THE CANCER LETTER

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NCI To Voluntarily Spend $196 Million On Breast Cancer; Will Require Reallocation

Interpreting the intent of Congress, NCI plans to conduct a voluntary reallocation of funds that would boost breast cancer research by $59.3 million above the President's budget request.

Sources confirmed that under the plan NCI will spend $196 million on breast cancer, an increase that will entail a reallocation from the Institute's other programs and will give breast cancer the largest dollar

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In Brief

Reginald Ho Assumes ACS Presidency; Board Calls On NCI To Fully Fund ASSIST Program

REGINALD HO, clinical professor of medicine at the Univ. of Hawaii and chief of oncology and hematology at Straub Hospital in Honolulu, assumed the presidency of the American Cancer Society at the organization's annual meeting last week. He replaces **Walter Lawrence. IRVIN FLEMING**, clinical associate professor of surgical oncology at the Univ. of Tennessee College of Medicine, was named vice president and president and president elect. . . . **ACS BOARD** of Directors has approved a resolution calling on NCI to fully fund ASSIST, the nationwide, seven year, $150 million smoking cessation and prevention program being carried out jointly by the Society and NCI. NCI is considering cutting FY 1993 funding of the program by $5.1 million, or 20 percent, delaying some of the planned implementation effort (**The Cancer Letter,** Nov. 6). NCI Director **Samuel Broder** discussed the issue when he addressed the ACS board Saturday but did not commit to full funding of the program during the current fiscal year as originally planned. . . . **TWO RADIOLOGISTS** are expected to be added to the President's Cancer Panel Special Commission on Breast Cancer in response to requests from mammography specialists: **Gerald Dodd** and **Dorit Adler.** Also to be added to the commission is **Fran Visco**, president of the National Breast Cancer Coalition. The appointments are not yet official, but the three are expected to attend the commission's meeting this week. . . . **JOB OPPORTUNITY:** Univ. of California, Irvine, seeks professor or associate with major laboratory/clinical research interest to lead newly established Dept. of Radiation Oncology (formerly Division). Candidates may submit a statement of interest, curriculum vitae and list of five references to Dr. Frank Meyskens, Chair, Search Committee for Radiation Oncology, c/o Janet Nash, Univ. of California, Irvine, College of Medicine, Vice Chancellor's Office, 246 Irvine Hall, Irvine, CA 92717-3950.

NCI Voluntarily Reallocates Money To Favor Breast Cancer Research

(Continued from page 1)
amount of any cancer site.

During the Congressional appropriations process, the professional societies opposed such a reallocation.

The Institute's plan for spending its $1.99 billion FY93 appropriation has been submitted to NIH and the White House Office of Management & Budget. The NCI Executive Committee and other key officials are expected to finalize the spending plan at a retreat in mid-January.

The figures have not been released by NCI's budget office.

According to NCI sources, the emphasis on breast cancer will require redirection of resources from other areas.

"It's not gloom and doom, but it's not the party of '92," said one administrator, refering to the 16 percent increase the Institute received last year.

Besides breast cancer, the House and Senate, in their budget reports, asked NCI to increase funding for ovarian, cervical, and prostate cancer.

$274 Million More

The move for an increase in breast cancer funding was spearheaded by the National Breast Cancer Coalition, a patient advocacy group that initially convinced both the House and Senate to earmark increases in breast cancer funding at the expense of other programs.

The House mandated a 30 percent increase (**The Cancer Letter**, July 31) and Senate mandated the bypass budget level of $220 million (**The Cancer Letter**, Sept. 18).

Ultimately, the earmarks were abandoned in the House-Senate conference (**The Cancer Letter**, Oct. 9). At the same time, Congress directed the Department of Defense to spend $210 million on breast cancer research.

Together, NCI and Defense plan to spend $406 million on breast cancer research, a $274 million increase from fiscal 1992. The National Breast Cancer Coalition demanded a $300 million increase.

Ideas For Defense

Sources said NCI Director Samuel Broder took a packet of proposals for the Defense breast cancer money to a meeting with department officials. Each NCI division was asked to submit ideas.

One proposal included in the package was to increase the accrual of military women to cooperative group clinical trials, according to Cancer Therapy Evaluation Program Director Michael Friedman.

Other proposals included establishing a tissue bank and bone marrow transplant programs in regional military hospitals. These proposals were not in NCI's bypass budget.

FDA Commissioner Proposes Office For Life Threatening Diseases

FDA is proposing to establish an office for liaison with advocates for people with serious or life threatening diseases, which would be located in the Office of the Commissioner.

FDA Commissioner David Kessler, in a letter to representatives from cancer patient advocacy groups, proposed that the new office be modelled on FDA's existing Office of AIDS Coordination, "with comparable responsibilities for a number of serious and life threatening diseases."

Cancer patient organizations had requested that FDA establish an office for cancer similar to the Office of AIDS Coordination, which works with AIDS patient advocacy groups. Representatives from cancer organizations met with Kessler and other FDA officials last July to discuss the request, as well as other issues (**The Cancer Letter**, Aug. 14).

"After careful review of our experiences with AIDS and other diseases and after projecting the likely needs of people with other serious and life threatening diseases, we believe that we should explore the creation of a single office located with the Office of the Commissioner," Kessler wrote in the Sept. 3 letter.

Kessler invited comments and suggestions, which may be directed to Elyse Summers, special assistant to the deputy commissioner for external affairs, at 301/443-3184.

THE CANCER LETTER

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DCT Board Sends Letter On RU 486 Opposing Bill Requiring Research

NCI's Div. of Cancer Treatment Board of Scientific Counselors has sent a letter to Congressmen Ron Wyden (D-OR) and Patricia Schroeder (D-CO) opposing a bill that would require NIH to test RU 486 in breast cancer as well as other indications.

The bill was introduced early last month (**The Cancer Letter,** Oct. 23).

The board, Chairman Ronald Levy, Stanford Univ., wrote, "unanimously expresses its concern that special interest groups from outside the scientific community have attempted to influence the conduct of medical research through the legislative process. The peer review mechanisms for evaluating proposed research and for establishing scientific priorities must be protected from non-scientific influences if they are to remain effective for assuring top quality research and efficient utilization of limited resources....

"The board, after reviewing the existing clinical data, finds little evidence that [RU 486] will be an important agent for treating breast cancer and finds no reason to question the 1991 decision of the National Cancer Institute not to sponsor clinical testing of RU 486 at that time. The board finds no evidence to suggest that political considerations played any part in that decision. Further, and most important, this board emphatically disapproves of legislative efforts that would either require or prohibit the study of this or any other drug with patients. Such a decision should be made only by qualified medical researchers in the absence of political constraints."

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NCI Director Samuel Broder, commenting to the DCT board at its meeting last month on the $210 million earmarked for breast cancer research in the Dept. of Defense FY 1993 appropriation: "We might establish the 'Army Corps of Genetic Engineers.' I can't tell you how this is going to be spent. This is in DOD and we don't have any standing to request it."

Broder on the bypass budget: "For those of you who think the bypass budget doesn't mean anything, think again. But a new use is being made of it, to focus on subsets of the bypass budget rather than the bypass as an organic whole. Now that Congress and others are focusing on specific aspects of the bypass budget, we will have to develop appropriate strategies so the totality of the Institute won't suffer."

• • •

DCT board members discussed NCI's policy of setting aside a percentage of money from the research project grant pool (R01s and P01s)--about 10 to 15 percent--to fund grants submitted in response to Requests for Applications (RFAs) developed by NCI staff.

"The RFA set-aside and funding exceptions to the payline are a tremendous prerogative for the management," board chairman Levy said.

Broder pointed out that RFAs are issued only after approval by the division boards of scientific counselors, and are "driven by a perceived need of the community."

"The problems P01s face is not because of RFAs, but R01s," Broder said. "The Institute as a whole has made the decision to support and protect the R01 mechanism. Something has to give and it is P01s.... I don't share your concern about the RFA mechanism." (For an extensive overview of P01 funding, refer to **The Cancer Letter,** Oct. 2.)

Broder said RFAs should be used to "jump-start" research in a field.

Board member Clara Bloomfield suggested that the board should have the opportunity to suggest topics for RFAs.

"That's a wonderful idea," DCT Director Bruce Chabner said. "I get the feeling we do too much preaching and not enough listening."

• • •

"**It seems** we are getting more and more mandated research from Congress," DCT board member Lester Peters said.

DCPC Board Ok's 3 Grant Programs In Surveillance, Diet, Survivors

NCI's Div. of Cancer Prevention & Control Board of Scientific Counselors have given concept approval to three new grant programs and two new contract projects.

The board approved new grant programs for research in surveillance, dietary factors in cancer prevention, and adult survivors of cancer.

The board also gave concept approval to a contract with the Chinese Academy of Medical Sciences for "Studies to Evaluate Potential Components of a Protocol for the Early Detection and Treatment of Squamous Dysplasia and Early Squamous Cancer of the Esophagus," for a total of $498,595 over five years.

The board tabled discussion of a proposed randomized trial of the clinical management of atypical squamous cells of undetermined significance (ASCUS) and low grade squamous intraepithelial lesions (LSIL) of the uterine cervix until its next meeting scheduled for January.

Following are the concept statements:

[Reports on concept reviews by the boards of scientific counselors of NCI divisions provide readers with advance notice of the Institute's spending plans. Notices of Requests for Proposals, Requests for Applications, or Program Announcements are published in **The Cancer Letter** as they are released; proposals need not be submitted until that time.]

Surveillance Research: Breast Cancer Screening Performance, Diagnosis, Biological Characteristics, Treatment, and Outcome. Proposed RFA, cooperative agreements, $5.2 million total over 5 years, three awards. Project officer: Larry Kessler, Chief, Applied Research Branch.

The objectives of the Breast Cancer Surveillance Research Project are:

a) to conduct an observational study of screening in order to assess the operation screening programs and policies in the U.S. by utilizing comparable data on: recommended screening policies, target groups for screening, rates of women screened, influence of screening on trends in breast cancer incidence and breast cancer mortality, quality assurance procedures, use of state-of-the-art technology;

b) to conduct analytic research on the operational aspects of screening to direct health policy and programmatic decisions and to generate health policy research particularly regarding: results of screening examinations, including predictive values, sensitivity, and specificity, follow-up of screened women, effect of screening on changes in breast cancer prognosis;

c) to track the utilization of state-of-the-art and emerging, new technologies in breast cancer screening and diagnosis with outcome. Technology of interest includes but is not limited to the following: improvements in conventional mammography such as technological developments in grid design and composition, magnetic resonance imaging/spectroscopy, ultrasound, lesion localization and stereotactic fine needle aspiration and biopsy, cytology of nipple aspirate;

d) to facilitate investigator initiated studies of genetic alterations among women with breast cancer detected through screening and those with breast cancer which was non-screen detected.

Data will need to be collected from each mammography facility in an area and reported to a centralized data collection site for an area. The centralized data collection site will need to be linked to the cancer registry for the area. If possible, these areas will be among those funded by the CDC that provided screening services to low-income women. It is preferable that these areas also be the ones which serve as demonstration sites for the ACR program on standardization of mammography reporting. Additionally, it may be preferable that these states have laws mandating tracking systems for mammography results as well as high quality cancer registration systems already in place.

The following steps will be necessary to establish the database needed to conduct the research on surveillance:

1) Identify Current Data Collection Efforts; Consider Modification. Staff from the NCI and the Principal Investigators from individual sites would convene to determine how to modify current data collection practices in each area to conform to the standards developed jointly by the NCI staff and the Principal Investigators. In both the tumor registration and radiologist practices, software and data collection procedures exist which are generally compatible with this project. However, this is not likely the case in pathology offices. In some cases, new software or other data collection methods would have to be created to suit these needs.

2) Obtain Cooperation and Assess Needs. In each area, the project requires the cooperation of radiologists, pathologists, surgeons, and tumor registrars. Currently, although clinical breast examination is an essential part of breast cancer screening, collecting routine data on this procedure appears impractical because the exam is generally performed in primary care physicians' offices. Several pilot studies may be needed during the establishment of the Database to determine the feasibility of collecting clinical breast exam data and coordinating these data with registry and mammography screening data. Large HMOs may be used to track this information.

3) Establish Standard Definitions; Modify Table Forms. The glossary (definitions and rules for classification) and table forms developed for the International Database for Breast Cancer Screening will be modified as necessary for this project. Software will be developed using the glossary and table forms.

4) Collection of Data. Once table forms, data collection forms, and software have been developed, personnel will need to be trained in data collection methods. It will be necessary to link all data on each woman so that multiple visits to multiple sites will be included in the database and one record will be used across multiple facilities. Data collection will be done using computers in mammography facilities with moderate to high volume. In other mammography facilities with low volume and in clinicians' offices and pathologists laboratories, data collection may include use of optical scanning forms. After data are collected in each facility, linkage will be required to a centralized area and then to the cancer registry. Data sets from the mammography facilities will be handled in a confidential manner by the centralized data management center and in accordance with existing procedures in the limited-access cancer registry center.

5) Analysis of Data. Assessment of the effectiveness of breast cancer screening and identification of barriers to achievement of expected effects would include analyses of variability among geographically defined areas (states or large metropolitan areas) comparing population screening/stage of disease/mortality between areas and with the HIP and Swedish trials. Also needed are analyses of data by clinic and by geographically defined area; for example, proportion women from target population attending, proportion of screened women referred for additional exams, disposition of mammography results "abnormality-probably benign," benign to malignant biopsy ratios, numbers of women lost to followup and determination of reasons, proportion of women screened found to have cancer, proportion of women screened found to have cancer < 10 mm diameter pathology, proportion of women who develop cancer in 12 months following screening.

Then these results will be analyzed by comparing achievements of screening programs in geographically defined areas to achievements in randomized controlled trials and in other countries with established screening programs where similar data have been collected and standards established. These findings can then be used to establish program standards for the U.S.

It is not likely that a single institution can meet the wide ranging goals of this project. We propose that investigators with expertise in the establishment an management of registry data, investigators from screening and treatment practice form a group within a geographical area to conduct the research proposed. There will be up to three groups funded. The groups will form one consortium. A system of data collecting and reporting on breast cancer screening by mammography and clinical breast exam, pathology of biopsied lesions, and outcome will need to be established in each of the three areas of the consortium; i.e., geographical area of the U.S. which already have population-based cancer registries. Further, that these systems be maintained for a minimum of five years.

Phase 1 clinical trials of new chemopreventive agents. Proposed RFP, master agreements, total $7.5 million over five years. Project officer: Marjorie Perloff, Chemoprevention Branch.

The major thrust of the Chemoprevention Branch is to identify potential chemopreventive agents, and to conduct preclinical and clinical research with the ultimate objective of conducting phase 3 risk reduction trials. Presently, approximately 200 agents or regimens are being studied; testing on an additional 25 new compounds will begin this year. Several of these compounds will be appropriate for phase 1 clinical trials during the next year. Thus, the capability to initiate phase 1 clinical trials is a high priority. The progress of the chemoprevention program will be delayed if the phase 1 clinical trial mechanism is not available for introducing new compounds into phase 2 and 3 trials.

Master agreement orders will be issued to all investigators or institutions who are deemed via peer review qualified for carrying out the proposed tasks. The award will be for five years. As agents become available, applications will be requested and reviewed, and the best proposals will be selected for funding and implementation. Three to five new agents will be studied per year; the number of subjects will be determined as necessary for each compound evaluated. All master agreement order holders will be asked to submit a master protocol for phase 1 studies in their technical proposals which details all aspects of the study except those determined by the specific agents.

Dietary factors, steroid hormone metabolism, and cancer prevention. Proposed new RFA, five to six awards, total $4.5 million over three years. Project officer: Carolyn Clifford, Diet & Cancer Branch.

This concept seeks to encourage the submission of R01 applications for the conduct of carefully controlled human experimental dietary studies to evaluate the role of dietary macro- and/or micronutrients and their interactions in relation to the circulating levels of steroid hormones, their bioavailability, metabolism and excretory patterns and to better define the mechanisms by which dietary factors can affect hormone metabolism.

Some interesting unanswered questions include:

1. What is the relative role of dietary fat and dietary fiber in modulating steroid hormone metabolism?

2. Why does a low fat diet alter plasma estrone levels in premenopausal women and not postmenopausal women?

3. What are the qualitative and quantitative responses to circulating steroid hormone levels to changes in dietary factors?

4. What impact does age, obesity, lean body mass, and weight loss have on the dietary modulation of steroid hormone metabolism in males and females?

The overall goal of this research is to provide more definitive data for developing quantitative dietary guidance and translation into optimal and desirable eating patterns and food choices that have the potential for a substantial reduction in the risk of the diet-hormone related cancers (breast and prostate cancer).

Biorepository in the Prostate, Lung, Colorectal, and Ovarian cancer screening trial. Proposed RFP, total $5.9 million over seven years, one biorepository contract award and approximately 12 supplemental contracts to PLCO screening centers. Project officer: John Gohagan, Early Detection Branch.

Purpose of this concept is to establish a biorepository for the identification and development of biomarkers for studies of cancer etiology, risk assessment and early detection. DCPC initiated a study of the effectiveness of selected screening techniques for prostate, lung, colon and ovarian cancers in the Early Detection and Community Oncology Program. In May 1991, the BSC recommended that a serum bank or biorepository be added to the trial. The trial involves recruitment of 148,000 subjects (men and women) aged 60-74 years, randomizing to screening and control arms, screening annually over three years for prostate cancer by digital rectal exam and serum PSA, for lung cancer by chest x-ray, for colon cancer by flexible sigmoidoscopy, and for ovarian cancer by pelvic exam, serum CA125, and transvaginal ultrasound. At each screening exam, blood will be collected to assay for PSA and CA125. Full scale recruitment, screening and followup will take place in years three to five, screening and followup in years six to eight for cancer incidence and mortality, and followup through years nine to sixteen.

A serial, prospective collection of whole blood and serum samples from PLCO screened subjects will make possible studies to evaluate new early detection markers of prostate, lung, colorectal and ovarian cancers inexpensively, and rapidly. It will also make possible molecular epidemiologic and etiologic risk assessment studies of the highest scientific quality.

The proposed repository will provide a unique resource for studies of cancer etiology and cancer prevention and control. Biologic samples (serum, white blood cells in buffy coat, and red blood cells in whole blood) will be collected from 74,000 screened subjects at the base line screening exam, and at the following two annual screening exams (serum only). A specialized questionnaire associated with the anticipated use of repository materials will be designed for and incorporated into the intake process. In depth interview studies of risk factors will be conducted for cases of lung and prostate cancer and for selected controls.

The repository will contain serum, plasma, RBC, and whole blood, and buffy coat from the intake draw (45ml) and serum only from the two subsequent draws (12ml) will be accumulated in the repository for subsequent analyses. Etiology components will be stored initially in 2.5 ml alliquots. These may be further divided upon the first thaw. Early detection components (serum) will be stored initially in 1 ml alliquots.

Storage of the samples to year 8 of the PLCO trial is planned. Continuation beyond year 8 will depend on scientific need and availability of funding.

Upon receipt, biologic samples will be inventoried. Plasma, serum and blood will be separated for storage, allowing for backup, in minus 70 degree C freezers.

The contractor shall be responsible for all operations and shall be represented on the steering committee of the PLCO trial along with representatives of the screening centers, coordinating center, and LAB. An NCI scientific oversight team specific to the biorepository will be established to oversee scientific practices including research panel composition and distribution for analysis.

Support from the Div. of Cancer Etiology also will be sought. Other divisions of NCI may eventually find use for some of this material; how they would share in the costs would be established by a biorepository managing committee.

Budget estimates include phlebotomy, prerepository processing and shipping, freezer acquisition, freezer maintenance, personnel, processing of samples arriving and leaving the repository for analysis, quality control, record keeping, and related costs. DCE is expected to share in biorepository costs on a pro rata basis.

Adult survivors of cancer. Proposed new RFA, total $10 million over four years, four to five awards. Program director: Claudette Varricchio, Community Oncology & Rehabilitation Branch.

The goal of this initiative is to decrease the functional and psychosocial morbidity associated with cancer survivorship by testing interventions to facilitate rehabilitation of adult cancer survivors and to enhance their re-entry into society.

The concept proposes to invite R01 applications to test interventions in a two phase approach:

1. Descriptive phase to gather detailed baseline information and refine propose interventions as indicated by findings.

2. Evaluative phase in which intervention is implemented and the impact is determined and assessed.

Adult cancer survivors are defined as persons diagnosed and treated for cancer after age 21, who have completed therapy and have a good prognosis for cure or long term survival.

Applications should reflect a strong research orientation with attention to psychosocial variables, vocational rehabilitation, and adaptation to long term physical impairment or functional rehabilitation. The approach should be interdisciplinary in nature and have the potential to be transferred effectively to diverse practice settings.

Applicants are requested to develop, implement and evaluate interventions aimed at improving the rehabilitation and quality of life of cancer survivors in psychosocial sequelae, vocational rehabilitation, or adaptation to long term functional impairment.

Proposals should define the population of interest, document the problem, describe the intervention and the evaluation plan. The design may include qualitative or quantitative methodologies and must include a systematic documentation of the problem. The research hypotheses should be based on relevant conceptual models or theories and should address issues in at least one of the following areas: long term physical impairment; self-image, sexuality, reproductive potential; interpersonal relationships and social functioning; vocational rehabilitation, employment or insurability; medical uncertainties; cultural and ethnic background and values as influences on adaptation to cancer.

The proposed interventions may be drawn from those which have been shown to have been of benefit in the long term rehabilitation of patients in other disease categories. This intervention study may incorporate a descriptive phase for collection of baseline data, or a short pilot phase for refining the proposed intervention. However, the principal focus of the research should be to predict problems and evaluate interventions to accomplish the rehabilitation and reintegration of the adult survivor of cancer.

Existing measures of the outcome variables of interest, with established validity and reliability must be used. These may be drawn from other disciplines in the social sciences. Focus groups and other sociologic approaches may be suitable.

Research designs should allow rigorous evaluation of the study intervention. An experimental design is the preferred approach. Quasi-experimental designs may be appropriate. Outcome variables must be clearly defined and assessed by valid and reliable techniques. Analysis will include descriptions of the population of adult survivors and the needs identified by this group. Usual evaluative methods can be used to determine the effectiveness of interventions. Some of these evaluative methods may be drawn from education, social sciences or health services research. Investigators are expected to select endpoints which reflect the quality of long term survival, for example: functional status, changes in the use of services, or degree of return to premorbid lifestyle, work and activities.

RFAs Available

RFA AI-92-16

Title: **National cooperative drug discovery groups for treatment of HIV**

Letter of Intent Receipt Date: Jan. 15

Application Receipt Date: March 17

The National Institute of Allergy and Infectious Diseases invites applications for the establishment of National Cooperative Drug Discovery Groups for the Treatment of HIV. The objective is to support innovative research of sound scientific rationale, which requires intra-group interactions and that is likely to result in the discovery of more effective therapeutic strategies against HIV. This RFA will support original and/or under-exploited studies that are at the cutting edge of biomedical research. Applications that include research projects or core components from the private sector are strongly encouraged. Applications may be submitted by domestic and foreign for-profit and non-profit organization, private and public. Awards will be made as Cooperative Agreements (U01s). NIAID has set aside $3 million for the initial year's funding. Three to four awards anticipated. New awards are subject to a first year limit of $800,000 in total costs.

As of last August, 18 groups were funded under the NCDDG-HIV program. Eight of these Groups are eligible for competitive renewals in 1993 in response to this RFA.

Research directed toward drug discovery in the following major areas will be considered responsive to this RFA:

--Discovery, elucidation and application of modalities that inhibit HIV gene expression via interference with HIV regulatory elements.

--Inhibition of critical steps in HIV replication via intracellular delivery and expression of antagonists using viral vectors or other delivery strategies (gene therapy).

--Intervention with cellular biochemical pathways required for induction of HIV from a 'latent' or non-replicative state and/or for enhancement of HIV replication.

--Structure-based drug design encompassing novel chemistry, synthesis and development of stable, small molecules that block HIV infection or impair virus replication.

--Innovative exploitation of the humoral and cellular arms of the immune system for a targeted anti-HIV affront and immune system reconstitution.

--Studies of non-T cells compartment(s) that may serve in the initial infection by HIV, and which may play an essential role in free virus transport, cell-cell transmission, and general dissemination of HIV in the body.

--New and sound conceptual strategies which are not or minimally pursued for the discovery of new entities (or combinations) with potential for the treatment of HIV infection.

Inquiries and letter of intent may be directed to: Dr. Nava Sarver, Chief, Targeted Drug Discovery Section, Developmental Therapeutics Branch, Basic Research and Developmental Program, Div. of AIDS, National Institute of Allergy and Infectious Diseases, 6003 Executive Boulevard, Room 2C11, Bethesda, MD 20892; phone 301/496-8197, fax 301/402-3211.

RFA AI-92-10

Title: **Pediatric AIDS clinical trials program**

Letter of Intent Receipt Date: Nov. 13

Preapplication Meeting Date: Dec. 7

Application Receipt Date: Jan. 21

The purpose of this RFA is to recompete the Pediatric AIDS Clinical Trials Program in order to further stimulate pediatric AIDS research. This program, initiated in 1988, is supported by the Div. of AIDS of the National Institute of Allergy and Infectious Diseases.

The RFA calls for an emphasis on the development and evaluation of pediatric therapeutic research in three major areas, namely: 1) interruption of perinatal transmission of HIV, 2) antiretroviral therapy, and 3) therapy and prophylaxis against opportunistic infection in HIV disease. The target populations include: infants (0 to 12 months of age), children (13 months to 12 years of age), and adolescents (13 through 18 years of age).

Applications may be submitted by domestic, for-profit and non-profit organizations, public and private. Existing pediatric AIDS Clinical Trial Units (ACTUs), pediatric components of adult

ACTUs, as well as new applicants are invited to apply.

Awards will be supported through NIH cooperative agreements (U01). Approximately $23 million will be available for the first year funding. Approximately 10-14 pediatric ACTUs will be funded for a total project period of four years. Anticipated earliest award date is September 1, 1993.

The primary research objectives are to evaluate the pharmacokinetics, safety, tolerance, and efficacy of agents in order to: reduce the rate of perinatal transmission of HIV; develop effective antiretroviral treatment of primary HIV infection; and develop effective treatment and prophylaxis of opportunistic infections.

These research aims will be addressed through a multi-center clinical trials network in which Principal Investigators work collectively and cooperatively with NIAID staff to devise and implement the most appropriate studies for these objectives.

Awardees must conduct clinical trials that focus on the three research areas listed above. At least 25 new patients per year must be accrued onto pediatric protocols. The majority of the pediatric protocols include patients to ages 17 or 18.

In addition to the 25 patients mentioned above, awardees who have a particular interest in unique aspects of research on adolescents will implement specific studies designed to focus on this population. Institutions with a special interest in neurological and neuropsychological testing will conduct studies of new and efficient methods that could be used as measures of effectiveness in clinical trials of antivirals.

Inquiries and letter of intent may be directed to: Tina Johnson, Clinical Research Management Branch, Div. of AIDS, NIAID, Solar Building, Room 2A09, Bethesda, MD 20892; phone 301/496-8214.

RFA AI-92-14

Title: **AIDS clinical trials units at minority institutions**

Letter of Intent Receipt Date: Nov. 16

Application Receipt Date: Jan. 21

The National Institute of Allergy and Infectious Diseases announces the availability of an RFA for AIDS Clinical Trials Units (ACTUs) at Minority Institutions. The purpose of this RFA is to solicit applications from minority institutions to establish adult ACTUs and to become part of the AIDS Clinical Trials Group (ACTG).

Institutions that have more than 50 percent minority student enrollment and award the M.D., D.D.S., D.V.M., or other doctoral degree in the health professions are encouraged to apply. The ACTG is a network of 35 domestic biomedical research institutions that, in aggregate, has the capabilities to develop new therapeutic interventions from initial clinical trials in human subjects to their final approval by the Food and Drug Administration.

The ACTG evaluates the safety and efficacy of therapeutic interventions for the treatment of HIV, associated opportunistic infections and malignancies, and neurological complications of AIDS.

This competition is limited to domestic universities or colleges that possess the capabilities to conduct clinical research on HIV infection and AIDS. Applications may not contain an international component. Preference will be given to institutions that have more than 50% minority student enrollment.

Awards will be made as cooperative agreements (U01). The total project period for applications submitted in response to this RFA will not exceed four years. The anticipated award date is Sept. 1, 1993. NIAID anticipates that $3,800,000 will be available in the initial year for funding applications in response to this RFA. Three to four applications will be funded. All awardees must be capable of enrolling a minimum of 60 new patients annually on to ACTG clinical protocols for each year of the award.

Inquiries and letter of intent may be directed to: Dr. Frederick Batzold, Div. of AIDS, NIAID, 6003 Executive Blvd., Bethesda, MD 20892; phone 301/496-8214.

RFA CA-93-04

Title: **Interactive research project grants for nutrition and cancer prevention**

Letter of Intent Receipt Date: Nov. 24

Aplication Receipt Date: Jan. 19

NCI's Div. of Cancer Prevention and Control invites Interactive Research Project Grants to encourage and facilitate formal interdisciplinary collaborations through the coordinated submission of related research project applications that share a common research focus relevant to nutrition and cancer prevention 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 submitted from either a single institution or a consortium of institutions. Applications will be reviewed independently for scientific merit.

Domestic and foreign non-profit and for-profit organizations and institutions, governments and their agencies are eligible to apply. Project period should not exceed five years. Approximately $2.5 million in total costs per year for up to five years will be committed. Six to nine awards will be made.

Representative areas of particular interest for this RFA focus on innovative research approaches for the development, evaluation and/or application of specific methodologies for elucidating the mechanisms of action and quantification of the role of diet and dietary components in cancer prevention.

Several examples of research areas relevant to nutrition and cancer prevention in which the IRPG concept may be applied are:

--Metabolic effectors of dietary origin. Basic science projects may be combined that integrate multiple aspects of dietary factors that modulate signal transduction, DNA repair, antioxidants, hormonal regulation and gene regulation.

--Interaction of diet and dietary components with drugs, hormones, metabolites and genes--synergistic and antagonistic effects.

--Development of new and better methods to quantify dietary intake in individuals.

--Further identification and evaluation of overall dietary patterns, foods and food constituents that alter cancer risk and elucidation of their mechanisms of action.

--Identification of markers of dietary exposure and early indicators of risk.

--Quantification of optimal ranges of dietary constituents that affect cancer risk.

--Social behavioral research to identify motivation factors and barriers to changing food habits.

--Nutrition as one component of healthy lifestyle modification. Studies of fundamental relationships between diet, nutrition and cancer and behavioral change affiliated with modification.

Prospective applicants are encouraged to explore other areas of potential for the Interactive Research Project Grant mechanism with the NCI Program Director.

Inquiries and letter of intent may be directed to: Dr. Carolyn Clifford, Diet & Cancer Branch, Div. of Cancer Prevention & Control, NCI, Executive Plaza North, Room 212, Bethesda, MD 20892-6130, phone 301/496-8573.

RFA CA-93-06

Title: **Developmental research in native Pacific populations**

Letter of Intent Receipt Date: Dec. 4
Application Receipt Date: Jan. 25

The Special Populations Studies Branch of NCI's Div. of Cancer Prevention & Control invites applications from various organizations for developmental studies that:

1) assess cancer control need, 2) determine barriers to cancer control, and/or 3) validate intervention methods and assessment instruments in native Pacific populations; i.e., American Samoans, Guamanians (Chamorros), Palauians, and Northern Marianians. This initiative will define the cancer prevention and control needs of native Pacific populations and those of similar ancestry located in the Pacific as well as the U.S. mainland.

Applications may be submitted by domestic (including U.S. Territorial possessions) public and private, for-profit and non-profit organizations serving native Pacific populations. Teams of applicants are encouraged. Support will be the NIH research project grant (R01). It is anticipated that four awards will be made at approximately $300,000 total costs per year. Approximately $1.2 million in total costs per year for three years will be set-aside to fund applications. Up to four awards will be made. The total project period of these awards may not exceed three years.

Studies conducted under this RFA will seek to define cancer prevention and control needs/services of the native Pacific population segments (Phase I).

Studies to test ways in which existing intervention methods can be used or adapted for the target populations (Phase II); or studies of new methods designed to be sensitive to the needs of the target populations (Phase II); or methodologic research on validation of assessment instruments in target populations (Phase II) are eligible for consideration under the RFA.

The research of interest in this RFA falls into either Phase I or Phase II studies. Hypothesis development (Phase I) studies should focus on the assessment of cancer prevention and control needs in communities or organizations within native Pacific populations or studies that identify barriers to cancer prevention and control within these indigenous populations.

Methods development and testing studies, Phase II, should focus on: 1) validating the use of existing intervention methods (e.g., dietary modification, health services, tobacco cessation) applied in the target populations described above; 2) developing and pilot testing unique methods that are sensitive to the needs of the target populations described above; or 3) developing and validating assessment instruments to measure the cancer control related needs of the target populations or for use in evaluating the effectiveness of intervention methods in the target populations.

Inquiries and letter of intent may be directed to:

Dr. George Alexander, Chief, Special Populations Studies Branch, Cancer Control Science Program, Division of Cancer Prevention and Control, National Cancer Institute, Executive Plaza North, Room 240, Bethesda, MD 20892-4200; phone 301/496-8589.

Breast Cancer Incidence Fell In 1989: NCI's 'Cancer Statistics Review'

The incidence rate for breast cancer declined for the second straight year in 1989 and mortality rates increased for black women of any age, while declining for white women under age 50.

The findings are reported in NCI's annual "Cancer Statistics Review," published each year using data from the Surveillance, Epidemiology & End Results program (SEER). The document covers 1973-1989, the most current year for which data are available.

According to the review, the incidence rate for breast cancer fell from 109.6 cases per 100,000 in 1988 to 104.6 in 1989. Breast cancer incidence increased dramatically through much of the 1980s, rising from 85.2 cases per 100,000 in 1980 to 112.4 in 1987.

For white women, the breast cancer mortality rate from 1973-1989 decreased 12.5 percent for ages under 50 and increased 5.4 percent for ages 50 and older. For black women during the same period, the rate increased 5.3 percent for ages under 50 and 21.9 percent for those 50 and older.

For all women, the breast cancer mortality rate increased 2.7 percent between 1973-1989. Mortality over the 16 year period increased 2 percent for whites, while it rose 17.7 percent for blacks.

NCI said the gradual, long term increase in breast cancer incidence is difficult to explain. About 60 percent of women diagnosed have no known risk factors such as family history of the disease or those associated with reproductive history, such as late child bearing, early menarche, late menopause, and use of exogenous hormones such as oral contraceptives and postmenopausal replacement estrogen. Other possible causes include lifestyle and environmental risk factors.

NCI said there is evidence that the marked increase in breast cancer incidence that began in the early 1980s was due primarily to a nationwide increase in mammography screening, particularly in women over age 50. The earlier detection of cases through mammography is expected to result in improvements in mortality by the mid-1990s.

However, NCI said, the recent decline in incidence among whites suggests that screening may be stabilizing at lower levels than had been projected, which would correspondingly reduce expected mortality benefits.

For the first time, the 1992 "CSR" is organized into sections according to cancer site. Twenty-four sections each contain incidence, mortality, and survival data for a specific type of cancer. Other sections deal with cancer in children, cancer mortality by state, and SEER studies of cancer treatment patterns.

Other additions are a new section on the probability of developing cancer, median ages at death, by race and sex, for patients with various types of cancer and treatment patterns for selected stages of cancer.

Single copies of "Cancer Statistics Review 1973-1989" may be obtained by writing the Office of Cancer Communications, Building 31 Room 10A24, Bethesda, MD 20892, or calling 1-800-4-CANCER.