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## Senate Passes NIH Reauthorization 87-10; $2.5 Bil. Authority For NCI, New Line Items

The Senate last week passed a bill authorizing $2.5 billion in funding for NCI in fiscal 1993, including $100 million targeted to prostate cancer research, $350 million for breast cancer research, and $30 million for the establishment of cancer registries in every state. The funding authorization for NCI was included in the NIH Reauthorization Act of 1992, which provided the authority for appropriations for the institutes

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*In Brief*

## William McGuire, Breast Cancer Researcher, Dead Of Heart Attack; Attracted Large Group To Texas

**WILLIAM McGUIRE,** of Univ. of Texas Health Science Center at San Antonio and one of the world's foremost breast cancer researchers, died March 25 of an apparent heart attack while scuba diving in Cozumel, Mexico. He was 54. McGuire's research on prognostic factors in recurrent breast cancer earned him national and international stature. The large research group he attracted to San Antonio identified and confirmed a number of these variables, including estrogen and progesterone receptors. He was also known for his bank of 7,000 frozen breast tumors collected over the past 20 years. "He was a remarkable individual, a unique curmudgeon who cared deeply about science," said Helene Smith, director of the Geraldine Bush Cancer Research Institute, speaking at the American Cancer Society's Science Writers' Seminar last week in St. Petersburg, FL, where McGuire was scheduled to discuss his research. Gary Clark, one of McGuire's co-authors, came to the meeting in his place. McGuire spent two years as a clinical associate at NCI before going to San Antonio in 1969. In 1975, he became chief of the oncology division. With Charles Coltman, McGuire coordinated the annual San Antonio Breast Cancer Symposium. He also founded and edited the journal "Breast Cancer Research and Treatment." Survivors include two sons, Bill and Sean. . . . **TOBACCO PRODUCT** sales and distribution would be regulated under the Food, Drug & Cosmetic Act in legislation proposed by Sen. Jeff Bingaman (D-NM). The bill, S.2298, would require manufacturers to provide a complete list of additives to HHS. If HHS determines the additives are unsafe, the product could be removed. . . **REP. CARL PURSELL** (R-MI), ranking minority member of the House Labor, HHS, Education Appropriations Subcommittee, announced he will not seek reelection in November. . . **GREGORIO DELGADO** was named chairman of obstetrics and gynecology at Loyola Univ. Stritch School of Medicine. He was chief of gyncologic oncology at Georgetown Univ.

## Senate Authorizes $2.5 Bil. For NCI, Targets Prostate, Breast Ca. Research

(Continued from page 1)

through 1997. The House passed its version of NIH reauthorization last year.

The act, passed on a vote of 87-10, also lifted the four-year federal ban on fetal tissue research, allowing the government to resume funding for medical research that uses tissue from aborted fetuses.

NIH reauthorization has been stalled for about two years due to the controversy over fetal tissue research. But in a sudden turnaround, the Senate voted 77-22 to reject an amendment by Sen. Orrin Hatch (R-UT) that would have restricted federally funded research to tissue from spontaneously aborted fetuses. Sixteen antiabortion senators voted in favor of fetal research.

Provisions in the legislation specific to NCI include:

▶Authorization of $2.5 billion in FY 1993 and such sums as necessary for FY 1994-97. Authorizes $156.6 million for cancer prevention and control programs for FY93 and such sums as necessary for FY94-97.

▶An amendment by Sens. Robert Dole (R-KS), Ted Stevens (R-AK), Jesse Helms (R-NC), and Alan Cranston (D-CA)--all of whom have been diagnosed with prostate cancer--creates a specific line item in NCI's budget for prostate cancer research. The amendment authorizes an increase in NCI's prostate cancer funding from $28 million to $100 million, and $20 million in new prostate cancer funds to the Centers for Disease Control. The funds enable CDC to implement grants (awarded through peer review) to states for prostate cancer screening, referrals, and education, similar to the program on breast cancer screening begun last year.

▶A provision establishes a research program on breast cancer and cancers of the reproductive system of women, and authorizes $155 million for FY93 and such sums as necessary for FY94-97 for the program. The authority for the new program is in addition to the existing authority for breast cancer research, for which NCI expects to spend $196 million this year. Thus, the Institute has the authority to spend more than $350 million on breast cancer and reproductive system cancers.

▶An amendment by Sen. Patrick Leahy (D-VT) authorizes $30 million for funding cancer registries in every state. States would provide matching funds, and the grants would be awarded through the NIH peer review system. The amendment provides that the new registries shall not supplant, replace or diminish NCI's existing SEER program or transfer its responsibility from NCI.

▶Directs NCI to conduct a study to determine the factors contributing to the elevated breast cancer mortality rates reported in Connecticut, Delaware, Maryland, Massachusetts, New Hampshire, New Jersey, New York, Rhode Island, Vermont, and the District of Columbia. The bill requires that the study begin no later than FY94 and data collection may continue through FY98. Findings are to be submitted to Congress by Sept. 30, 1999. NCI is directed to spend at least $1 million per year for each year of the study.

**Cancer program advocates** said they were pleased with the legislation, the amendments, and the level of authorized funding, even though the total amount authorized for NCI is $200 million less than NCI's bypass budget (professional needs budget).

"These are great programs to have authorized, but the challenge now is to get the appropriation," said Marguerite Donoghue, vice president for research and regulatory affairs of Capitol Associates, which works on behalf of the National Coalition for Cancer Research.

Since at least 1984, the Senate NIH reauthorization bills have authorized amounts for NCI that are lower than the bypass request, Donoghue noted.

It is doubtful that NCI could fully implement the prostate cancer, breast cancer, or cancer registries initiatives under the President's proposed budget of $2.01 billion for FY93, without major redistribution of funds.

The powerful chairman of the House Labor-HHS-Education Appropriations Subcommittee, Rep. William Natcher (D-KY), always has opposed "earmarking," or targeting specific amounts of money to certain research areas; he could block appropriations to the prostate and breast line items.

**THE CANCER LETTER**

*Editor:* **Kirsten Boyd Goldberg**
Founder & Contributing Editor:
**Jerry D. Boyd**

*Editorial/Subscriptions Office*
**PO Box 15189, Washington, DC 20003**
**Tel: (202) 543-7665 Fax: (202) 543-6879**

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### Revitalizing Intramural Research

For NIH overall, the bill authorizes $6 billion for FY93 and such sums as necessary in FY94-97, including $25 million for the NIH director's discretionary fund. Included in the legislation is a new section on "Revitalization of Intramural Research Program," which provides:

--a requirement for NIH to conduct a study of the retention, recruitment, vacancy and turnover rates of support staff;

--encourages the NIH director to study the replacement or renovation of the NIH Clinical Center;

--allows the HHS secretary to transfer to NIH 26 acres of federal land presently owned by the Navy for construction of a new research hospital;

--allows NIH to establish a comprehensive program for replacement and repair of buildings on the Bethesda campus;

--allows NIH to buy 300 acres of land for establishment of a satellite campus in Maryland for enhancing intramural research;

--allows NIH to establish a day care program for use by employees and research subjects.

Another provision raises the limit on the number of NIH employees who may be designated members of the Senior Biomedical Research Service, which provides pay raises to senior scientists.

The bill also authorizes $415 million for the National Research Service Awards in FY93 and such sums as necessary for FY94-97. Funding for NRSAs has remained flat for the past two years because the program had not been reauthorized.

### AIDS Research

For AIDS research, the bill reauthorizes the program to repay the educational loans of health professionals who agree to conduct AIDS research at NIH and authorizes $3 million to expand that program to include research in other areas of need.

The bill also:

--expands the authority of the AIDS Advisory Committee of the National Institute of Allergy & Infectious Diseases to make recommendations on research on opportunistic infections and cancers;

--directs NIH's clinical evaluation units to conduct trials of treatments for opportunistic infections and cancers;

--requires the NIH director to develop and implement a comprehensive plan for AIDS activities and their evaluation;

--requires NIH to conduct three studies on AIDS drug development and approval, and reimbursement for care provided in clinical trials.

## ACS President Lawrence Emphasizes Cancer Prevention Gains Since 1971

Over the past 20 years since the signing of the National Cancer Act, the largest gains in the "war on cancer" have been in cancer prevention, American Cancer Society President Walter Lawrence told a meeting of science writers last week.

While tremendous gains have been made in treatment of childhood leukemia, other childhood cancers, testicular cancers, and breast cancer, there has been modest progress in treatment results for all sites of cancer, Lawrence said. "Clearly, we are far from being able to declare victory in this campaign. My own view is that our biggest gain in this arena is our increased appreciation of, and focus on, cancer prevention strategies," Lawrence said.

His remarks were made at the ACS Science Writers' Seminar in St. Petersburg, FL, last week. Lawrence later told **The Cancer Letter** that he intends to increase attention on cancer prevention and control this year. Lawrence, emeritus director of the Massey Cancer Center at the Medical College of Virginia, also is a member of the National Cancer Advisory Board.

ACS supports an increasing amount of prevention research, including new clinical trials of diet and chemoprevention.

"Basic research in the area of causation, particularly the identification of various cellular gene alterations, is moving at a rapid pace," Lawrence said. "This knowledge will aid us in developing prevention strategies in the future and will also very soon allow identification of high risk subpopulations among us" who would be candidates for aggressive screening and early detection methods, or involvement in chemoprevention clinical trials.

### Increasing Breast Cancer Incidence

Offsetting gains in early diagnosis of breast cancer is the increasing incidence of the disease, Lawrence said.

"The report we made to the nation in early 1991--that the lifetime risk of breast cancer for women had increased to one in nine--was not meant to be a scare tactic, but a means of pointing out the urgency of early detection of breast cancer," Lawrence said, referring to a recent article in "The New York Times" critical of the Society's report.

"These figures are certainly accurate when one considers a life expectancy of 85 years and that the major escalation of this risk occurs in the older citizen age range," Lawrence said.

"Although we have incomplete information on the cause of this increasing risk, the increasing mean age

of our population must be considered a major factor. It is our view that awareness of this one in nine estimate by women is important rather than frightening. It helps us break down barriers that prevent women from availing themselves of life-saving mammograms."

On the issue of silicone gel breast implants, ACS has urged continued research on the safety of the devices, but recommended that FDA allow the implants to remain available to women who have had a mastectomy, Lawrence said.

ACS is supporting two major cancer prevention studies. The first, led by Daniel Nixon, ACS vice president for professional education, will test the hypothesis that added wheat fiber in a controlled dietary study will reduce the recurrence rate of colon polyps in patients who have had colon polyps removed. The pilot project, a randomized, controlled, double-blind clinical trial, is being conducted in Virginia.

The treatment agent is a wheat fiber supplement which will allow an intake of 32-35 grams of dietary fiber per day. All study subjects will be encouraged to follow ACS dietary guidelines. Both groups will be followed with colonoscopy for recurrence of polyps, one and three years following the original removal of polyps, or annually if their first follow-up exam reveals new polyps.

The intervention group will receive fiber cereal packets each containing 20 grams of fiber. Controls will get a placebo cereal packet. The pilot phase will take about two years, and if successful, the full implementation phase will begin, and will take about four years.

The second project, also led by Nixon, will study the prevention of breast cancer recurrence through control of dietary fat and weight management. Subjects on adjuvant breast cancer chemotherapy will be randomized to a calorie controlled, low fat diet.

The feasibility study will enroll 180 postmenopausal breast cancer patients in one ACS division, and take about one and a half years. The second phase of the study will involve 1,800 patients and take approximately five years.

"The concepts being examined by these two pilot studies are not really new, but these trials should tell us whether such dietary interventions are both realistic and feasible," Lawrence said.

The ACS projects will use trained volunteers to assist in dietary counseling, data management, and patient follow-up. Cost of both projects is estimated at $400,000 per year with the use of volunteers. Nixon estimated the studies would cost more than $1 million per year without volunteers.

## National Cancer Act History, Cancer Letter Index, Available

A limited number of copies of "The National Cancer Act of 1971: The First 20 Years of the War on Cancer...As Reported By **The Cancer Letter**" still are available for purchase.

This 120-page publication contains year-by-year overviews of the major policy developments and cancer news events since the National Cancer Program was created in 1971. The special issue includes a complete index to articles published in **The Cancer Letter** from 1973 through 1990. In addition, there are introductory notes from Sen. Edward Kennedy, former President Richard Nixon, and former Congressman Paul Rogers.

Copies of the publication are $15 each (U.S. funds only) postage and handling included. Payment may be sent to The Cancer Letter, PO Box 15189, Washington, D.C. 20003.

## RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD. RFP announcements from other agencies will include the complete mailing address at the end of each.

**RFP NCI-CP-61016-02**

Title: Support services for studies of emergent cancer issues

Deadline: Approximately May 6

NCI intends to recompete its master agreements in search of additional qualified offerors capable of providing needed support services on emergent cancer issues. Existing MA holders already in the Emergent Cancer Issues pool need not respond to this solicitation. Offerors scheduled for award of a MA will be eligible to compete for future Master Agreement Orders. Contractors selected for award of a MAO shall provide managerial, data collection, and data processing support for epidemiologic studies to be designed and executed alone or in collaboration with other research organizations.

Specific tasks may include: study planning and liaison activities, data collection forms design, development of data collection manuals, data abstracting and coding, identification, location, and interviewing of study subjects, exposure assessment, quality control activities, and the submission of computerized data and associated reports or deliverables.

Multiple MAOs may be issued each year. MA holder is free to respond to any particular RFP without having any effect on its MA. MAs awarded will be issued for four years.

Contract specialist: Michael Loewe
RCB Executive Plaza South Rm 620
301/496-8611

**RFP NCI-CB-21002-32**

Title: Development of an advanced flow cytometry data system
Deadline: Approximately May 15

NCI is seeking a qualified small business contractor to develop and maintain during development an advanced flow cytometry data system. The system shall consist of customized software, specialized hardware configurations, and specialized operating system configurations necessary to provide comprehensive data transfer, data storage and retrieval, data analysis, and system management capabilities for flow cytometry instrumentation at NCI, including the Becton-Dickinson Immunocytometry Systems, Facstar Plus.

The contractor shall produce a flow cytometry data system which can be operated and maintained by NCI staff in the flow cytometry laboratory who are not professionally trained in computer science. During the development period, the flow cytometry instrumentation and associated computers shall be used for research projects utilizing existing software versions and functional versions of modules of the Advanced Flow Cytometry Data System as they are developed by the contractor. The modules of the AFCDS include: a data transfer module which shall fully and automatically integrate BDIS Facstar Plus data collection software with VAX/VMS systems, a data storage and retrieval module which shall fully integrate storage and retrieval of flow cytometry data with the data transfer module, the data analysis module and the system management modules, and data analysis module, which shall provide software for analyses of histogram and list mode flow cytometry data files, a system management module which shall include user friendly software, compatible with the data transfer, data storage and data analysis modules, and an system analysis module.

Contract specialist: Richard Hartmann
RCB Executive Plaza South Rm 620
301/496-8611

**RFP NIH-ES-92-25**

Title: Oncogene analysis for molecular toxicology studies
Deadline: Approximately May 12

The primary purpose of this project will be to provide laboratory support by the application of assays to screen for and verify mutations in oncogenes, such as ras or p53, in samples of frozen or fixed tissues using a variety of molecular techniques. Specific methods to be in place include polymerase chain reaction (PCR) amplification, oligonucleotide hybridization, restriction fragment length polymorphism (RFLP) analysis, direct sequencing of PCR products, and single stranded conformation polymorphism (SSCP). Specific tasks include, but are not limited to, DNA extraction, amplification of regions of p53 or other genes, screening for mutational activities of ras or other genes or mutational deactivation of tumor suppressor genes, and assay for loss of heterozygosity. All responsible sources may submit a proposal that will be considered. Estimated five-year competitive procurement. Copies of the complete RFP may be obtained from: National Institute of Environmental Health Sciences, Contracts and Procurement Management Branch, Thomas Hardee, Contracting Officer, 79 T.W. Alexander Drive, 4401 Building, PO Box 12874 Research Triangle Park, NC 27709, phone 919-541-7893.

## RFAs Available

**RFA HS-92-03**

Title: **Study of patient outcomes associated with pharmaceutical therapy**
Application Receipt Date: July 15

The purpose of this announcement is to solicit applications from non-profit organizations to conduct research on the outcomes of pharmaceutical therapy. The Agency for Health Care Policy and Research (AHCPR) is encouraging innovative and timely health services research on the effectiveness of pharmaceutical treatment and care.

Applications may be submitted by domestic and foreign non-profit organizations, public and private. The RFA will use the research grant mechanism (R01). The total project period may not exceed five years. AHCPR expects to commit up to $3 million for six to ten competitive awards.

The purpose of this RFA is to encourage studies on the outcomes of pharmaceutical therapy.

This RFA emphasizes the relationship between prescription drugs, related services, and patient outcomes in ambulatory care settings. Of particular importance is the need to increase the availability and use of data and empirical methods in research on the patient outcomes of pharmaceutical therapy.

Three general areas of research are of interest:

- o data and analytic methods;
- o factors affecting the appropriateness of drug prescribing; and
- o the role of the patient.

Described below, the issues and questions raised are illustrative only, and other study topics relevant to this RFA are welcome.

Data and Analytic Methods: There is a critical need for comprehensive, comparative assessment of the appropriateness and effectiveness of alternative pharmaceutical therapies. Researchers should consider using existing data collected for either administrative or research purposes. These sources can be supplemented with primary data collection. Emphasis is to be given to the study of clinical conditions that meet the following criteria:

- o the predominant mode of therapy is pharmaceutical;
- o a large number of patients are affected;
- o the use of health care resources is substantial; and
- o a variety of therapeutic choices exist.

AHCPR encourages studies of the following:

- o What is the feasibility of using and/or developing comprehensive databases to address questions concerning the outcomes of pharmaceutical treatment?
- o Accurate ascertainment of drug exposure is essential. How valid are currently used measures of drug exposure?
- o How can the association between pharmaceutical treatment to achieve surrogate endpoints and patient outcomes be validated?
- o Comparative cost-effectiveness studies that can be used by the industry and research community as models or standards for analysis would be especially useful.
- o What hypotheses on the outcomes of pharmaceutical therapy can be tested using international sources of data?

Factors Affecting the Appropriateness of Drug Prescribing: Previous studies have explored the effects of policy and educational interventions on drug prescribing. Many questions remain about the long-term effects of private and public programs that monitor and intervene in the prescribing process. AHCPR is interested in research on the effects on patient outcomes of programs designed to improve the appropriateness of drug prescribing.

AHCPR encourages studies of the following:

- o Of particular interest to this RFA are questions dealing with the link between drug utilization review (DUR) and patient outcomes in Medicaid or other programs in the ambulatory care setting.
- o Evaluative questions regarding the relationship of pharmaceutical care, specifically pharmacists' cognitive services, and patient outcomes are encouraged.
- o Interventions to change prescribing behavior range from academic detailing to less costly computer-generated letters.

Further study of the effects of these interventions on prescribing behavior and on patient outcomes is needed.

The Role of the Patient: Therapeutic goals are condition- and patient-specific, and desired outcomes will vary by disease, severity of illness, consequences of therapy, and associated treatment costs. In addition to objectively measured consequences of treatment, outcomes of importance include subjective measures of patients' quality of life, satisfaction, and perceived functional status.

AHCPR is interested in studies that will address the following:

o How does patient compliance with a drug regimen vary with respect to changes in quality of life and functional status?

o What is the association between objective and subjective measures for specific conditions?

o To what extent can existing databases, or new primary data collection, be used to examine the relationship between self-care and patient outcomes?

o How can existing models and instruments measuring patient satisfaction, quality of life, functional status, and utility be used to compare outcomes among alternative therapies?

Applications should specifically address the appropriateness and/or effectiveness of pharmaceuticals or related services. Projects should include investigator(s) and key staff who reflect the multidisciplinary nature of outcomes research.

AHCPR plans to convene a conference in Chicago on April 30, 1992, prior to the application receipt date. Attendance is not a prerequisite for applying. All personal travel costs and accommodations are the responsibility of the attendees.

Written and telephone requests for and inquiries concerning this RFA are encouraged and may be directed to: Lynn Bosco, MD or Eleanor Perfetto, PhD, Center for Medical Effectiveness Research, Agency for Health Care Policy and Research, 2101 East Jefferson Street, Suite 605, Rockville, MD 20852, phone 301-227-8485.

**RFA CA-92-17**

Title: **5-a-Day for better health**

Letter of Intent Receipt Date: April 24

Application Receipt Date: June 9

NCI's Div. of Cancer Prevention and Control invites applications for grants to develop, implement, and evaluate interventions in specific community channels and/or for specific target populations to increase the consumption of fruits and vegetables, using the 5-A-Day message. The 5-A-Day message is "Eat 5 servings of fruits and vegetables a day for better health." Fruits and vegetables are promoted in the program in a manner that retains their integrity as low-fat foods and as part of an overall healthy eating pattern that is low in fat and high in fiber.

A channel is defined for this application as a specific means or route for reaching consumers with messages and/or food for the purpose of creating the desired dietary behavior change. Examples are schools, food service (may include restaurants, and cafeterias) worksites, and food assistance programs. Within the channel, a target population must be selected. For example, if schools are selected as the channel, all students may be targeted or students in specific grades may be targeted.

Whenever it seems appropriate, applicants will be expected to utilize the mass media as a part of the intervention. In addition, complementary partnerships with the fruit and vegetable industry are encouraged.

The intent of the announcement is 1) to encourage research in the development of effective community level interventions for changing dietary patterns, using a simple, positive, actionable message; and 2) to develop the community-level component of the national 5-A-Day program, providing the complementary and necessary interactive and environmental elements of successful behavioral change interventions, such as skills development, local media placement, social support, and modifications of foods offered in local food systems.

These community interventions are an important component of the larger national program, that will provide national media coverage and industry-initiated activities. The national program is a partnership between the fruit and vegetable industry and NCI.

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as units of State and local governments, universities, colleges, hospitals, research institutions, consultant firms, or combinations thereof. Universities, colleges, research institutions, hospitals, and consultant firms must involve either a public health agency or some other public agency with a mandate to protect public health and the ability to access and intervene appropriately in the channel or community chosen. All applications will be expected to incorporate appropriate research design and analysis expertise, most frequently provided by universities, colleges, research institutions, and consultants.

Interdisciplinary teams of applicants are encouraged. Among a team of applicants, one institution must be proposed as the lead institution. Foreign applicants are not eligible. Applications from minority individuals and women are encouraged.

This RFA will use the NIH individual research grant (R01). The total project period for applications submitted in response to the present RFA may not exceed four years.

NCI anticipates that $4 million in total costs per year for four years will be available for this RFA. Up to 10 awards are planned.

The goal of this research is to develop, implement and evaluate interventions in specific community channels and/or for specific target populations to increase the consumption of fruits and vegetables using the 5-A-Day message. The primary objectives of this research are:

(1) To increase awareness in the target population of the importance of eating at least five servings of fruits and vegetables every day for better health.

(2) In channels chosen, whenever appropriate, to increase the supportiveness of the environment for increased fruit and vegetable consumption, either through increasing the offering of foods that meet the criteria for the 5-A-Day program, policy changes, or other structural or educational changes that would promote fruit and vegetable consumption.

(3) To increase the daily consumption of fruits and vegetables in the target population significantly more than in the control population.

Applications must address one of the following two design options. Designs other than those described below are allowed but will require justification:

(1) Interventions focused on a specific channel: The major research question to be answered is: Will the target groups (e.g., schools, worksites) in a specific channel receiving a 5-A-Day intervention, based on a selected model of dietary behavior change, demonstrate a significantly greater increase in fruit and vegetable consumption than the groups in the same channel not receiving the intervention?

Other research questions of interest are: Will the target groups in a specific channel receiving a 5-A-Day intervention demonstrate greater changes in dietary awareness, knowledge, attitudes, and behavior than the control groups? Will the organizations or entities in a specific channel receiving a 5-A-Day intervention (e.g., schools, school cafeterias, worksites, worksite cafeterias) demonstrate greater environmental support for increased fruit and vegetable consumption than the organizations or entities in the same channel not receiving the intervention? Other innovative

research questions are invited.

(2) Interventions focused on a specific hard-to-reach population: The major research question to be answered is: Will the groups in a specific hard-to-reach population receiving a 5-A-Day intervention, based on a selected model of behavioral change, demonstrate a significantly greater increase in fruit and vegetable consumption than groups in the same target population, not receiving the intervention? Choice of a single channel is preferable for this research question. However, more than one channel may be used with adequate justification of the specific channels as more appropriate for reaching the target population than a single channel. Examples of appropriate target populations might be ethnic groups, such as Blacks, Hispanics, and Asians, low income groups, low literacy groups, and groups at high risk. Other research questions of interest are the same as those enumerated in design option (1) above, applied to the hard-to-reach target population. Other innovative research questions are invited.

Networking among investigators will be expected. Thus, each grantee should include in her/his budget enough funds for at least two investigators to attend two meetings per year in Washington DC with fellow grantees. Investigators will be expected to supply a final report in a specific format that summarizes both successes and failures to contribute to the dissemination of community intervention research. In addition, grantees will be expected to participate in a joint summary of results of all grants. Grantees will be licensed to use the 5-A-Day logo.

Letter of intent may be sent to, and further information received from: Jerianne Heimendinger, NCI Div. of Cancer Prevention and Control, Executive Plaza North, Room 330, 9000 Rockville Pike, Bethesda, MD 20892, phone 301/496-8520, FAX 301/402-0816.

## Program Announcements

**PA-92-47**

Title: **Neurofibromatosis**

Application Receipt Dates: June 1, Oct. 1, and Feb. 1

The National Institute of Neurological Disorders and Stroke (NINDS) and the National Cancer Institute (NCI) encourage the submission of research grant applications in basic science and clinical investigations concerning all aspects of neurofibromatosis including molecular genetics, cell biology, pathophysiology, development of new animal models, diagnosis, and treatment.

Applications may be submitted by foreign and domestic, for-profit and nonprofit organizations, public and private. However, foreign institutions are not eligible to apply for the First Independent Research Support and Transition (FIRST) Award (R29).

Applicants may use the Research Project Grant (R01), Research Program Project (P01), Research Center Grant (P50), and FIRST Award (R29). Prospective applicants are encouraged to communicate with the NINDS and NCI program contacts listed at the end of the announcement regarding the appropriate funding mechanism.

Neurofibromatosis 1 (NF1), or von Recklinghausen's disease, is an autosomal dominant inherited disorder affecting the central and peripheral nervous system. Its prevalence is about 1 in 4,000. It is characterized by cafe au lait spots of the skin, neurofibromas, schwannomas, intracranial tumors, lisch nodules, and other associated lesions.

The NF1 gene on chromosome 17 has been cloned. Further studies are needed to characterize its gene product. The normal NF1 gene product may be an anti-oncogene that suppresses the ras oncogene. When disinhibited by the mutation of the NF1 gene, the ras oncogene may cause tumor formation.

At the present time, molecular genetic screening is of limited usefulness in counseling and clinical management of NF1. It requires familial markers (not available for all families or for sporadic cases), and it cannot predict the rate or degree of progression of the disorder in a given diagnosed individual.

Neurofibromatosis 2 (NF2), or bilateral acoustic neurofibromatosis, is an autosomal dominant disorder associated with vestibular schwannomas and other schwannomas, meningiomas, ependymomas, gliomas, and posterior subcapsular cataracts. Its prevalence is about 1 in 40,000.

The NF2 gene has been mapped to chromosome 22 in one published family. The gene has not yet been isolated. It is believed to normally function as a tumor suppressor gene.

Multidisciplinary and collaborative studies of neurofibromatosis are encouraged. Examples are given below, but applications are not limited to these areas of research:

o Improvement of diagnostic criteria and tests for use in genetic counseling and clinical management of NF1, NF2, and atypical or variant NF.

o Development of transgenic animal models to study the pathogenesis of NF1, NF2, and associated tumors.

o Studies to explain the variability of clinical expression of NF1 and NF2. Can genotype-phenotype correlations be made in an individual patient? Is the phenotype modulated by modifying genes? Does the expression of these disorders in a given individual depend not only on the precise genetic defect but also on the individual's sex, on the parent from whom the gene defect was inherited, or on other factors?

o Identification and analysis of the NF1 and NF2 gene products and their functions in normal cellular physiology, in the pathophysiology of neurofibromatosis, and in tumorigenesis.

o Basic studies of neurodevelopmental mechanisms affected by neurofibromatosis such as neural crest cell migration and differentiation.

o Understanding the nature and neurobiologic basis of the cognitive impairment associated with NF1.

o Development and assessment of new and innovative therapeutic strategies for the many associated manifestations of NF1 and NF2.

For further information contact Dr. Philip Sheridan, Developmental Neurology Branch, National Institute of Neurological Disorders and Stroke, Federal Building, Room 8C10, Bethesda, MD 20892, phone 301/496-6701; or, Dr. Michael Martin, Tumor Biology Program, National Cancer Institute, 6120 Executive Plaza South, Room 630, Rockville, MD 20852, phone 301/496-7028.

**PA-92-57**

Title: **National digital mammography development group**

Application Receipt Dates: June 1, Oct. 1, and Feb. 1

The Diagnostic Imaging Research Branch of NCI's Radiation Research Program seeks grant applications through Interactive Research Project Grants (IRPGs) in order to form a National Digital Mammography Development Group (NDMDG) that will consist of six major components: (1) software and hardware for digital mammography; (2) image processing; (3) computer-aided diagnosis; (4) telemammography; (5) pre-clinical and clinical technology evaluation; and (6) Headquarters for the scientific leadership (development of experimental design and data processing).

The objective of this PA is to establish a multi-institutional, multi-disciplinary scientific group to facilitate integrated development and evaluation of digital mammography and related technologies, such as image processing, computer-aided diagnosis (CAD), and tele-mammography, for improved breast cancer imaging and characterization.

Applications may be submitted by foreign and domestic,

for-profit and non-profit, public and private organizations. This program will be supported through the research project grant (R01) mechanism. NCI encourages the coordinated submission of related research project grant applications from investigators who want to collaborate on a common cancer research theme but do not require extensive shared physical resources or core functions. A minimum of three independent investigators with related research objectives are encouraged to submit concurrent, collaborative, cross-referenced individual research project grant applications (R01) that share a common research focus. Applications may be from either a single institution or a consortium of institutions. Applications will be reviewed independently for scientific merit. Meritorious applications
will be considered for funding both as independent awards and in the context of the overall proposed collaboration.

Applicants will be responsible for the planning, direction, and execution of the proposed projects. One Principal Investigator out of the group must be identified as the "Program Coordinator," and must be cited in all applications on page 2 of form PHS 398. Individual investigators may request funds for the time and effort contributed toward the coordination of the overall research and for collaborative resource activities.

The major thrust of this initiative is to facilitate integrated technologic development of digital mammographic systems. This PA encompasses a full range of studies from basic technology and instrumentation development through pre-clinical and clinical evaluation. The research agenda for the NDMDG encompasses the following goals:

o To develop and evaluate new technologic advances to increase image quality in digital mammography (e.g., spatial/contrast/time resolution);

o To develop and validate new digital imaging methodology (dynamic or "real time" imaging);

o To develop and validate new image processing techniques to increase the sensitivity of the detection of lesions;

o To develop and validate new algorithms, neural networks, and other forms of machine intelligence for CAD; and

o To develop and validate practical methods of data compression, storage, and image transmission for telemammography.

Written and telephone inquires may be directed to: Faina Shtern, MD, Chief, Diagnostic Imaging Research Branch, Radiation Research Program, NCI, Executive Plaza North, Suite 800, Bethesda, MD 20892, phone 301/496-9531.

**PA-92-61**

Title: Cancer prevention and control research

Application Receipt Dates: June 1, Oct. 1, and Feb. 1

The National Cancer Institute invites applications for studies covering a broad range of research related to cancer prevention and control. The Div. of Cancer Prevention and Control is mandated to conduct research on cancer prevention and control and the surveillance and monitoring of the incidence, mortality, and morbidity of cancer. A priority for DCPC is to develop the means for effective translation of the knowledge gained from research in prevention and control into disease prevention and health promotion activities for the benefit of the public. The goal of these efforts is to achieve significant reductions in cancer incidence, mortality, and morbidity with a concomitant increase in cancer survival.

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private.

DCPC conducts a broad array of cancer control research and application activities that emphasize validation, evaluation, and demonstration. The programs range from research on prevention, screening and early detection, to methods for applying the most effective regimens for cancer treatment, rehabilitation, and continuing care.

The primary research areas are:

o Chemoprevention - pre-clinical and clinical studies related to the identification and evaluation of agents including nutrients that may inhibit carcinogenesis, i.e., initiation, promotion, transformation and/or progression of the malignant process as presently understood. Biomarkers or cancer occurrence may serve as endpoints.

o Nutrition and Diet - Role of nutrients, foods or other dietary components in cancer incidence. Influence of dietary factors on the modulation of cancer risk markers, early indicators of cancer risk or intermediate endpoints. Define biochemical and molecular mechanisms by which dietary components may act as metabolic effectors that protect, control, or increase cancer risk. Absorption and metabolism of nutrients and other dietary components associated with cancer risk and prevention. Dietary assessment in human intervention trials. Development of biochemical or biological markers for dietary compliance and exposure. Improved nutritional and dietary assessment instruments including nutrient data bases. Development of reliable methods for analysis of nutrients and other components in foods, body fluids, and tissues.

o Screening and early detection of cancer - Research to significantly reduce cancer morbidity and mortality through early detection including identification of markers of risk, exposure, and pre-malignant events of progression that can be used to identify sub-populations at particularly high risk of developing cancer. Research is also encouraged in the use of artificial intelligence for image processing as well as new imaging technologies related to early detection. Research on quality control and quality assurance related to screening and early detection is also encouraged.

o Community Oncology - The primary objective is to stimulate research that will provide a basis to reduce the time between research advances in prevention, screening, early detection, patient management, and continuing care and the application of those advances in community settings.

o Rehabilitation and Pain Management - Research that focuses on the application of rehabilitative medicine and pain management for cancer patients.

o Cancer Control Applications - The development and testing of intervention strategies to modify personal, social, and lifestyle factors known to contribute to the development and/or increased risk of cancer.

o Special Populations - Multidisciplinary intervention research aimed at addressing and modifying the excessive cancer incidence and/or mortality rates, lower cancer survival rates, or inadequate cancer prevention and control services for minority, underserved and other special populations.

o Surveillance - Data collection, statistical analysis and mathematical modelling, health services research and information data base linkage studies are required to monitor progress toward cancer control, particularly as it pertains to national goals.

The mechanism of support will be the individual research project grant (R01).

Inquiries may be directed to the relevant Program Director:

Chemoprevention: Dr. Winfred Malone, 301/496-8567

Diet and nutrition: Dr. Carolyn Clifford, 301/496-8573

Screening & early detection: Dr. Barnett Kramer, 301/496-8544

Community oncology & continuing care: Dr. Susan Nayfield, 301/496-8541

Cancer control applications: Dr. Thomas Glynn, 301/496-8520

Special populations: Dr. George Alexander, 301/496-8589

Surveillance: Dr. Brenda Edwards, 301/496-8506

Program Directors are located at Executive Plaza North, 9000 Rockville Pike, Bethesda, MD 20892-4200.