA has initiated pilot studies of cancer pain with the goal of gathering valid data defining the incidence and natural history of pain in cancer. Under the contract program Pain Control in Cancer, seven institutions (Contract Nos. NO1-CN-95417, 95486, 95487, 95488, 95489, 95490, 95491) are participating in a collaborative study to demonstrate that pain control for cancer patients is best instituted early in its onset after careful planning and evaluation by a multidisciplinary team of experts. This program addresses the management of pain associated with advanced and metastatic disease and chronic pain associated with localized disease.

Projects Publications:

Kremer, E., Atkinson, J.H., and Ignelzi, R.J.: Measurement of pain: Patient preference does not confound pain measurement. Pain. (in press).

Kremer, E., Atkinson, J.H., and Ignelzi, R.J.: Pain measurement: Construct validity of the affective dimension of the McGill Pain Questionaire with clinic benign pain patients. Pain. (in press).

Kremer, E., Atkinson, J.H., and Ignelzi, R.J.: Pain measurement: The affective dimensional measure of the McGill Pain Questionnaire with a cancer pain population. Pain. (in press).

Atkinson, J.H., Kremer, E., and Ignelzi, R.J.: The diffusion of pain language with affective disturbance confounds differential diagnosis. Pain. (in press).

Daut, R.L. and Cleeland, C.S.: The prevalence and severity of pain in cancer. Cancer. (in press).

Pattern of Care Study in Radiation Therapy

This landmark study of the American College of Radiology is in its seventh year. This represents the first effort by a major cancer care specialty to systematically assess national patterns of care and develop educational strategies to improve quality of cancer care practices. Initial and follow up process surveys on ten cancer sites and outcome surveys on five sites have been completed. National benchmark outcomes with four year actuarial results have been completed for carcinoma of the cervix, Hodgkin's Disease and head and neck sites. Follow up process outcome surveys are planned. It is anticipated that this study will result in a permanent quality assurance program for radiation therapy when federal support is complete.

Projects Publications:

Kramer, S.: An overview of process and outcome data in the patterns of care study. Int. J. Radiat. Oncol. Biol. Phys. 7:795-800, 1981.

MacLean, C.J.: Variation in workup and treatment procedures among types of radiation therapy facilities: The patterns of care process survey for three head and neck sites. Cancer. 48:1346-52, 1981.

Hanks, G.E., Herring, D.F., and Kramer, S.: Patterns of care outcome studies: Results of the national practice in seminoma of the testis. Int. J. Radiat. Oncol. Biol. Phys. 7:1413-1417, 1981.

MacLean, C.J.: Discriminant analysis of radiation therapy procedures: The patterns of care process survey for carcinoma of the larynx. Cancer. 49:229-233, 1982.

Hanks, G.E., Kinzie, J.J., and Herring, D.F., Kramer, S.: Patterns of care outcome studies in Hodgkin's Disease: Results of the national practice and implications for management. Can. Treat. Rep. April, 1982.

Kramer, S., Hanks, G.E., Herring, D.F., and Davis, L.W.: Summary results from the facilities master list: Surveys conducted by the patterns of care study. Int. J. Radiat. Oncol. Biol Phys. April, 1982.

Hanks, G.E., Kramer, S., Diamond, J.J., and Herring, D.F.: Patterns of care outcome survey: National outcome data for six disease sites. Am. J. Clin. Oncol./Cancer Clin. Trials. May, 1982.

Hanks, G.E., Kinzie, J.J., White, R.L., and Herring, D.F., Kramer, S.: Patterns of care outcome studies: Results of the national practice in Hodgkin's Disease. Cancer. (in press).

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Community Clinical Oncology Program

A large scale cancer control effort, the Community Clinical Oncology Program (CCOP) which involves practicing community oncologists in the NCI clinical trials programs, will be initiated in Fiscal Year 1983. The purpose of the program is to utilize as a resource the increasing number of highly trained oncologic specialists who have entered community practice in recent years. Combining the expertise of community physicians with ongoing clinical research projects will result in a dynamic development and exchange of the newest clinical treatment research findings at the community level.

The CCOP initiative is intended to meet the needs of cancer patients by utilizing the trained specialists now practicing in community hospitals and clinics and establish a system of community clinical oncology programs which will participate in clinical research trials. Over 80 percent of patients with cancer are treated in the community with only a small number entering clinical trials. The Division of Cancer Treatment (DCT) of NCI supports a national

clinical trials program largely through academic centers. These have included (1) multimodal national and regional cooperative groups, (2) groups in which the investigators have a particular expertise (such as pediatricians), (3) groups that are designed to deal primarily with high technology single modality studies and (4) groups that are specifically disease-oriented. Additional large cancer centers are involved in implementation of local clinical research protocols.

Over the past decade, increasing numbers of highly trained clinical cancer specialists, experienced in clinical research and protocol care, have been entering private practice in the community. Experience within several Cooperative Groups has indicated that physicians caring for cancer patients in the community can maintain high quality clinical research activities similar to that of the academic centers. Evidence exists that new technology can be transferred effectively by having community physicians participate in clinical research activities.

CCOP And Research Base Affiliation

Each Community Clinical Oncology Program must have an affiliation with a nationally recognized clinical cancer research base. These may be clinical or comprehensive cancer centers, national or regional cooperative groups. Participating community programs will be required to enter or refer into NCI-approved clinical trials, designated as high priority by a research base with which the CCOP is affiliated. These research bases may be national or regional multi-disease cooperative groups, specialized cooperative groups or cancer centers currently participating in NCI approved clinical research protocols. Participants are encouraged to enter patients with early stage disease with common cancers and to enter or refer, if appropriate, patients with uncommon cancers.

Objectives of the Community Clinical Oncology Program

The CCOP initiative is designed:

A. To bring the advantages of clinical research to cancer patients in their own communities, by having practicing doctors and their patients participate in clinical treatment research protocols, and thus foster an exchange between clinical research and cancer control.

B. To reduce national mortality by speeding the transfer of newly developed cancer treatment technology to widespread community application.

C. To provide a basis for involving a wider segment of the community in cancer control activities and investigate the diffusion of cancer therapy advances in community medical practices. The diffusion hypothesis presumes that introduction of quality-controlled clinical research trials in the community will also benefit those patients not treated as part of this protocol.

D. To develop programs to serve as part of a broadly based nationwide resource for quality-controlled distribution of increasing numbers of experimental anti-cancer agents.

E. To facilitate community participation in future cancer control and prevention research activities planned by NCI.

Funding Mechanism and Amount of Support

Awards will be in the form of Cooperative Agreements, a preferred mechanism for funding NCI Clinical Trials Programs. The Cooperative Agreement is an assistance relationship which features substantial government involvement in the scientific conduct of a program. The clinical research activities planned by the CCOPs in conjunction with their affiliated research bases are similar to those conducted by the clinical cooperative group members supported by the Division of Cancer Treatment. Use of the cooperative agreement mechanism will assure consistency and quality control procedures in the application of clinical trials in the community setting. Cooperative agreements are essentially a partnership between the government and the recipients of the awards.

It is anticipated that up to ten million dollars will be allocated for the CCOP in FY 1983. Initially, CCOP will be a three-year program.

Unique Features of CCOP

The CCOP is a major long-term effort to stimulate cancer control activities through direct community support. This attempt should encourage cooperation among community physicians and clinical research resources (cancer centers and cooperative clinical trials groups). These initial community cancer control efforts are readily evaluated and should be followed by other systematic cancer control efforts in areas such as prevention and early detection.

Rehabilitation Program

This program seeks to reduce the morbidity from cancer and its treatment through stimulating study, demonstration, and research in new techniques of rehabilitation that have specific applicability to the physical, cosmetic, and functional problems associated with cancer.

The comprehensive nature of cancer rehabilitation determines support for a variety of projects which seek to achieve the cancer patients' early adjustment and re-entry into the everyday world of work, social activity, and physical functioning.

Contracts

Four contracts support a Training Program for Maxillofacial Prosthodontists and Maxillofacial Dental Technicians, (Contract Nos. NO1-CN-05458, 05522, 05523, 05524).

The projects funded by contract went beyond the training routinely available in the existing curricula of dental schools. Eligible applicants for this program were graduate dentists wishing to specialize in oro-facial restoration using non-living

materials. Didactic lectures, clinical experiences, and laboratory procedures are set out in the RFP workscope.

To ensure adequacy of performance, each contractor developed and submitted to the project officer: 1) an evaluation plan, 2) a training curriculum, 3) a patient access report, and 4) a semiannual training or progress report.

These documents will provide the basis for a model maxillofacial training program for dental schools wishing to initiate such a program independent of federal funding. The Evaluation Plan of the four contractors was reviewed by NCI and four expert consultants. Two contractors requested six month's extensions which were granted.

Grants

The Rehabilitation Program supports 21 grants which presently investigate six major areas of cancer rehabilitation.

1. Grants that develop, field test or demonstrate new skills, coping strategies, social support systems to improve the effectiveness of rehabilitation approaches. Seven grants fall in this category (Grant Nos. CA-20615, 26868, 26878, 27630, 27683, 27766, 27807).

2. Prostheses Development, Restoration, and Reconstruction - Cancer treatment frequently compromises anatomical structures and physiological functions. New devices and new procedures utilizing both living tissue and non-living materials are studied for specific application to cancer restorations. These projects pursue their investigation at both the laboratory and clinical stage. Five grants fall into this category (Grant Nos. CA-17945, 19761, 23571, 25650, 29046).

3. Host Maintenance - The patient's own physical strength and recuperative resources are an essential requisite for cancer rehabilitation. Clinicians and researchers increasingly recognize the potential of nutrition as a rehabilitation modality directly related to the success or failure of the rehabilitative endeavor. There are currently three active grants in this category (Grant Nos. CA-17928, 28005, 28072).

4. Patients' Reaction to Illness - Cancer patients exhibit a range and complexity of reactions to their illness in both the physical and psychological sphere. Such reactions need structured explorations for better understanding and planning. Exaggerated and untoward reactions mitigate against early, effective rehabilitation. Currently two grants study reaction to illness (Grant Nos. CA-19344, 24079).

5. Programmatic approaches involving demonstration of an institutional or department level plan for managing a major rehabilitation program in home care for terminal cancer, in which the objective is rehabilitation not nursing care or treatment. Such projects involve a variety of disciplines, resources, and services centrally coordinated and supervised. Two grants fall into this category (Grant Nos. CA-26779, 20396).

6. Measurement and Evaluation - While each funded project includes an evaluation component, there is a need to develop universal indexes of

measurements that can be applied independently to a given rehabilitation program or a single rehabilitation intervention. These projects address this need (Grant Nos. CA-27912, 25289).

The majority of these grants are in the final year, six having already submitted their final report. To ensure that every treated cancer patient has access to adequate, effective rehabilitation remains a primary NCI objective. There is an increased need for improved rehabilitation capabilities in the area of physical and physiological maintenance throughout the course of vigorous treatment as well as immediate initiation of restoration following treatment. Investigator initiated grant applications are encouraged over the next year.

Oncology Nursing Education Program

In 1979, San Jose State University (No. 95480) and the University of Alabama (No. 95428) were awarded contracts to develop and implement a model postmaster's one-year fellowship program in oncology nursing. The project faculty of the two schools of nursing have collaborated in designing a model curriculum and evaluating its effectiveness. The major objective of the program is to help resolve the nationwide shortage of qualified oncology nurse clinicians by providing advanced academic preparation to nurse educators who will then develop and upgrade oncology programs at the graduate, undergraduate and continuing education levels.

Participants were selected from all regions of the country. A second group of fellows is currently enrolled. A 15 month follow-up evaluation plan was implemented with the first group of fellows in April, 1982. In September 1982, a third group will be admitted to the University of Alabama program.

In 1979, a grant was awarded to the Fred Hutchinson Cancer Research Center to develop a Community-Based Cancer Nursing Education Program for Registered Nurses throughout the Pacific Northwest and Alaska. To date, over 324 nurses have completed the 80 hour curriculum in 13 communities. A pre and post program evaluation has been accomplished and the lecture series of the 80 hour curriculum along with the program's audio-visuals is in an exportable format for distribution.

Hospice Program

Three projects in Implementation of the Hospice Concept for the Care of Terminal Cancer Patients with a home care program and a backup in-house facility (Contract Nos. NO1-CN-85392, 85375, 75391) have been completed. These projects provided a demonstration of comprehensive terminal care given in three different settings, i.e., a nursing home, a community hospital, and a health maintenance organization.

A collaborative, descriptive study developed by the hospice contractors and NCI program staff was completed. The study focused on a thorough description of care in the three settings which included a longitudinal assessment of the patient and the bereaved family members (significant others). In describing the hospice patient population, age, sex, socio-economic status, medical condition, and other pertinent characteristics were recorded. The initial report with preliminary analyses will be available in the fall.

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NATIONAL ORGAN SITE PROGRAMS BRANCH

The National Organ Site Programs Branch currently consists of grant supported National Projects of targeted cancer research. Each Project is a planned research effort oriented towards cancer at a specific organ site. Currently there are National Organ Site Projects concerned with cancers of the urinary bladder, large bowel, pancreas, and prostate. The planning, direction, and coordination of each Project are provided at headquarters outside the NCI. The four National Project Directors are assisted in planning and administration by the headquarters staff and by a chartered committee of active research scientists recruited from institutions throughout the nation. Grant applications are received by the headquarters and are reviewed by the four individual committees with final review by the National Cancer Advisory Board. Applications which are judged scientifically meritorious and relevant to the aims of the Project are recommended to the NCI for funding.

Each National Project Director is a recognized clinical or laboratory scientist with a strong interest in, and professional identification with, a specific organ site cancer. The National Bladder Cancer Project is under the direction of Dr. Gilbert H. Friedell, St. Vincent Hospital, Worcester, Massachusetts; the National Large Bowel Cancer Project, Dr. Edward M. Copeland, M.D. Anderson Hospital and Tumor Institute, Houston Texas; the National Pancreatic Cancer Project, Dr.Isidore Cohn, Jr., Louisiana State University School of Medicine, New Orleans, Louisiana; and the National Prostatic Cancer Project, Dr. Gerald P. Murphy, Roswell Park Memorial Institute, Buffalo, New York.

In May 1982, the National Cancer Advisory Board recommended that the Organ Site Programs be reorganized as a National Organ Systems Program with a mission to focus on the four sites currently recognized, but to continuously appraise progress at other sites in order to identify those which might require specialized attention. In addition, the Breast Cancer Program will be integrated into the Organ Systems Program Branch. A single Coordinating Center external to the NCI would have two divisions at the outset: Genitourinary and Gastrointestinal. The Coordinating Center would be responsible for the organization, planning, coordination, and overview of the basic and clinical research components of the program. Communication between the clinical and laboratory segments would be maintained through workshops, and conferences, and fostered through other novel mechanisms yet to be developed. Peer review for the research grant applications would be performed by Study Sections within the Division of Research Grants.

NATIONAL BLADDER CANCER PROJECT

The primary goal of the National Bladder Cancer Project (NBCP) is to sponsor and encourage laboratory and clinical research directed toward improving the techniques available for detecting and diagnosing, preventing and/or controlling cancer of the urinary bladder.

The Project is based entirely on investigator-initiated grants. Qualified investigators are encouraged to submit grant applications to accomplish specific objectives. All grant applications submitted to the NBCP are evaluated by the Bladder Cancer Subcommittee (BCS) of the Bladder and Prostatic Cancer Review Committee for relevance to the needs of the project and for overall significance toward the achievement of the NBCP goals.

A collaborative effort is supported by the NBCP for prospective studies of patients with bladder carcinoma. The organization of the National Bladder Cancer Collaborative Group A (NBCCGA) is based upon the concept that bladder cancer is a progressive disease and that an increased understanding of the progression under treatment for various subgroups of patients will contribute to improved therapy through improved diagnosis and classification of patients. Consequently, a basic protocol of the NBCCGA is the surveillance of all patients with bladder cancer admitted by participating physicians. When the most suitable treatment selection is not known, randomized clinical trials are established to provide the data from which such a decision can be derived.

The broad goals of the NBCCGA are: to assess and characterize patients, their neoplasms, and the fields from which the neoplasms arise; to evaluate new diagnostic and marker techniques for better classification of the patients and their neoplasms; to verify application of existing treatment modalities; to clarify the role of radiation in combined therapy; and to evaluate a variety of agents singly and in combination, intravesically and systemically, alone and as adjuvant to surgery and/or radiation therapy.

Accomplishments

The results of investigator-initiated efforts in the NBCP have been outstanding. By expanding the close working relationship between the Headquarters and the BCS to include the larger scientific community, a total of 246 investigators (85 principal investigators) representing 24 different disciplines were recruited from 52 different institutions into the program. Nine additional institutions have been represented through membership on the BCS. A total of 354 grant applications have been reviewed to date, out of which 96 different projects have been funded. Twenty of these projects were intradepartmental, 54 were interdepartmental and 48 were interinstitutional.

With the encouragement and coordination provided by NBCP Headquarters and the BCS, laboratory investigators have provided essential basic information and have developed very useful experimental models of bladder cancer while a network of sensitized communicating and cooperating clinical research workers have made striking changes in the approach to the management of this disease by the practicing urologist.

Epidemiology

The accumulation of definitive new information on the epidemiology of bladder cancer has slowed considerably. This is due in part to the apparent confounding influence

of cigarette smoking as a major contributing factor in etiology of the disease. One recent study examined the hypothesis that defects in tryptophan metabolism might contribute to a higher incidence of bladder cancer based on the observed action of tryptophan as a tumor promotor in experimental animals (Friedlander and Morrison, 1981). This study showed that tryptophan excretion was not significantly different between bladder cancer patients and controls when adjusted for age, sex, and smoking status.

Carcinogenesis

Numerous bladder carcinogenesis studies are ongoing in the NBCP utilizing the following carcinogens and/or their metabolites: N-butyl-N-(4-hydroxybutyl)nitrosamine (BHBN) (Murphy and Irving, 1981), benzidine (Morton et al, 1981), phenacetin (Vaught et al, 1981), and N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide (FANFT) (Cohen et al, 1982; Mattammal et al, 1981; Swaminathan et al, 1981). These studies range from the identification of morphologic features in both preneoplastic and frank neoplastic lesions to metabolism and molecular interactions with cellular nucleic acids and proteins.

The activation of carcinogens -- or procarcinogens -- by various tissues and various pathways is gradually leading to a better understanding of molecular events in the carcinogenesis process for particular compounds. One of the more exciting findings has been the observation that prostaglandin endoperoxide synthetase (PES) from kidney or bladder tissue specifically transforms (oxidizes) a variety of compounds to carcinogenically active species (Cohen et al, 1981; Davis et al, 1981; Zenser et al, 1981; Zenser et al, 1982). The separable characteristics of the cyclooxygenase and hydroperoxidase activities of PES, combined with substrate and inhibitor studies, implicated the prostaglandin hydroperoxidase activity as the activating catalyst.

Other studies using FANFT (Swaminathan et al, 1981) and liver microsomal metabolites of phenacetin (Vaught et al, 1981) have demonstrated that these bladder carcinogens can covalently bind to nucleic acids and cause mutagenicity in a restricted subline of Salmonella typhymurium. Further investigations of the nucleic acid adducts formed and of the actions of antagonists and nucleic acid repair processes are currently underway.

Recent progress has been made by several laboratories toward establishing normal transitional epithelial cells in culture as model systems for bladder carcinogenesis. Those efforts employing a growth substratum derived from connective tissue have been most successful. An in vitro system for cell growth using salt-extracted bovine articular cartilage has also been employed to discriminate normal non-invasive cells from invasive and highly metastatic cells according to the depth and rate of cellular invasion of the substratum (Pauli et al, 1981). It was further found that the natural resistance of unextracted cartilage to tumor invasion is due at least in part to the presence of tissue derived proteinase inhibitors (Pauli et al, 1981).

Further studies of multi-stage carcinogenesis have shown that the simple ulceration of urinary bladders of Fischer 344 rats (by freezing) was found sufficient to effect tumor initiation in 30 percent of animals fed a routine laboratory diet. That is, FANFT or other known exogenous initiators were not necessary to induce bladder tumors in these animals (Cohen et al, 1982). These observations extend the importance of cell division in the process of tumor initiation.

Diagnosis/Classification

Recent advances in cytogenetic techniques have shown that up to 70 percent of solid bladder tumors may now be accessed for the detection of abnormalities. Using these methods it was shown that 32 of 50 papillary tumors had marker chromosomes and 11 of 12 of these tumors which recurred had at least one marker (Sandberg, 1981). Thus, the presence of markers in these tumors may be indicative of the likelihood of recurrence and/or of progression of such tumors.

Improvements in flow cytometric (FCM) evaluation of bladder irrigation specimens have made this technique a viable adjunct to cystoscopy and cytology for patient evaluation. FCM agreed with cystoscopy and cytometry in 80 percent of the cases investigated with regard to tumor stage and grade (Devonec et al, 1982). Further, evaluation of patients receiving intravesical BCG therapy for superficial bladder cancer indicated that FCM could predict tumor recurrence by as much as 12 months before it is evident cystoscopically (Klein et al, 1981).

Immunology

A variety of immunologic approaches have been used to understand, evaluate, and treat bladder cancer patients. Two separate studies showed that tumor antigen-induced suppressor cells are responsible to a large extent for the impaired immune response seen in bladder cancer patients as judged by decreased lymphocyte proliferation and cytotoxicity (Bean, 1981; Spina et al, 1981).

After considerable effort, there is now promise that bladder tumor-enriched antibodies can be produced by hybridoma cells prepared from animals challenged with either established in vitro cell lines or with cells isolated from fresh tumors (Boxer et al, 1981; Hellstrom et al, 1982). One of these antibodies, identified as 2H5, gave significant binding to membranes from five of seven transitional cell carcinomas but not to membranes from any other tissues. The antigen bound to a 140,000 dalton protein which is detectable in bladder transitional cell carcinomas but to a much lesser extent in normal bladder tissue.

Studies of interferon showed that both T- and null cell lymphocytes can be stimulated by Staphylococcus aureus protein A to produce γ-interferon, although phytohemagglutinin is the best stimulus for this purpose (Catalona et al, 1981; McCool et al, 1981). Interestingly, cells from bladder cancer patients showed a greater response to protein A than did cells from controls or from patients with other urologic tumors.

Related studies developed a T-cell hybridoma which produces macrophage activation factor (MAF), a substance capable of activating macrophages to be tumoricidal (Ratliff et al, 1982). This factor requires a lipopolysaccharide for its action and is distinct from γ-interferon.

Chemotherapy

A variety of methods have been utilized to evaluate chemotherapy approaches and devise individualized therapy regimens. Thus, tumor tissues are either dispersed and introduced into monolayer or soft agar culture systems or minced and innoculated into athymic (nude) mice for examinations of the tumoricidal effects of various cytotoxic agents. Each of these systems has recently demonstrated the potential of predicting the best chemotherapy for the individual tumor or tumor patients (Day et al, 1981; Stanisic et al, 1981).

A recent study was carried out comparing radiation vs cis-platinum actions against

human bladder transitional cell carcinomas grown in nude mice (Kyriazis et al, 1982). This study demonstrated a synergistic effect of the two treatment regimens with optimal results obtained when cis-platinum was given at 6 days post-radiation. These results offer encouraging guidelines for chemotherapy regimens in humans.

Clinical Studies

In a longitudinal study conducted in several collaborating institutions, an analysis was made of recurrence of disease in patients with transitional cell carcinoma. The probability of early recurrence was found to be associated with the number and size of visible tumors, the histologic grade and depth of invasion, and the presence of dysplasia and hyperplasia in the non-tumor bearing areas of the bladder. Progression of disease with respect to depth of invasion and extension beyond the bladder was found to be related to depth of invasion at initial diagnosis, histologic grade, tumor size, and the presence of moderate to severe dysplasia (Cutler et al, 1982).

Urinary cytology has taken an important place in the evaluation of patients with transitional cell carcinoma. Cytology can provide highly useful prognostic information as a supplement to cystoscopy and bladder biopsy in the clinical evaluation of each patient. Positive cytology appears to be a predictive factor in patients at high risk for recurrence of the primary bladder tumor (Friedell et al, 1982).

A prospective study of patient tolerance and pathologic downstaging was conducted in a collaborative effort using 4,000 RAD preoperative irradiation followed by prompt cystectomy and urinary diversion in patients with muscle-invading bladder cancer. The results supported the rationale of using full dose adjuvant preoperative radiation therapy to downstage and sterilize unresected pelvic micrometastases and yet maintain a short interval between diagnosis and cystectomy (Shipley et al, 1982).

A recent study of 52 patients has indicated that intravesical instillation of bacille Calmette-Guerin (BCG) as a site-directed immune stimulant (33 patients) is more effective in preventing superficial bladder tumor recurrence than is thio-TEPA (19 patients) over a prolonged period of therapy (Brosman, 1981).

Emphasis and Projections

Epidemiology

Considering the international opportunities and interdisciplinary approaches now available, more attention should be given to epidemiology. Epidemiologists need to work more closely with clinicians to discern epidemiologic correlates with the natural history of the disease(s) -- to determine factors associated with recurrence, with high grade and with low grade lesions. From such studies may come a new understanding of how the processes involved can be prevented, delayed, or reversed.

Carcinogenesis

A greater sensitivity to biologic events in studies of initiation, promotion, and invasion is needed in addition to the current emphasis on chemical events. Such events should include differentiation/dedifferentiation, tumor angiogenesis and stromal epithelial cell relationships and interactions. New studies should include lower dosage levels of carcinogens and co-carcinogens which are more in line with human exposure and should make further efforts to detect and evaluate the earlier, pre-malignant state of the disease. The period of support for selected animal studies should be increased from three to four or five years so that long term studies, particularly those with lower dosages of carcinogen and co-carcinogens can be conducted. Macromolecule interactions with carcinogens should be studied more

intensively at a mechanistic level. The qualitative, quantitative, and kinetic relationships between carcinogen-macromolecule interaction and tumor induction should be examined.

Diagnosis

Sufficient technology (i.e., flow cytometry) and cytologic markers (i.e., ABH antigens, hyperploidy, and marker chromosomes) for malignant cells are now available to justify clinical trials using the cellular content of urine samples as the basis for classification and prognostic evaluation. Having established markers for overt bladder cancer lesions, there is now a need to develop systems most effective for the diagnosis of early lesions, particularly for diagnosing pre-high grade lesions. With the aid of the newly developing computer model, optimal screening strategies for populations at given probabilities of risk should be defined.

Treatment

Studies on the pathogenesis and etiology of the silent lesions which are diagnosed late after muscle invasion and metastases should be specifically emphasized. It is important to define further the need for and efficacy of individualization of therapy by matching a specific drug regimen to the individual tumor. New drugs should be sought which have a high propensity to concentrate in urine. The search for potentially effective drugs beyond the current arsenal being tested with other cancers should continue. Intravesical and systemic approaches should be compared using a variety of agents singly and in combination. Treatment regimens should be developed in concert with efforts to detect *in situ* lesions earlier in order to provide alternatives to cystectomy for this phenotype when found widespread in the bladder epithelium. The effect of reducing exposures to all known bladder carcinogens or promoters in patients who have already had an initial bladder tumor should be evaluated.

Other Program Activities

Since 1974, the NBCP has sponsored annual Investigators' Workshops for the purpose of facilitating communication and interaction among the laboratory and clinical elements in the Project. This effort has been one important means through which a coordinated project effort is achieved. It not only encourages the exchange of ideas and materials, but several collaborative efforts have developed from the workshop discussions.

The next workshop, scheduled as the Second National Bladder Cancer Conference to be held in January 1983, is currently being developed. This conference will be co-sponsored by the American Urological Association and will "double" as one of the AUA regional meetings. Major addresses will be given on triggering the cellular change to neoplasia, altered gene products, mechanism of invasion, metastatic process, flow cytometry, ploidy and nuclear changes. General discussion sessions and mini-workshops as well as poster sessions will be used to present the latest and most important research findings which provide a scientific basis for advances in the clinical management of bladder cancer. The meeting will be open to anyone interested in attending.

Members of the Headquarters Staff have continued collaboration with Dr. Leon Ellwein of Science Applications, Inc., in the development of a computerized simulation model of bladder cancer (clinical disease) which can be used as a tool for planning and for testing hypotheses of various diagnostic and therapeutic intervention strategies.

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NATIONAL LARGE BOWEL CANCER PROJECT

The National Large Bowel Cancer Project, with headquarters at The University of Texas System Cancer Center, M. D. Anderson Hospital and Tumor Institute, sponsors multidisciplinary basic and clinical programs of investigator-initiated research designed to examine the biology and promote the control of colon and rectal cancer.

Accomplishments

Biology, Cause, and Prevention of Large Bowel Cancer

The identity and isolation of mutagens formed during the cooking of meat has progressed (Weisburger et al. 1981). Efforts are now being directed at blocking mutagen formation. Soy protein (15%) reduces the amount of extractable mutagenic activity by more than 90%. Chlorogenic acid and butylated hydroxyanisole (BHA) are also highly inhibitory. Wilkins et al. (1980) are continuing their efforts to characterize mutagenic bacterial products from human feces.

Inhibition of methylazoxymethanol (MAM) acetate-induced colonic neoplasms in mice has been demonstrated using several phenols that are widely consumed in the diet as food additives or are naturally occurring constituents of fruits and vegetables (Wattenberg 1981a, 1981b). These phenolic compounds had varied effects on the NAD^+-dependent alcohol dehydrogenase activity in the mouse liver and large bowel *in vitro*.

Onishi et al. (1982) are investigating the biotransformation of quercetin, a naturally occurring product with carcinogenic activity, by rat tissues (liver, kidney and intestinal mucosa). One non-mutagenic kidney metabolite was tentatively identified as isorhamnetin; a second unidentified metabolite of quercetin was mutagenic, and the structural features which appear to be essential for mutagenic activity have been identified. The formation of azoxymethane and other azoxy compounds during the biological oxidation of amines has also been studied (Fiala et al. 1981).

The inhibition of chemically induced colon carcinogenesis at various stages of neoplastic transformation by a variety of compounds is under intense study. Particular attention is being directed at fiber, vitamins, and at various minerals (Jacobs et al. 1981). Using an epidemiologic approach, Enstrom (1981, 1982) is assessing the role of diet in colorectal cancer etiology. Experiments conducted by Goldin and Gorbach (1981) suggest that a variety of factors, including antibiotics and diet, affect the metabolism and excretion of three different classes of procarcinogens and that a concommitant reduction in fecal bacterial enzyme activity explains these metabolic and excretory changes. The acute and chronic effects of dietary cholic acid on colonic epithelial cell proliferation have been described (Deschner et al. 1981), as has the effects of various bile acids on the absorption of carcinogens in the colon of rats and guinea pigs (Rose and Nahrwold 1982).

It has been determined that the colon is an active site of prostaglandin (PG) synthesis (Craven and DeRubertis 1981a), products which induce changes in cAMP and cGMP metabolism in this tissue. These latter factors have been implicated in the control of colonic epithelial cell proliferation (Craven and DeRubertis (1981b). Further studies in rat colon support the existence of an arachidonic acid responsive pathway for carcinogen activation which is in part coupled to cyclooxygenase and PG synthesis. This may represent an important alternative route of local colonic xenobiotic metabolism that is potentially subject to dietary and hormonal influence.

Fang and Strobel (1981) have demonstrated the control of carcinogen hydroxylation in rat colon by gastrointestinal hormones, and have accumulated evidence for the presence of multiple forms of cytochrome P-450 in colon microsomes.

Boffa et al. (1981a) have demonstrated that exposure of colon tumors to butyrate suppresses the malignant phenotype and leads to an expression of differentiated functions. Post-synthetic modification of chromosomal proteins represents a primary target of the butyrate action. In addition to inhibiting histone deacetylase activity directly, butyrate progressively but reversibly inhibits the phosphorylation of histones H1 and H2A. Other investigations on the role of the nucleolus and of ribosomal RNA in the control of cell proliferation are in progress (Baserga, 1981). Data presented by Augenlicht and Kobrin (1982) suggest that 1,2-dimethylhydrazine(DMH)-induced transformation of mouse colon cells is associated with extensive changes in gene expression.

Efforts have been directed at developing methods for the culture of human colonic carcinoma (Brattain et al. 1981a). The isolation of heterogenous malignant cell types with different biological properties from a single tumor has been described (Brattain et al. 1981b). Efforts are also directed at establishing epithelial cell cultures from normal human colon (CA 30185).

Detection, Early Diagnosis, and Prognosis of Large Bowel Cancer

Recognizing the importance of surface glycoproteins in the biological behavior of epithelial cells, Ahnen et al. (1982) demonstrated that CEA, normally localized to the microvillus surface, was diffusely distributed over colon cancer cells and that secretory component, normally localized to the basolateral surface, is diminished in amount or is absent in colon tumor cells. The data suggest that CEA or possibly other topographically restricted substances might serve as antigenic markers for the colonic microvillus surface.

The differential effects of sodium butyrate, dimethylsulfoxide (DMSO) and retinoic acid on membrane-associated antigens, enzymes, and glycoproteins of human rectal adenocarcinoma cells (HRT-18) has been investigated (Tsao et al. 1982).

Changes in the immunospecificity of nuclear antigens were demonstrated in the colon chromatin of rats treated with DMH. The level of nuclear antigen activity could be modulated in response to tumor promoters and inhibitors (Gabryelak et al. 1981). In related studies, the tumor-associated chromatin antigens of two human colon adenocarcinoma cell lines, HT29 and LoVo, were studied (Duhl et al. 1982). Antiserum immunoabsorbed with either LoVo or HT29 chromatin, failed to show any immunoreactivity, suggesting that the antigenic sites residing on these proteins are identical.

Considerable effort has been applied to the establishment of tissue cultures of human epithelial cells from benign colonic tumors (Friedman et al. 1981). The differential response of premalignant colonic epithelial cells to tumor promoters has been investigated (Friedman 1981).

In a continuing effort to identify high-risk individuals with hereditary colorectal cancer, the effects of TPA and EGF on proliferation of human mutant fibroblasts have been studied in vitro (Gansler and Kopelovich 1981). The results suggest that EGF and TPA may share only one class of receptors and that TPA may be used to monitor cancer progression. The suppression of tumorigenicity in human X mouse hybrids has

been reported by Chopan and Kopelovich (1981). The transformation-related traits expressed in the hybrid clones closely resembled the malignant mouse (A9) parental line. However, all hybrids displayed partial to complete suppression of tumorigenicity.

Diagnostic criteria for kindreds with familial polyposis coli and Gardner syndrome have been investigated at the cellular level. Chromosomes from individuals with these syndromes show excessive instability characterized by random structural and numerical aberrations. One member of the number 2 chromosome pair carries a consistent heteromorphism, tentatively identified as a deletion in the long arm at q14.3-21.3 (Gardner et al. 1982). Additional diagnostic criteria, in the form of extracolonic lesions that appear before adenomas in the colorectum, have also been described (Richards et al. 1981, Naylor and Gardner 1981). Further studies on the in vitro tetraploidy in heritable colon cancer syndromes have been conducted by Danes (1981) and in vitro evidence of genetic heterogeneity within the heritable colon cancer syndromes with polyposis have been more extensively studied (Danes and Alm 1981). Balis et al. (1981) continue to study enzyme variants of normal, premalignant, and malignant colonic cells.

As a part of an on-going study to detect early colon cancer, 21,961 individuals have been entered in a prospective controlled clinical trial to demonstrate the feasibility of screening for fecal occult blood in a standard risk, asymptomatic population over the past 6 years to detect colorectal cancers at an early (localized) stage, thereby increasing survival and reducing mortality. The program is unique in that it evaluates the benefit of both fecal occult blood testing and proctosigmoidoscopy as screening techniques. Follow-up continues in an effort to obtain reliable estimates of the incidence rates of colon/rectal cancers, survival rates, and total mortality due to colorectal cancer in the study and control groups (Winawer et al. 1982, Winawer and Fleisher 1982).

Using an orthotopic transplant of syngeneic murine adenocarcinoma cells (MCA-38), Raina et al. 1981 have observed that the dynamic changes detected by the Winn neutralization test parallel the alteration of specific antitumor immunity observed in vitro in the microplate leukocyte adherence inhibition assay. The selective loss of immunity in the local and regional compartments may play a permissive role in metastasis formation. Sjogren (1981) has found that administration of pure protein A to rats bearing colon cancer isografts inhibits tumor growth. He has observed that Cimetadine increases the natural killer (NK) cell activity in vitro and potentiates the interferon-induced activation of NK cells. The identification and characterization of the CEA-related antigen, TEX, has been described and a radioimmunoassay (RIA) specific for TEX has been developed (Shively et al. 1982). The nature of the carbohydrate determinants in CEA have been more clearly defined by developing a polyethylene glycol-based RIA (Pompecki et al. 1981a). Using this immunoassay, elevated levels of anti-Lewis antibodies in the sera of cancer patients have been demonstrated (Pompecki et al. 1981b).

Developmental and Clinical Therapy for Large Bowel Cancer

In conjunction with Dr. Hynes, who is synthesizing new folate analogs directed toward improved chemotherapy of colon adenocarcinoma (Yang et al. 1981, Hynes et al. 1982), Dr. Bertino is evaluating the effectiveness of this series of 2-amino-4- hydroxyquinazoline for activity against human colon cancer line HCT8 propagated in vitro. One compound, H338 (IAHQ), has shown good activity in this system and against a mouse colon adenocarcinoma (No. 38) (Fernandes et al. 1981). The data

suggest a new mechanism for its antitumor effect, namely the conversion of the analog intracellularly by polyglutamate synthetase to a potent inhibitor of thymidylate synthetase.

Using autochthonous tumors induced by a variety of colon carcinogens, it has been demonstrated that oral administration of indomethacin (20mg/L), a prostaglandin inhibitor, has antitumor or antipromotional activity and causes reductions in colon tumor incidence (Pollard and Luckert 1981a, 1981b). As the tumor burden was reduced by reducing the dosages of carcinogen, the efficacy of indomethacin therapy was increased. Peroxicam, a prostaglandin blocking agent with low toxicity, was equally inhibitory.

Using a transplantable murine colon tumor, T36, the selective inhibition of protein synthesis by sodium cyanate has been demonstrated (Allfrey et al. 1981) and its activation has been studied in culture (Boffa et al. 1981b). No inhibition of protein synthesis was observed in butyrate-treated tumor cells exposed to the cyanate/S9 system, whereas cells cultured in the absence of butyrate remained cyanate-sensitive (Boffa et al. 1981b). Using human colon carcinoma cell lines and their subclones, Leith et al. (1982) have demonstrated differential drug sensitivities as well as differential responses to x-irradiation and hyperthermia. Using several differentiation modulating agents, maturational effects on tumor cells have been noted. Several established colon carcinoma cell lines have been well characterized (Stragand et al. 1981) and their differential response to therapeutic agents has been evaluated as a function of cell differentiation and proliferative status (Drewinko et al. 1981, Drewinko and Barlogie 1982).

Biochemical determinants and responsiveness of particular tumors to specific agents and the mechanisms of tumor inhibition are being studied. The mechanism of tumor inhibition by alanosine, an aspartate analog which inhibits adenosine 5' -monophosphate synthesis, has been investigated (Hurlbert et al. 1982a). Studies to identify the biochemical determinants of responsiveness of 5-fluorouracil and its derivatives in human colorectal adenocarcinoma xenografts suggest that the response relates to the inhibition of thymidylate synthetase, and not to the level of incorporation of the triphosphate, or the frequency of its substitutions into total RNA at dose levels toxicologically acceptable to the host (Houghton et al. 1981). Preliminary studies of uridine kinase activity in human colorectal adenocarcinomas has been completed (Ahmed et al. 1981). The efficacy of the de novo synthesis of uridine 5' -monophosphate (UMP) is being studied in a large number of human neoplasms. The development and improvement of quantitative techniques for measuring treatment effectiveness on apparent or subclinical disease continues to receive emphasis.

Developing Resources

Synthetic bile acid reference standards are available to interested investigators (CA 21656). A cell bank of human and experimental colon tissue has been established at the ATCC to promote large bowel cancer research (CA 25635).

Emphases and Projections

A major emphasis has been on programs aimed at the prevention of large bowel cancer, with special emphasis on: 1) identifying and characterizing mutagens (potential carcinogens), 2) assessing "high-risk" populations and dietary factors believed to exert an influence on large bowel carcinogenesis; 3) developing immunopreventive approaches; and 4) studying drugs which may interfere with the

carcinogenic process.

Model systems, now well developed, are expected to expand our concepts and knowledge concerning large bowel cancer. Such models are now being used to: 1) identify and test new anticancer drugs, 2) identify potential inhibitors of carcinogenesis, 3) develop approaches to immunoprevention, 4) discern factors associated with transformation of colon epithelium to precancerous lesions and carcinoma of the large bowel, using molecular genetic approaches, and 5) assess the influence of dietary factors and the microflora in the initiation, promotion, or inhibition of large bowel cancer.

Methods derived from research in cellular biology will be utilized to ascertain alterations in cellular behavior and to identify phenotypic expressions characteristic of high-risk individuals. Identification of cellular and biochemical properties related to growth and metastatic potential of large bowel cancer will be encouraged. Programs in screening and early diagnosis of large bowel cancer will also be fostered with particular emphasis on evaluating the factors affecting their implementation and efficacy.

The National Large Bowel Cancer Project will foster development of new chemotherapeutic drugs to treat large bowel cancer. Research will be pursued to identify targets dealing with metabolic pathways involved in nucleic acid and protein synthesis. Cell surface glycoproteins and fundamental studies of membrane structure will be continued to uncover abnormal, exploitable, cellular functions.

Other Program Activities

The eighth workshop, "The Large Bowel Cancer Program: Its Achievements and Future Directions of Investigation", was published in The Cancer Bulletin, 33 (4), July-August, 1981. The revised annual Announcement of programmatic priorities was a result of the workshop. The NLBCP has co-sponsored a conference on "Prevention of Hereditary Large Bowel Cancer." A workshop on Markers of Colonic Cell Differentiation will be sponsored in the Fall at Southwest Harbor, Maine. The Proceedings of these workshops will be published.

The National Large Bowel Cancer Project and the American College of Surgeons jointly sponsor an exhibit on colorectal cancer entitled, "Large Bowel Cancer - Biology and Control". The exhibit has been updated, and has been shown at 27 meetings with 2,625 companion brochures having been circulated.

The activities of the National Large Bowel Cancer Project are publicized and distributed in a quarterly Newsletter and an annual Announcement.

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NATIONAL PANCREATIC CANCER PROJECT

The National Pancreatic Cancer Project (NPaCP) is an Organ Site Program established by the National Cancer Institute to stimulate research in the underdeveloped area of pancreatic cancer research. The Project began functioning in 1975 with its headquarters at the Louisiana State University Medical Center. Functions of the NPaCP include promotion and review of grants for pancreatic cancer research, dissemination of information to scientists, physicians, and the general public, and stimulation of scientific collaboration through conferences and workshops.

Pancreatic cancer is the fourth leading cause of death due to cancer and has the highest mortality to incidence ratio among major cancers. Due to the anatomic location of the pancreas and the relatively asymptomatic early stages, diagnosis of pancreatic cancer is extremely difficult. Treatment of pancreatic cancer also is hindered by the location of the pancreas and by the resistance of the disease toward conventional therapeutic regimes. While early diagnosis, effective treatment, and prevention are ultimate goals of the NPaCP, the current primary aim of the Project is to stimulate basic research which will lay the foundation for studies which will directly address the problems of pancreatic cancer.

Accomplishments

To date the NPaCP has reviewed 244 grant applications of which 75 have been funded. Now in its eighth year of operation, the Project is currently funding 32 research projects and eight others have been approved with recommendations for funding. In accordance with statements made in the above introduction, much of the work funded by the NPaCP is for basic research. This includes projects involved in experimental biology, carcinogenesis, pathology, epidemiology, immunology and tumor markers. While the clinical and applied fields of diagnosis and treatment are de-emphasized at present, important studies in these areas also are being funded. This emphasis on basic research is evident in the following summary of project accomplishments for the fiscal year of 1982.

Characterization of the normal pancreas has been conducted by DiMagno (CA 25064). It has been postulated that pancreatic cancer may result from reflux of carcinogenic agents from the duodenum into the bile duct. DiMagno et al have disproved this theory by showing that an efficient antireflux mechanism exists (Keane, 1981). Reflux is prevented by a sphincter at the opening of the pancreatic duct. In other experiments, these investigators have shown that physiological doses of nicotine shorten the cycle of interdigestive secretion and duodenal motility and, thus, increase duodenal motility and pancreatic secretion of trypsin and bicarbonate (Keane, in press). These effects of nicotine may be related to pancreatic cancer due to the positive correlation between cigarette smoking and pancreatic neoplasia. DiMagno et al also found that pancreatic secretion and duodenal motility in humans are cyclical and serve to clear the stomach of refluxed duodenal secretions (Keane, 1981).

The study of carcinogenesis has been a primary emphasis of the NPaCP. When the Project began in 1975, there were no acceptable animal models with which to study pancreatic cancer. Now that a number of good models are available, the Project has encouraged their characterization and use in innovative experimental studies.

Black (CA 16263), Gunther (CA 26561), Iqbal (CA 20914), Parsa (CA 22682), Pour (CA 20198) and Reddy (CA 23055) are among the investigators funded by the NPaCP to utilize these animal models for study of carcinogenesis (aspects of pancreatic neoplasia). A review of accomplishments in this field has been published by Reddy (Reddy, 1981).

Black et al have demonstrated that the rat pancreas responds with changes in DNA and RNA content to treatment (in vivo) with the pancreatic carcinogen 7, 12-dimethylbenz(A)anthracene (Black, in press). There appears to be a biphasic response with an initial depression of DNA, RNA and protein synthesis occurring from 2 to 16 hours post-treatment followed by an increase in DNA synthesis from 16 to 48 hours. While DNA replication was depressed during the first phase, repair synthesis was increased almost two-fold. RNA content in both nuclear and cytoplasmic compartments was significantly depressed at 5 and 22 hours. Additionally, the cytoplasmic content was depressed at 48 hours. These observations are consistent with findings in neoplastic tissues of other organs and with the theory of macromolecular control of the carcinogenic processes.

Gunther has examined the effects of the tumor promoting agent 12-O-tetradecanoyl-phorbol-13-acetate (TPA) on calcium efflux in guinea pig phorbol acinar cells (Gunther, in press). Secretagogues such as caerulein (an analogue of CCK), carbamylcholine (cholinergic agonist) and calcium ionophore A23187 stimulate rapid release of calcium into the cytoplasm which triggers an increase in the level of cGMP and, by a separate series of events, protein discharge. In contrast, TPA appears to stimulate protein discharge independent of either increased cGMP or calcium discharge. This finding may help elucidate the physiological significance of the phorbol ester in normal acinar cell function, and its potential role in the etiology of pancreatic cancer.

Iqbal has been investigating the metabolism of nitrosamines in the Syrian hamster model of pancreatic cancer. Following injection of the pancreatic carcinogen N-nitrosobis(2-oxopropyl)amine (BOP), Iqbal et al found that the metabolite N-nitroso(2-hydroxypropyl) (2-oxopropyl)amine) (HPOP) has a higher concentration and a longer half-life in the pancreas than in other affected tissues (Whalley, 1981). N-nitrosobis(2-hydroxypropyl)amine (BHP), another important metabolite of BOP, was found in significantly smaller concentrations than HPOP in both the pancreas and plasma. These observations are consistent with the theory that HPOP is a more proximate carcinogen than BOP.

Parsa has produced the first in vitro model of pancreatic neoplasia. Carcinomas in organ cultures of human pancreas explants were induced by dimethylnitrosamine (DMNA) (Parsa, 1981). DMNA induced both ductal hyperplasia and atypia of the epithelial linings of main ducts, smaller ducts, and ductules within 6 weeks. Cells derived from 10-week-old DMNA-treated explants produced multiple nodules of carcinoma when injected subcutaneously into nude mice.

Pour et al have continued to characterize the Syrian hamster models of pancreatic cancer which they developed. As would be expected, DNA damage due to BOP was found to be greater in the pancreas than in the liver or salivary gland (Lawson, 1981). Furthermore, repair mechanisms in the pancreas, unlike those of other tissues, were not able to mend the damage caused by high concentrations of BOP. Differences in alkylation of BOP in target (pancreas) and non-target (liver) tissues were noted (Lawson, 1981). There are two alkylating agents in the liver, a methylating

agent and a 2-oxopropylating agent. The pancreas, however, appears to only methylate a one-carbon alkyl group. Following BOP injection, a potential methylating metabolite, N-nitrosomethyl (2-oxopropyl)amine (MOP) was identified in both the pancreas and liver (Lawson, 1981). The investigators also have identified several other carcinogenic agents in the hamster model; N-nitrosobis(2-oxobutyl) amine (BOB), N-nitroso(2-oxobutyl)(2-oxopropyl)amine (OBOP) and N-nitroso-2-methoxy-2,6-dimethylmorpholine (Pour, 1981).

Kim (CA 24321) and Yunis (CA 19182) have used in vitro techniques to study various biological aspects of pancreatic cancer. Kim et al demonstrated that three pancreatic cancer cell lines (PANC-1, CAPAN-1 and MIA-PaCa-2) attach to collagen in vitro (McIntyre, 1981). Anchorage independent growth, such as this , is the in vitro property which has been found to correlate best with tumor formation in vivo. Yunis et al have found that both Acinetobacter glutaminase-asparaginase and L-(αS, 5S)-α amino-3-chloro-4,5-dihydro-5-isoxozoleacetic acid (Acivicin) are effective inhibitors of MIA PaCa-2 cell growth (Meck, 1981 and Wu, in press). One mode of action for Acivicin appears to be a partially irreversible binding with gamma-glutamyl transpeptidase (Allen, in press). Yunis et al also have immunologically and functionally characterized colony stimulating factors I and II (Wu, 1981).

Using the tools of immunology, Chu (CA 18410) and Scheele (CA 22582) have identified pancreas-specific antigens and pancreas-associated proteins. Chu and co-workers have identified and characterized three different human pancreas-specific antigens and one human pancreatic cancer-associated antigen (PCAA) (Loor, 1981; Papsidero, in press and Tan, 1981). These antigens are now being used as potential markers for pancreatic cancer and for studies of pancreatic secretion. Chu et al also have established a human pancreatic tumor cell line, AsPC-1 (Chen, 1982). These cells also express PCAA. Novel approaches for protein isolation have been described by Chu and Scheele. Chu et al used isoelectric focusing of immune complexes bound to Protein A-Sepharose to separate IgG immunoglobulins from human biological fluids (Maidment, 1981). Scheele et al identified 15 discrete proteins from human pancreatic juice by two-dimensional isoelectric focusing/sodium dodecyl sulfate gel electrophoresis (Scheele, 1981).

Danes (CA 25662), Goodale (CA 20115), Hubner (CA 29490) and Rinderknecht (CA 20222) have been investigating possible avenues of early diagnosis. Since diagnosis of pancreatic cancer could be enhanced by the identification of risk factors, Danes is studying the possibility of genetic risk (Danes, 1981). Initial findings indicate that a small genetic risk may exist and that this risk may be identified by hyperploidy in monolayer dermal cultures (Danes, in press). Goodale et al found that endoscopic retrograde cholangiopancreatography was 80% effective in diagnosing symptomatic patients with pancreatic cancer (Goodale, 1981). The investigators also found that pancreatic secretions from cancer patients had a 10-fold greater concentration of albumin, 2- to 7-fold greater IgG concentration and a 6- to 15-fold greater concentration of IgA than secretions from patients with pancreatitis. Hubner et al have described the diagnostic method of positron emission tomography (Hubner, in press). Rinderknecht has described a method of diagnosing pancreatic disease by fluorometric determination of plasma trypsinogen (Rinderknecht, in press).

Treatment protocols have been described by Dobelbower (CA 25733) and Goldson (CA 26658). Dobelbower et al have used a combination of ^{125}I-implantation and

precision high-dose (PHD) external beam radiotherapy for treating patients with non-resectable pancreatic carcinoma (Whittington, 1981). This regime has a median survival of 10½ months and appears to be more effective than PHD alone. Goldson is using intraoperative radiotherapy (IOR) for treatment of pancreatic carcinoma (Goldson, 1981). Clinical data suggest that pre-operative percutaneous biliary decompression and hyperalimentation improve patient tolerance and hasten surgical recovery. The median survival for these patients, 80% of whom had distant disease, was six months.

Gold (CA 29489) and Longnecker (CA 19410) also have published data supported by the NPaCP. Gold et al found that human colonic adenocarcinomas produce an alpha-1-proteinase inhibitor which is capable of inhibiting pancreatic elastase (Lee, in press). Longnecker et al found that islet amyloid occurs in 12% of nondiabetics, in 59% of diabetics, and in 89% of diabetics undergoing insulin treatment (Maloy, 1981).

Other Program Activities

In addition to supporting the research discussed in the Accomplishments section, the NPaCP has stimulated interest, collaboration and research in the field of pancreatic cancer through Project supported literature and meetings. During the past year the NPaCP has published the proceedings of the International Union Against Cancer Workshop on Pancreatic Cancer (Cohn, 1981), the proceedings of the Workshop on Radiation Therapy (Cohn, 1981), proceedings of the Workshop on Pancreatic Tumor Markers (Kupchik, 1982), and an overview of pancreatic cancer (Beazley, 1981). The NPaCP has also published its biannual Newsletter which has a circulation of approximately 1100 readers, and the abstracts of the 1981 NPaCP-APA (American Pancreatic Association) meeting. The NPaCP-APA meeting featured 37 presentations on various aspects of pancreatic cancer including a keynote speech by Dr. Brian McMahon on risk factors. In March of 1982 the NPaCP sponsored an Epidemiology Workshop at NCI. Approximately 50 experts attended this meeting to discuss the volatile issues of methodological problems in pancreatic cancer epidemiology, current epidemiological findings and their etiological relevance. Results from the two largest case-control studies along with those of smaller case-control studies and preliminary results of prospective cohort studies implicate a triad of risk factors in the etiology of pancreatic cancer; tobacco, alcohol and coffee. In April of 1982 the NPaCP held a symposium entitled "Experimental Approaches to Pancreatic Cancer Research: Transformation in Acinar Cell Surface Properties" in conjunction with the meetings of the Federation of American Societies for Experimental Biology. Talks by headquarters staff and grantees focused on basic cellular transformations occurring in pancreatic carcinogenesis. These presentations were used to highlight questions facing the field of pancreatic cancer which could be addressed by basic researchers. This was the first attempt that has been made to open avenues which could lead basic researchers into this field. Other activities conducted by the Project include three meetings of the NPaCP Subcommittee to review grants and establish priorities, and numerous presentations by the Principle Investigator, Dr. Cohn, on the topic of pancreatic cancer. These publications, conferences, and workshops in addition to the scientific research sponsored by the NPaCP have had an impact on the field of pancreatic cancer and it is expected that future work by the NPaCP will be of the same value.

Emphases and Projections

The immediate goals of the NPaCP are to generate research which will result in a better understanding of the pancreas and the basic nature of pancreatic cancer. There are three major reasons for the Project's emphasis on basic research. First, the unique problems presented by pancreatic cancer and the lack of basic information dictate the need for more fundamental knowledge. Secondly, there is a lack of investigators in this aspect of research. The third reason is that there are attractive avenues for funding of clinical projects whereas there are limited resources for basic experimentation. This is evidenced by the $2.86 million spent by NCI on clinical contracts for the study of pancreatic cancer as compared to the $0.95 million spent on basic research (R01). Thus, the NPaCP has filled and will continue to fill this vacuum. Innovative experimentation, characterization of cancer models, and the development of tumor markers and biological probes will be stressed. To aid in these endeavors the NPaCP plans to establish a specimen and cell bank which will allow investigators easier access to materials needed for study. It is expected that such an easy access to samples in addition to the availability of research models will encourage more investigators to study pancreatic cancer. The Project also will continue to sponsor conferences and workshops, publish literature for the scientific community, encourage collaboration and stimulate interest in the field of pancreatic cancer.

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NATIONAL PROSTATIC CANCER PROJECT

The National Prostatic Cancer Project (NPCP), initiated in 1972, represents an integrated effort in which the planning, coordination, and scientific administration of its programs are conducted at the Project Headquarters located at Roswell Park Memorial Institute, under the direction of Dr. Gerald P. Murphy. The overall strategy of the NPCP has been to share major responsibilities between the National Cancer Institute and scientists throughout the nation for development and implementation of a program aimed at prevention and decreased mortality due to prostate cancer. This involves a multidisciplinary research program which addresses high priority projects that have been identified by the scientific and clinical community. The major result toward which these studies are providing progress is measured in terms of increased survival time and delay in the development of progressive disease.

On a continual basis, and in concert with annual planning meetings of the Working Cadre, new areas in need of research are identified and publicized as a mechanism for attracting grant applications into targeted and high priority areas relevant to prostate cancer. The NPCP continued to investigate and implement programs and strategies for experimental and clinical research which, based on the evaluation and analysis of current knowledge and information, offered the best opportunities for immediate and visible success at all levels of endeavor.

Accomplishments

Significant accomplishments were reported during the current period in the Etiology/Prevention, Detection/Diagnosis and Treatment categories of NPCP research grant activity.

Etiology/Prevention

Greater emphasis has been focused on the causal and preventive factors related to prostate cancer, particularly in the fields of nutrition and chemoprevention e.g. retinoids. Of particular note is a new epidemiologic study in progress at the University of Hawaii which will compare cases of prostatic cancer and controls on selected dietary components (fats, vitamin A, vitamin A precursors, and zinc-to-cadmium ratio). Cases are identified through seven major hospitals on Oahu, Hawaii, and controls matched on age and sex are selected by a random-digit procedure. Quantitative dietary histories, from which nutrient intakes can be assessed, are administered to all subjects. During the past year, interviews were completed on 205 cases and 224 controls. Food composition data includes all of the foods and nutrients particular to this study. Analysis of the case-control data will be carried out during the next year, after interviews are completed on a projected 400 cases and 800 controls. At Howard University, investigators are examining whether dietary and/or lifestyle habits of American black males are related to the high incidence of prostatic cancer. Thus far, a total of 163 patients have been enrolled in this study. In the nutritional portion of the study the observations suggested that patients ate more yellow vegetables than controls, and that prostate cancer patients from ages 30-49 consumed less fruit juices.

Animal models for studies of prostate cancer have been developed by investigators supported by the NPCP. Their use in furthering our understanding of basic mechanisms involved with prostate cancer and metastasis have led to some important findings (Coffey, Isaacs 1981; Isaacs et al, 1981). For example, investigations

of several distinct sublines developed from the original Dunning rat prostatic R-3327-H tumor suggests that acquisition of some characteristics by the tumors represents a process of tumor progression into fully developed malignancies (Isaacs et al, 1981). Comparison of chromosomal changes and characteristics observed in the tumors suggested that the growth rate, dedifferentiation and attainment of metastatic ability were related to chromosome variation (Wake et al, 1982). These results point to the importance of chromosome changes in the early development of tumors (Sandberg 1981). Studies of defined human populations have clearly shown a familial association with prostatic cancer (Meikle, Stanish 1981) further suggesting genetic involvement.

Other investigators have made discoveries in animal prostate that may lead ultimately to further understanding and applications to the normal human prostate and the disease (Pollard, et al 1981). Alpha-protein has been identified as a non-receptor steroid-binding protein in the rat ventral prostate which could, in vitro, inhibit the association of an androgen-receptor complex with nuclear chromatin (Liao, et al 1981). This protein is a major secretory protein in the prostate, which can be used as an excellent specific marker for rat prostate with possible applications, ultimately, to the human. Progress has been reported in the use of established in vitro human prostatic adenocarcinoma cells as a new model in nude mice for studies on etiology, biology, detection and therapy of human prostatic neoplasia (Horoszewicz, et al 1982). This is clearly a valuable model which closely resembles human prostate cancer.

Detection/Diagnosis

During the current year, there has been further characterization of established markers for human prostate (Anderson, et al 1981; Bolton, et al 1981; Catalona, Menon 1981). Moreover, significant results have been obtained from the following areas of investigation on the human prostate-specific antigen (PA): biochemical characterization of PA, identification of PA isoantigens, clinical evaluation of PA (alone and in combination with prostatic acid phosphatase, PAP), generation of hybridoma-derived monoclonal antibodies to PA and in vivo radioimmunodetection of prostate carcinoma xenograft with the use of PA xenoantibodies (Nadji, et al 1981; Papsidero, et al 1981). Serologic evaluation of PA has revealed that pretreatment level of PA is of prognostic value in regards to patients' survival (Kuriyama, et al 1981). Serial PA levels also are of value in early detection of disease recurrence and monitoring of treatment response (Nadji, et al 1981). Simultaneous determination of PA and PAP has demonstrated an additive clinical value of PA and PAP in various stages of prostate cancer.

The need for non-invasive means of diagnosing prostate cancer has resulted in specific applications of bone scans for prostatic cancer response criteria (Pollen, et al 1981). Another study on prostatic fluid subjected to analysis for a variety of substances was undertaken in an effort to identify changes that would differentiate individuals with a high risk of carcinoma of the prostate from patients with benign prostatic hyperplasia, inflammatory disease of the prostate, and normal males (Grayhack, Lee 1981). Among the compounds studied the lactic dehydrogenase (LDH) isoenzymes, the C_3 component of complement, and transferrin had demonstrated alterations in concentration in patients with carcinoma.

Each year studies of steroid hormone receptors in human prostate specimens bring this technology closer to actually being of value in predicting which cancers will respond to hormonal therapy (MacLaughlin, et al 1981; Mobbs, et al 1981; Pertschuk, et al 1982). Reliable and specific assays have been developed for the characterization and quantitation of androgen receptors in the cytosol and

soluble KCl extracts of nuclei prepared from human prostatic tissue (Trachenberg, et al 1982). The measurement of nuclear resistant receptors may improve, as suggested by some clinical studies, the usefulness of receptor levels to predict the hormonal responsiveness of prostatic cancer (Trachenberg, Walsh 1982). Moreover, it was recently reported that estrogen receptors, when detected in prostate cancer specimens, may play a significant role in identifying a subset of hormonally sensitive tumors with a specific histologic tumor grade (Pontes, et al 1982).

Other studies for markers for prostate cancer have suggested that tissue levels of dihydrotestosterone in Stage D_2 prostate cancer patients may be useful for predicting the clinical response of prostate cancer to anti-androgen therapy (Geller, et al 1981; Geller, et al 1981). Additional support for this conclusion must await further follow-up of additional patients entered into the study with dihydrotestosterone levels less than 2.0 ng/gm.

Treatment

The Cooperative Clinical Trials Program of the NPCP have established that favorable responses and acceptable degrees of toxicity can be obtained with cytotoxic treatment and that chemotherapy can be recommended as a legitimate option for patients with endocrine-resistant prostatic carcinoma (Murphy, et al 1982). Presently, while there is a continued effort to evaluate single agent drug therapy, additional studies are in progress to evaluate combinations of agents that have proved effective. Also, adjuvant chemotherapy protocols for earlier stages of cancer and adjuvant therapy to surgery or irradiation have been added to the studies. Ten studies have been completed in terms of patient accrual but surviving patients are still being followed and evaluated. The results to date warrant the following conclusions (Loening, et al 1982; Loening, et al 1982; Murphy, et al 1982; Soloway, et al 1982; Soloway, et al 1982): 1) On the basis of both objective and subjective criteria, chemotherapy has demonstrated advantage over conventional therapy in hormonally resistant advanced Stage D disease; 2) Patients who respond to chemotherapy survive significantly longer than non-responders; 3) In patients with advanced disease, objective partial regressions were only observed in those treated with chemotherapy; 4) Active single agents with acceptable and manageable side effects are Cytoxan, 5-FU, Estracyt, DTIC, Methotrexate, cis-Platinum and Streptozotocin. Minimal activity and excessive side effects were observed for Hydroxyurea, MethylCCNU and Procarbazine. Vincristine and Leo 1031 alone exhibited minimal activity and in combination with Estracyt did not improve response or survival over either agents alone. The combination of cis-Platinum and Estracyt was superior to either agent used alone; 5) In patients with previously untreated advanced disease there is evidence that adding chemotherapy to hormones for the initial treatment is advantageous, particularly for patients with symptoms of pain.

The NPCP is currently conducting chemotherapy trials for several types of disease, including 1) Advanced disease (Stage D_2) that is refractory to hormones (at least orchiectomy) and has not been treated with radiotherapy (<2000 rads to pelvis) or chemotherapy; 2) Advanced disease (Stage D_2) that is refractory to hormones (at least orchiectomy) and has been treated with radiotherapy (<2000 rads to pelvis) or chemotherapy; 3) Newly diagnosed and untreated advanced disease (Stage D_2); 4) Advanced disease (Stage D_2) that is stable to orchiectomy or estrogenic hormone treatment; 5) Non-metastatic disease, Stage B_2-D_1 treated definitively with a prostatectomy plus pelvic lymph node resection followed by adjuvant chemotherapy; 6) Non-metastatic disease, Stages B_2-D_1 treated definitively with external or internal radiotherapy plus pelvic lymph node resection followed by adjuvant

chemotherapy; 7) Patients with Stage A_2 disease with negative lymph nodes will receive definitive surgery or external radiotherapy. In addition to these, two protocols have been recently activated to 1) survey patients with Stage A_1 prostate carcinoma and to 2) conduct a comparison of definitive therapies, surgery versus external irradiation, for Stage A_2 prostate adenocarcinoma. Over 2100 patients have now been admitted to these protocols.

Studies related to treatment of prostate cancer have involved the synthesis and testing of various agents with potential activity against prostate cancer (Batzold 1981; Petrow, et al 1981; Sandberg 1981). A study of androgen sensitive tumors in the Noble rat confirmed previous laboratory data by revealing that chemotherapy plus castration decreased both tumor volume and number of metastases more than in the castrated only groups (Drago, et al 1981).

Emphasis and Projections

The NPCP continues to investigate and implement programs and strategies for experimental and clinical research which, based on the evaluation and analysis of current knowledge and information, will offer the best opportunities for immediate and visible success at all levels of endeavor. In the Etiology/Prevention area, studies will focus on experimental biology and epidemiology of prostate cancer. Many of these studies will utilize animal tumor models and human prostate specimens provided by the NPCP. Particular emphasis will be placed on both nutritional and chemopreventive aspects of prostate cancer. Areas of priority are: identification of risk factors and prevention approaches in populations with differing risks of prostatic cancer; environment and occupational factors which affect the development of prostatic cancer; development and aging of the prostate: role in prostatic cancer; role of cellular and intrinsic factors in prostatic carcinogenesis; analysis of prostatic fluid for determination of acinar cell milieu and the detection of carcinogens, biological markers and promoters of prostate cancer; trace metals in prostatic cancer; cytogenetic factors in prostate cancer; further characterization of hormone receptors, steroid levels and enzyme profiles in normal, BPH and cancerous prostatic tissue; endocrine alteration associated with the development of prostatic cancer; role of peptide hormones in growth regulation of normal and malignant prostatic epithelium; growth and maintenance of normal, benign and malignant human prostatic epithelium *in vitro*; genetic regulation and expression in prostatic cancer; the progression of prostatic cancer and the development of metastasis; prostatic binding systems for substances other than hormones (polyamines, prostaglandins, drugs); the availability of animal models for the study of prevention, initiation and modulation of prostate cancer; the surface of normal and malignant prostatic cells; subcellular alterations in prostate carcinoma; and interaction between stroma and epithelium of the normal and neoplastic prostate gland.

In the Detection/Diagnosis area, studies dealing with earlier detection and more accurate diagnosis of the stage (clinical and pathological) of prostate cancer, and the response to therapy are being emphasized. Many of these studies will involve new techniques that have evolved from basic advances in tumor immunology. In addition, research aimed at improving the precision of predicting the biological potential of both newly diagnosed tumors and those undergoing therapy will be implemented. Priority areas for the upcoming year are: biochemical and other markers for detection of patients with prostatic cancer; evaluation of non-invasive imaging techniques for the detection of prostatic cancer; development of radioisotope agents for detection and staging of metastatic prostate cancer; morphologic

definition of lesions associated with and precursor to the development and progression of adenocarcinoma of the prostate; evaluation of the use of histochemical techniques for the localization of receptors and other binding proteins in the prostate gland; comparison of new analytical methods of prostate cancer detection; cytogenetics of prostate cancer; human hybridoma to prostatic carcinoma; and kinetics of prostatic carcinoma.

In the Treatment area, the NPCP has defined among its objectives 1) the evaluation and improvement of additional therapy modalities on prostatic cancer by testing and selection of new agents and procedures, and the determination of their therapeutic effectiveness, and 2) the development of combination therapeutic modalities where appropriate, based upon new information, and the evaluation of their usefulness in clinical disease states involving local, regional, and metastatic disease. Emphasis continues to be placed on: evaluation and comparison of therapeutic modalities for prostatic cancer; clinical demonstration studies of newer treatment approaches in nodes positive and/or high grade histopathology (Gleason staging 7, 8, 9, & 10) prostate cancer; evaluation of nutritional status and nutritional intervention in advanced prostatic cancer; the development and evaluation of new concepts to control prostatic growth; studies on the development of resistance and tumor cell heterogeneity in prostatic cancer; and biology of invasiveness and metastatic spread in prostate cancer. Increasing both survival time and time to development of progressive disease, as well as obtaining objective and subjective responses in prostatic cancer, are major goals.

Other Program Activities

Periodically, the NPCP identifies topics of growing investigational activity and importance in prostatic cancer. In response, authorities are called on to review the pertinent subjects and to provide direction for future programmatic implementation and impact. On March 8-9, 1982, at Roswell Park Memorial Institute, over 30 investigators participated in an assessment of the current status of the histopathology of prostate cancer. Recently, the NPCP sponsored part of the faculty for the subject oriented seminar of the American Urological Association entitled "Clinical Status of Prostatic Carcinoma", held in Washington, D.C. on April 1-3, 1982.

The NPCP has continued to inform the scientific community of its activities by means of a quarterly Prostatic Cancer Newsletter that describes the Project's activities and publishes brief summaries of continuing research progress by investigators receiving support through this Project. Over 8,700 copies of five issues of the newsletter have been distributed nationally and abroad during the year to a readership of over 2,500 individuals. The NPCP Reprint File has been enlarged to over 5,000 reprints of articles on and related to the prostate, and is catalogued on the computer of the Central Statistical Office. Over 600 of the articles are by investigators supported through the NPCP. The Reprint File has been, and is proving to be a valuable resource for investigators and Working Cadre members.

Through programs supported by the NPCP, investigators are supplied with sera from prostate cancer patients, human prostate tissues and cultures, and R3327 tumor bearing rats. These have proven to be highly valuable resources for research projects which might not otherwise have been implemented had they not existed. These programs characterize the unique capability of the NPCP to both support and respond to investigators conducting research on prostate cancer.

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Objectives

The Cancer Construction Program's objectives are to support the National Cancer Program by assisting the extramural research effort in the following ways:

a. support new facilities to house cancer research activities including basic, applied, and clinical research;

b. upgrade existing research laboratories;

c. upgrade existing animal research facilities to comply with current DHHS criteria for animal care and employee safety;

d. upgrade clinical areas for applied cancer research;

e. provide biohazard containment units;

f. provide advice concerning biohazard safety and facility modifications to cancer researchers; and

g. provide advice to other NIH institutes concerning their research facility improvement programs.

Accomplishments

The NCI Construction Program continues to accomplish its stated goals. In the years since 1972 much has been accomplished; however, recent budget priorities have reduced the Construction Program to a smaller segment of the NCI's overall budget. The program provides grant support which requires that the grantee institution match the NCI-funding with an equal amount of non-Federal funding.

In FY 82, seven construction applications were received by NCI; they requested a total NCI-funding of $5,644,000. After a thorough evaluation by the peer review system, seven applications were recommended for approval and four were recommended with strong enthusiasm; total recommended NCI funding = $2,006,000. The available NCI Construction Program's funding of $1,225,000 was awarded to four of these institutions for renovation type projects involving the upgrading of existing cancer research laboratories.

CONSTRUCTION PROGRAM'S ACHIEVEMENT RECORD (1972-1982)

Goal	Achievements (No. of Projects) 1972-1981	1982
a. Build new cancer research buildings	44	0
b. Upgrade existing laboratories	20	4
c. Upgrade existing animal facilities	9	0
d. Upgrade clinical research facilities	8	0
e. Provide biohazard containment units	19	0
f. Provide technical advice to NCI	continuing	continuing
g. Provide technical advice to NIH	continuing	continuing

Projections

The earlier emphasis on the construction of cancer research buildings has changed to the renovation and upgrading of existing laboratories and animal facilities. The currently available annual funding of $1,250,000 has been awarded to renovation projects which are clearly justified on the basis of high quality scientific research, cancer relevance, and need for facility improvements.

Funding by Program Activities

In FY 82, four construction grants were awarded. Each of these grants was for the renovation of existing cancer research laboratories to upgrade the effectiveness of their research efforts and to improve the safety of the laboratory.

A summary of each of the FY 82 grants is given below:

1. University of Washington (1 C06 CA32596-01)
The University of Washington was awarded $220,000 in partial support of minor renovations to existing space in the Department of Biological Structure. The NCI funding was matched by $220,000 in University of Washington funding. The remodeled space accomodated the expansion of the cell differentiation and cellular immunohematology programs which were focused on the role of bone marrow derived cells in tumor resistance. A pathogen-free animal facility was included in the renovation project.

2. University of North Carolina (1 C06 CA32623-01)
The University of North Carolina School of Medicine was awarded $219,010 in partial support of the completion of research laboratories in their new Lineberger Cancer Research Building. The NCI funding was matched by $219,010 by the University of North Carolina.

The remodeled space was for the Virology and Cancer Cell Biology programs. The virology program had strong emphasis on molecular biology, human cytomegalovirus, and DNA-protein complexes. The cancer cell biology program is focused on the regulation of the mammalian cell cycle and tumorogenic retroviruses.

3. Albert Einstein School of Medicine (1 C06 CA32573-01)
Albert Einstein College of Medicine was awarded $639,785 in partial support of major renovations to the Leo Forchheimer Medical Science Building. The NCI-funding was matched by $639,785 in Albert Einstein College of Medicine funding.

The cancer research performed in the renovated spaces included the following areas: carcinogenic and chemotherapeutic agents; immunology; nucleic acid synthesis and viral oncology; membrane synthesis, structure, and function; gene expression in malignant cells; cell structure, function and regulation.

4. Boston University (1 C06 CA32573-01)
The Hubert H. Humphrey Cancer Research Center was awarded $146,205 in partial support of renovations. The NCI-funding was matched by $359,020 in Boston University funding.

The cancer research performed in the renovated spaces included the following research areas: DNA replication and control; biology of the tumor cell; and tumor immunology.

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IV.

EDUCATION PROGRAM

CANCER COMMUNICATIONS NETWORK

The Cancer Communications Network (CCN) was established in 1976 for the purpose of assuring that accurate, up-to-date information on cancer cause, prevention, early detection, diagnosis, treatment, rehabilitation and continuing care is readily available and accessible to the public and health professionals. The CCN contracts were recently recompeted for an additional three years of funding and currently consist of 18 regional offices funded by NCI (Nos. 95471, 25566, 25567, 25568, 25569, 25570, 25571, 25572, 25573, 25574, 25575, 25576, 25577, 25578, 25579, 25580, 25581, and 25582). Three additional offices receive no funds from NCI but actively participate in the information exchange that occurs throughout the network.

Each network office is responsible for:

1. Establishing a Communications Office to plan, administer, promote, develop support materials for, and evaluate activities undertaken by the contract staff;

2. Developing and maintaining a resource directory of agencies and services available to cancer patients and their families within the defined service area of the center;

3. Establishing and operating a toll-free telephone service (The Cancer Information Service or CIS) for immediate access to answers on cancer-related questions from the public; and

4. Identifying, developing, implementing and evaluating a limited number of special projects to meet specific cancer information/education needs within the service area.

While the basic conceptual nature of the CCN program has not changed as a result of the recent procurement, some differences are evident in the new contracts. The new workscope represents program requirements in a more detailed fashion, provides for standardization among network offices in several areas, increases the NCI management role, and stresses the importance of quality control and evaluation. In addition, Special Project requirements have become more targeted, thus reducing to forty-four the number of Special Projects in which the network is involved.

Work continued on the national evaluation of the Cancer Information Service portion of the networks' operations. The quality assessment program has undergone pretesting, and the standardized call record form will be pretested soon.

The National Publicity and Promotion Task Force continued to advise NCI on promotional materials developed for the network. Revisions on the National Plan for Publicity and Promotion of the Cancer Information Service were completed. That document is now used as background and guidance for the network and for NCI. The task force is currently undertaking the development of a marketing plan for the Cancer Information Service, which will be completed in the next fiscal year. Two public service announcements (PSA's) were developed for the network by NCI, one of these in conjunction with the Decade of Discovery program. This PSA was co-sponsored by the Candlelighter's Foundation, Inc. It is currently a finalist

in a national competition for public service announcements. Other PSA's produced by various CIS offices, were replicated by NCI for use by the entire network.

The Staff and Volunteer Training Task Force has been established to develop a uniform staff and volunteer training program for use by the network. This task force will review all training programs currently in operation and use this information, coupled with new information, to develop a standard program.

At the end of this fiscal year, over 800,000 callers have been served by the Cancer Information Service since its inception. The CIS currently averages 11,500 calls each month, with over 135,000 total calls. Examples of Special Projects currently underway throughout the network include a series of leaders forums, Seniors Team Up Against Cancer health education project, A PAP smear education program for high risk women, cancer risk self-assessments, a cancer program for older citizens, cancer education programs targeted towards the Black and Hispanic community, an information dissemination campaign for rural audiences, and many newsletters, radio programs, and mass media campaigns providing cancer information and education to various target audiences. In addition, a Psychosocial Cancer Counseling Line (PCCL) has been developed by one office to meet the psychological and emotional needs of cancer patients and their families.

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RESEARCH MANPOWER BRANCH

Overview

Objectives

The primary function and objective of the Research Manpower Branch is to provide, plan, organize and support a concentrated effort for quality research training and development for fellows and trainees ranging from the predoctoral level to the nearly-established investigator. Experience can be gained in applied and/or basic science areas. The branch also manages the cancer clinical education program which provides continuing education for health professionals and cancer curriculum improvement for medical students and others.

Accomplishments

In fiscal year 1980 under the Institutional Training Grants (T32) 518 predoctorals 707 postdoctorals (including 180 M.D.s) received training. The Individual Postdoctoral Fellowship Program supported 216 postdoctorals including 22 M.D.s. In addition, two short courses were held on the Pathobiology of Cancer, one in Keystone, Colorado the other in Lake Placid, New York. Research trainees and fellows lacking previous training in the actual disease mechanisms of cancer actively participated in these courses. In the case of the Cancer Clinical Education Program, 91 institutions received awards, including schools of medicine, dentistry and public health and specialized cancer institutions.

Program Projections

In 1982-83 the Research Manpower Branch proposes to do the following things: a) continue the development of the nutrition training grant effort which was begun in 1982; b) rethink the objectives of the Cancer Clinical Education Program; c) plan a new award of the Career (K) series designed to stimulate recruitment of more physicians into research, especially surgical oncologists; d) stimulate additional training applications in prevention and epidemiology.

Funding by Program Activities in FY 1982

Program	Number of Grants	Amount (millions)
National Research Service Awards		
Institutional	168	$19.2
Individual	165	2.9
Research Career Development Awards	106	4.1
Research Career Award Program	5	.16
Clinical Cancer Education Program	74	5.1
Contracts - Preventive Education	13	1.4
Veterinary Pathology Program	2	.29

Examples of Research Accomplishments by NRSA Trainees, Fellows and Research Career Development Awardees

At Yale University postdoctoral trainee Alexander Waldrop, has applied for a patent for "Modified Nucleotides and Method of Preparing and Using Same." This invention is expected to be of immense value in diagnosing infectious and genetic disorders. It will also be an invaluable research tool in nucleic acid sequencing and gene isolation procedures.

Dr. William Pearson at Johns Hopkins has shown that butylhydroxyanisole potentially increases the production of glutathione S-transferase (GST) in mouse liver 25 fold. GSTs are drug-detoxifying enzymes which protects animals against chemical carcinogens.

Dr. James Griffin working at the Sidney Farber Cancer Institute is defining the cell surface antigens of normal and malignant myeloid cells. He has developed a panel of monoclonal antibodies which recognize differentiation-linked markers of human myeloid cells. These are being used to define subsets of human acute nonlymphocytic leukemias. It is hoped that these efforts eventually will lead to clinical correlations such as those which already have been so useful in understanding acute lymphocytic leukemia.

S. Schwarzbaum is developing techniques for natural killer cell (NK) purification so that their characteristics may be studied. NK cells in humans are mononuclear cells which occur in peripheral blood and which are cytotoxic for certain tumor cells. Because NK cells comprise less than one percent of the total peripheral blood mononuclear cells, their study has been inhibited. Differential density gradient centrifugation techniques have been used to concentrate NK cells. Hybridoma techniques have been used to secure monoclonal antibodies which appear to be NK specific determinants. These antibodies are being used to further purify NK effector cells so that their structure and activity may be better defined. This work is being conducted at Albert Einstein College of Medicine.

Dr. Samuel Ahn is studying the first trial of immunization of human beings specifically directed against a characterized tumor-associated antigen. Oncolofetal antigen (OFA) is present in 80 percent of melanoma biopsy specimens. IgM antibodies directed against OFA produce in vitro lysis of melanoma cells in the presence of complement. After preliminary studies showed that patients who developed a strongly elevated IgM anti-OFA titer after immunization had a lengthy disease-free interval, studies were begun in Stage III melanoma patients. Because OFA is present in several other neoplasms, a successful vaccine would have potential use in those cancers also. These studies are being conducted at the University of California in Los Angeles.

At the M.D. Anderson Hospital and Tumor Institute, Dr. John Knapp has been studying the utility of cis-diamine-dichloroplatinum II (CDP) in malignant solid tumors. In a pilot study, four previously treated pediatric patients with unresected primary tumors were studied. CDP was administered intra-arterially via the major artery feeding the primary tumor. Treatment was administered at intervals of about two weeks for two to four courses. The primary tumor in all four patients responded clinically with more than 70 percent tumor destruction in two patients and less than 40 percent in the remaining two. Pulmonary

metastases were nonresponsive. A more definitive study has begun. Where tumor destruction is more than 60 percent, the concentration of CDP in the tumor is 17-40 micrograms/gram dry weight. With destruction of less than 60 percent, CDP measures 12 micrograms or less.

Activities by Program Areas

The Research Manpower Branch is responsible for the following programs: National Research Service Awards; (including research training grants and research fellowships) Research Career Development Awards; Clinical Cancer Education Grants and Contracts; and Short-Term Training.

NRSA-Research Training Grants

These institutional grants provide universities an opportunity to develop or enhance research training at the predoctoral and/or postdoctoral level. The applicant must have the staff and facilities for the proposed program. After the award is made, the institution's training program director has the responsibility for selection and evaluation of trainees. The administration of the institutional training grant is handled by the program director at the institution. Predoctoral students may receive up to eight years of support (five years as a predoctoral and three years as a postdoctoral) under the National Research Service Act (NRSA). The stipend for predoctorals is $5,040. Postdoctoral stipends depend on experience and range from $13,380 to $18,760. Postdoctoral candidates are limited to a maximum of three years of support under NRSA.

	Number of Grants	Trainees Pre	Trainees Post
Cancer Biology	17	36	87
Etiology & Prevention	94	459	456
Detection & Diagnosis	26	54	80
Treatment & Restorative Care	31	6	148
TOTAL	168	555	771

NRSA Research Fellowships and Other Individual Awards

The Individual Postdoctoral Fellowship Program provides the opportunity for those who have attained the research doctorate or a professional degree to broaden their scientific background. Applications are received in the same disciplines as the Institutional Training Grants. The postdoctoral fellow

receives the same stipend level as a postdoctoral trainee. An applicant for a postdoctoral fellowship must establish his acceptance by a preceptor and must present a detailed description of the research project which he will undertake as part of his research training. The individual fellow is limited to three years of support. A senior postdoctoral fellowship is available to faculty members and others having more than seven years postdoctoral experience.

	Number Awarded
Cancer Etiology & Prevention	129
Cancer Detection & Diagnosis	4
Cancer Treatment & Restorative Care	73
TOTAL	206

Research Career Development Awards

The purpose of the Research Career Development Awards is to provide very promising young investigators the opportunity to devote full-time to their development as independent cancer investigators. Applicants must demonstrate appropriate scientific experience and achievement and must have outstanding research potential. Each candidate must be nominated by his/her sponsoring institution. The salary support is set individually with a maximum of $30,000 each year.

	Number Awarded
Cancer Etiology and Prevention	88
Cancer Detection and Diagnosis	5
Cancer Treatment and Restorative Care	13
TOTAL	106

Research Career Awards

This program provides an annual salary of $25,000 to selected cancer investigators for the duration of their research careers. No new awards have been made since 1964. NCI presently makes five such awards annually.

Clinical Cancer Education Program

In 1974 the Clinical Cancer Education Program was initiated under the present guidelines. The purpose of the grants are: (a) to encourage planning and development of educational programs aimed at the ultimate achievement of optimal care of the cancer patient; (b) to enable students in the health professions to acquire basic knowledge of neoplastic disease and of preventive measures, and diagnostic and therapeutic skills and experience in optimal care; (c) to stimulate and expand efforts in cancer education and teaching which will be relevant to changing needs in medical education. Applicants are from medical schools, dental schools, schools of osteopathy, specialized cancer institutions, principal

affiliated hospitals of medical schools and schools of public health. Usually, there is only one award per institution for this program. The object of this support is to provide new curricula for the teaching of students, house officers, nurses, etc. Continuing education in oncology for practicing physicians is also an important part of the program.

There are presently 74 active clinical education grants. In addition to the 74 grants, a contract with the American Association for Cancer Education was completed. The purpose of that project was to develop a methodology for the systematic evaluation of the effectiveness of Clinical Cancer Education Grants. The recommendations are: (a) the development of program goals and cancer educational objectives for physicians and dentists in training (b) the development of new data forms for recording the activities supported by the grants; (c) proposal of two alternative systems of data storage and retrieval to handle information and document the achievements of the clinical cancer education program.

Cancer Prevention Education

Thirteen contracts were awarded in 1979 for the development of courses in cancer prevention. The major objective of twelve of them was to develop and evaluate course(s) in cancer prevention within three years. This objective was accomplished by several means such as: development of audio-visual aids, course modules, case presentations, supplemental reading lists, self-instructional materials, examinations, guidelines for instructors. A thirteenth contract involved fostering cancer prevention and detection through public education and school health education.

The final products of the contracts are presently being reviewed by consultants and NCI staff. After the evaluation is complete, the material will be made available to interested institutions/universities by the contractors and the NCI.

Categorization of the thirteen contracts are as follows:

Occupational Health, Smoking, Breast Self-Exam.	1
Education for Medical Students	4
Education for Medical Students & Residents	3
Nurse Practitioner	1
Nurse Practitioner & Physician Assistants	1
Physician Assistants	3
Total	13

Short-Term Research Training

Short-Term Research Training is of two kinds. The first kind, a program for Students in Health Professional Schools (T35), was designed to ameliorate the shortage of clinical investigators by attracting highly qualified medical students into biomedical and behavioral careers. Funding was made to the University of Chicago in July 1980 for five years. The award was made to support 26 medical students each year for three months. The second kind consisted of targeted short courses up to one week in duration which are offered

to all National Cancer Institute research trainees. These courses include a) Epidemiology, b) Histopathobiology of Neoplasia, c) Culture of Macrophages and Human Monocytes.

Veterinary Pathology Training Program

This program was initiated in 1980. The purpose is to increase the production of board-certified veterinary pathologists, and otherwise to increase the national pool of comparative pathologists. The National Cancer Institute in conjunction with the National Institute of Environmental Health Sciences supports five grants. Two of these are funded by NCI. This program will expire at the end of the present project period.

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☆U.S. GOVERNMENT PRINTING OFFICE: 1982-361-132:663