THE CANCER LETTER

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Army Will Outspend NCI On Breast Cancer In FY93, But How To Apply For A Grant?

The Department of the Army will outspend NCI on breast cancer research in fiscal 1993.

Under the budget signed by the President last week the Army will have $210 million to spend on the disease, nearly $73 million more than NCI.

How does one apply for a grant? At this point no definitive answer exists. The legislation passed in the final days of the 102nd Congress

(Continued to page 2)

In Brief

Broder Wins ARC's Griffuel Prize; Lawyers Trained To Help Low-Income Breast Ca. Patients

SAMUEL BRODER, NCI director, was awarded the Griffuel Prize by the French Assn. for Research on Cancer. The award, of 500,000 francs, roughly $100,000, was given in recognition of Broder's work on the relationship between cancer and immunodeficiency states and antiretroviral chemotherapy. . . . **VOLUNTEER LAWYERS** will be trained to assist low-income women with breast cancer in a program initiated by the Judges and Lawyers Breast Cancer Alert, based in New York City. Key aspect of the training is sensitizing lawyers to the emotional experiences of women with breast cancer so they can be better advocates for their legal needs, the organization said. The training is held at the Assn. of the Bar of the City of New York. . . . **MATILDA CUOMO**, wife of NY Gov. Mario Cuomo, dedicated Memorial Sloan-Kettering Cancer Center's new outpatient breast cancer and diagnostic imaging center recently. . . . **STAFF CHANGES** in NCI's Div. of Cancer Treatment: **Barbara Temeck** was promoted to surgery branch medical officer, **Louis Malspeis** was promoted to chief of the Laboratory of Pharmaceutical Chemistry; **Thomas Delaney**, senior investigator in the Radiation Oncology Branch, is chief of radiation medicine at Boston Univ. Hospital; **Lori Pierce**, senior investigator in the ROB, is assistant professor at Univ. of Michigan Medical School; **Michelle Evans**, senior clinical investigator, transferred to the National Institute on Aging; **Daniel Zaharko** retired as chief of the Pharmacology Branch; **Jeffrey Norton**, medical officer in the Surgery Branch, is chief of endocrine and oncologic surgery at Washington Univ. School of Medicine; **Rina Zakut**, expert in the Tumor Immunology Section, accepted a position at the Weizmann Institite of Science; **Eric Whitman**, IV access surgeon, accepted a position at St. Louis Univ. Medical Center; **Vilhelm Bohr**, medical officer, will transfer to the National Institute on Aging.

DOD To Outspend NCI By $73 Mil. On Breast Cancer Research In FY93

(Continued from page 1)

mandates that the Army's breast cancer research would have to be peer reviewed, but makes no mention of an interagency agreement with NCI.

This smoke screen was deployed to keep the Administration from scoring the funds as domestic discretionary, rather than defense spending, but after the bill was signed into law the smoke remains to clear.

Consider the language of the defense appropriations bill:

"...$210 million of the funds shall be available for a peer reviewed breast cancer program with the Department of the Army as executive agent. [The] Army shall coordinate with the Armed Services Biomedical Research and Evaluation Management Committee to involve facilities and research personnel of the Department of the Navy and the Department of the Air Force, or other entities, in addition to facilities, medical and research personnel, and resources of the Department of the Army in the breast cancer research program. The Department of the Army, as executive agent, shall provide a report to the congressional defense committee no later than June 1, 1993, setting forth the details of the breast cancer research program, noting inter alta the benefits which may be achieved through such research in the reduction of future costs of the Civilian Health and Medical Program of the Uniformed Services."

This Army-centric language leaves open the door for an interagency agreement: "The Army shall... involve... [the Navy, Air Force] or other entities..." However, it does not guarantee that an agreement with NCI would be made.

The optimists among observers said the agreement would be inevitable since the Army does not have the peer review system capable of distributing the money.

Even the scenario of an interagency agreement poses a challenge to NCI: under the bypass budget, which represents the professional judgment of funding needed to meet all research opportunities, the Institute asked Congress and the President for $220 million for breast cancer research in fiscal 1993.

Now NCI and DOD together will be obligated to spend an estimated $345.6 million.

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"I personally appreciate the need for more money for breast cancer research," American Society of Clinical Oncology President Bernard Fisher wrote to the conferees reconciling the House and Senate versions of the defense appropriations bill.

"We are confident proper use of these DOD funds could be ensured by establishing an interagency agreement with NCI. With such an agreement, DOD could take advantage of NCI's excellent network of qualified researchers and its peer review system."

American Assn. for Cancer Research is preparing a letter on the subject, sources said.

Similarly, the Breast Cancer Coalition, a new group representing politicized breast cancer patients (**The Cancer Letter**, Aug.7), is developing an elaborate system for monitoring the spending of the DOD--and NCI--money.

"It's not a matter of how much; it's a matter of how," Terry Lierman, president of Capitol Associates, the lobbying group for the National Coalition for Cancer Research, described the logistical problem faced by cancer researchers.

In the final days of the appropriations debates, NCCR and the Breast Cancer Coalition worked together to ensure the passage of the DOD breast cancer appropriation.

The amendment to the DOD bill was introduced by Sen. Tom Harkin (D-IA), chairman of the Labor, HHS and Education Appropriations Subcommittee and one of the conferees on the DOD measure.

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Even its adversaries concede that the Breast Cancer Coalition was crucial to obtaining the windfall for breast cancer research.

The coalition's write-to-Washington campaign generated 600,000 letters, its demonstrations lined the halls of Congress with breast cancer survivors. The result was a political climate best summarized in an off-the-cuff remark by Sen. Dale Bumpers (D-AR): "This isn't the year to treat women unfairly," Bumpers (D-AR) quipped at the final session of the Labor, HHS, Education Appropriations Subcommittee.

THE CANCER LETTER

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At the outset of the DOD appropriations conference, the coalition staged a vigil on the steps leading to the Senate chamber. "We'll get that money," the coalition's lobbyist Joanne Howes said to a reporter shortly after a chat with Harkin.

Five hours later, Sen. Daniel Inouye (D-HA), chairman of the Defense Appropriations Committee, descended the steps with a dispatch that would have puzzled anyone unfamiliar with television advertising of spaghetti sauces:

"It's like Ragu. It's in there," the Senator said.

"Go home," said a Hill staff member coming down the steps moments later. "Can't you take yes for an answer?"

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Odd as that may sound, the breast cancer windfall is only a partial victory for the Breast Cancer Coalition. Partial because the final appropriation for breast cancer research fell $87 below its goal.

Actually, the coalition came very close to getting the $433 million. It had succeeded at getting both the House and Senate to mandate NCI to increase spending on breast cancer at the expense of other programs.

These provisions, opposed by NCCR, were dropped from the Labor, HHS and Education conference report when Harkin's DOD amendment was gaining momentum in the Senate. Still, the Breast Cancer Coalition fought to the end, attempting to keep the increases in the Labor, HHS bill.

Now, with the session over, the Breast Cancer Coalition has demanded a role in determining the manner in which the funds will be spent.

"A lot of people are looking at this and saying, well, they got all this money and they will go away happy," Fran Visco, president of the coalition, said to **The Cancer Letter.** "Well, we are not going away. We want to work with NCI, the appropriate representatives of the Army and the members of Congress in determining how the money will be spent. And we want to be on the ground floor."

Later this week the Breast Cancer Coalition will arrive at a plan for monitoring the NCI and DOD breast cancer funding.

However, Visco said, the coalition is likely to appoint several committees to deal with the key players in charting the program.

Each committee will include seven members and each would target a key player.

So far, the officials slated for such meetings include NIH Director Bernadine Healy, NCI Director Samuel Broder, and NCI Div. of Cancer Treatment Director Bruce Chabner.

Broder is likely to be asked to schedule monthly meetings with the coalition. Chabner will be asked for quarterly meetings. The coalition is yet to identify the DOD officials and legislators who would be asked for similar meetings, Visco said.

To ensure continuity, four members will serve on all teams at once.

The coalition's other goals include lobbying for formation of a standing subcommittee on breast cancer under the National Cancer Advisory Board as well as placing its representatives on study sections.

"We do have patient advocates who are also scientists," Visco said.

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The appropriations for all NIH institutes were reduced by a .8 percent cut by the House and Senate conferees.

The final budgets for all NIH institutes follow:

NIH total--$10.363 billion

NCI--$1.991 billion

National Heart, Lung and Blood Inst.--$1.219 billion

National Inst. of Dental Research--$162 million

National Inst. of Diabetes, Digestive & Kidney Diseases--$683.1 million

National Inst. of Neurological Disorders & Stroke--$601.7 million

National Inst. of Allergy & Infectious Disease--$983.9 million

National Inst. of General Medical Sciences--$833.1 million

National Inst. of Child Health and Human Development--$529.8 million

National Eye Inst.--$276.9 million

National Inst. of Environmental Health Sciences--$253.1 million

National Inst. on Aging--$401.2 million

National Inst. of Arthritis and Musculoskeletal and Skin Disease--$212.9 million

National Inst. On Deafness & Other Communication Disorders--$155.1 million

National Inst. of Nursing Research--$48.2 million

National Inst. on Alcoholism and Alcohol Abuse--$177.3 million

National Inst. on Drug Abuse--$405.7 million

National Inst. of Mental Health--$585.7 million

National Center for Research Resources--$312.7 million

National Center for Human Genome Research--$106.4 million

John Fogarty International Center--$19.8 million

National Library of Medicine--$104.2 million

Office of the Director--$191.2 million

Buildings and Facilities--$108.7 million

In Congress

Congress Passes Mammography Quality Standards, FDA User Fees

Congress approved a set of national standards for mammography advocated by the American Cancer Society, American College of Radiology, the Susan Komen Foundation and the Breast Cancer Coalition. The measure was expected to be signed by the President.

Under the act, all mammography facilities will be required to have a certificate to operate, which is conditioned on the facility having been accredited and inspected.

The accreditation program will include requirements for equipment, personnel experience and training, routine quality control procedures, annual survey by a qualified medical physicist and peer review of clinical images.

Penalties for noncompliance were set at up to $10,000 a day.

Under the act, HHS will form a national advisory committee of at least 13 members. At least four members of the group will represent breast cancer or consumer groups and at least two will be physicians who perform mammography.

The act also requires HHS to award screening surveillance and research grants to evaluate participation rates in screening mammography, diagnostic procedures, incidence of breast cancer, mode of detection, outcomes and followup information.

The requirements, which are expected to go into effect Oct. 1, 1994, do not apply to the Dept. of Veterans Affairs.

The measure was introduced by Sen. Brock Adams (D-WA) and House members John Dingell (D-MI), Henry Waxman (D-CA), Pat Schroeder (D-CO) and Marilyn Lloyd (D-TN).

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Drug sponsors will be required to pay FDA "user fees" under a measure introduced by Sen. Edward Kennedy (D-MA) and Rep. Henry Waxman (D-CA) and supported by FDA.

Under the new law, FDA will be able to generate $300 million in new funds in the next five years, applying the money raised through the fees to speeding the drug approval process. The agency's target is to review breakthrough drugs in six months. All other drugs would be reviewed in 12 months.

FDA's plans include increasing its drug review staff from 1,000 to 1,600 in the next four years.

Drug sponsors will pay $100,000 for each new drug application this year. Within five years, the fee will rise to $233,000. Every manufacturing facility approved by FDA will be charged $60,000 a year. This fee will increase to $138,000 within five years.

A third kind of fee will require drug companies to pay FDA $5,000 a year for every drug they have on the market. This is scheduled to increase to $14,000.

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Under tax legislation passed by Congress at the end of the session, Medicare is required to cover **self-administered oral cancer drugs** which are used for the same indication and contain the same active ingredients as drugs that would be covered if they were administered intravenously in a physician's office. The change goes into effect Jan. 1.

The language was part of S.1996, the Medicare Cancer Coverage Improvement Act of 1991, introduced by Sens. John Rockefeller (D-WVa) and John Chafee (R-RI). The requirement could save money for Medicare by avoiding physician charges; in addition, oral administration is preferred by patients and physicians, and saves travel costs for patients, the sponsors said. The House version, H.R.3826, was introduced by Rep. Sander Levin (D-MI).

The legislation was endorsed by the National Alliance of Breast Cancer Organizations, the National Coalition for Cancer Survivorship, Cancer Care Inc., Assn. of Community Cancer Centers, the American Society of Clinical Oncology, and the Assn. of American Cancer Institutes.

Two provisions which were cut from the final legislation included in the tax bill H.R. 11, would have required the Medicare program to adopt a uniform policy on "off-label" uses of FDA-approved anticancer drugs, based on the medical compendia, and required Medicare to evaluate payment for the patient care costs of beneficiaries enrolled in clinical trials.

The Congressional Budget Office estimated that all three provisions would have required no additional cost to the Medicare program. However, the White House Office of Management & Budget estimated the act would cost $30 million, a figure called "outrageous" by supporters of the legislation.

Harmon Eyre, chairman of ASCO's Public Issues Committee, in a letter to Rockefeller and Levin, said, "The benefits of your legislation come at no significant additional cost to the Medicare program. If unlabeled indications and patient costs associated with clinical trials are not covered, patients and their physicians will likely opt for a reimbursable therapy. Covering [these costs] will mean that patients get therapy with the greatest potential to help them."

Tamoxifen Trial Enrolls 19% Of Total Needed, But Few Minorities: Fisher

The NCI-sponsored Breast Cancer Prevention Trial has randomized 3,088 women as of Oct. 12, slightly more than 19 percent of the 16,000 women needed for the study, principal investigator Bernard Fisher told **The Cancer Letter** this week.

"We are very excited about that; we are nearly at 20 percent since enrollment began on June 1," Fisher said.

The $60 million, placebo-controlled study to evaluate the preventive effects of tamoxifen in women at increased risk for breast cancer is being conducted at more than 270 sites in the U.S. and Canada, and is coordinated by the National Surgical Adjuvant Breast & Bowel Project, which Fisher chairs (**The Cancer Letter**, May 8).

In a recent presentation to the National Cancer Advisory Board, Fisher said that as of Aug. 31, investigators had done 28,837 risk assessments, finding that two-thirds of the women, or 19,246, are eligible for participation based on the risk assessment.

Of the women who are eligible based on the risk assessment, 36 percent are in the youngest age group (35-49), 30 percent are in the 50-59 age group, and 33 percent are over 60, Fisher said.

However, more younger women are enrolling. Of the women randomized as of late last month, 43 percent are in the younger age group, 28 percent are in the middle group and 29 percent are over 60.

The risk profile on each potential subject comes into the trial's central data center by facsimile, and the information is entered into a computer, which, Fisher said, "spits out the risk profile, which is faxed back to the clinic." The risk assessment is based on a model developed by Mitchell Gail of NCI and is designed to identify women who are at increased risk of getting breast cancer based on their family history and history of biopsies or diagnosis of lobular carcinoma in situ.

Fisher pointed out that once a woman is determined eligible based on her risk assessment, she then goes through a total health assessment involving gynecological exam, mammogram, and other tests, which can take a few months to complete.

"Newspapers have said, 'Aha, you're getting 30,000 risk assessments and you only have 2,000 women participating. The NCAB and NCI are having a hard time getting patients into this study.' That is just another misconception of numbers," Fisher told the NCAB. Some women have not reached the point in the "pipeline" when they can be randomized, he said.

"All we can say is, of 6,000 risk assessments, 4,000 women were eligible, 1,302 were randomized, or 32 percent of patients have been randomized, which is higher than we had anticipated," Fisher said. "We thought if we got 10 percent into the study, we would be on target."

Minority Enrollment Low

A major problem the investigators have encountered is the low participation of minority women, Fisher said. Of the risk assessments that have been done, only 4 percent have been for non-white women. Only 2 percent of the women who have been randomized are non-white.

Each center participating in the study had to have a program to encourage entry of minority women and the socioeconomically disadvantaged, Fisher said.

"This is a common problem which has been noted in all studies, screening trials and so on, and is a most difficult problem," Fisher said. "We are making every effort we can. We will increase our efforts." He noted that most of the women entered onto the study so far have been self-referred.

Fisher said the problem of minority recruitment would be a major topic of discussion at an upcoming meeting of the trial's investigators. "The participation of minority women is low and we are unhappy about that," he said.

President's Cancer Panel Chairman Harold Freeman commented, "The study would be much more important in its conclusions if somehow you could separate out the meaning of this problem in poor women across race, and also sort out the meaning of race."

A related issue is the cost to women participating in the study. Unless their insurance covers preventive care, women have to pay for the pelvic exam, mammogram, and other tests prior to entry onto the trial.

"The fact is that insurance is geared to providing coverage of diagnosis and treatment of acute illness, and has focused on unpredictable catastrophic events rather than routine care," Fisher told the NCAB. "Very few insurance plans cover preventive services. There are some costs to this study, not many. The requirements are only related to what would be good health care. A woman gets a pelvic examination, she gets a mammogram, she gets the kinds of things that should be done anyhow."

Incidentally, Fisher said, "one of the rewards of this study, which is coming out now in these risk assessment programs, is that we are picking up women who do have breast cancer, who do have endometrial cancer, who have other problems. So this is a public health kind of an effort."

Fisher said the investigators have been "remarkably innovative" in their attempts to reduce the costs of the tests. For example, in Pittsburgh, a blood test that would normally cost $60 to $70 is being done for $8, he told **The Cancer Letter.** In addition, there is some money set aside for women who cannot afford to pay for the tests.

Investigators are planning several studies associated with the trial, including studies of ocular events, endometrial changes, bone changes, and genetic studies. The investigators also will collect blood from the subjects for long-term storage. "We think the trial will have tremendous implications for studies of genetics," Fisher said.

In summary, Fisher said, "This trial is very carefully conducted, closely monitored, and the alternative to this as far as I'm concerned--the use of tamoxifen in women to prevent breast cancer without such a study--would lead to therapeutic anarchy."

NCAB member Sydney Salmon said the Breast Cancer Prevention Trial "is perhaps the most important trial launched by NCI in the 1990s."

NCI Div. of Cancer Treatment Director Bruce Chabner asked about the projected incidence of endometrial cancer for those women taking tamoxifen. "My own conclusion from your data is that it is not statistically significant," he said.

"In our estimate in the risk-benefit analysis, we've looked at a two-fold increased risk of endometrial cancer, which is consistent with clinical trials data for women with breast cancer and also consistent with data for estrogen replacement therapy," said Leslie Ford, chief of the Community Oncology & Rehabilitation Branch in the Div. of Cancer Prevention & Control.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. 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.

Title: Consolidated Cancer Information Service
Deadline: Approximately Nov. 16

The International Cancer Information Center, National Cancer Institute, is seeking a contractor for a project with a primary objective to development and management of an information services for health professionals. Based on the responses received, this acquisition may be solicited as a 100 percent small business set aside, SIC code 7375 with a size standard of (14 million). This is not an RFP and does not commit NCI to award a contract now or in the future. No RFP is available at this time.

In an effort to improve the effectiveness of information dissemination, ICIC plans to unify the production and dissemination of its information services, through a single Membership Service, providing the public with access and assistance through one point of contact. The way ICIC plans to achieve these goals is by consolidating production and distribution of its information services by using a contract mechanism to develop and maintain a service program which has yet to be named. It will be referred to in this document as the "Membership Service."

Specifically, under this contract mechanism, a contractor shall extensively plan and provide: 1) a service desk system and a fulfillment system for responding to customer initiated telephone, mail, fax or E-mail requests for information, membership, and information products/services, 2) publications, graphic design, typesetting, printing, and mail/delivery services, 3) membership service marketing services, 4) member billing, accounting, collection, and rebate services.

The contractor shall collect from a customer who wishes to be a member of the Membership Service--including any individual or organization located anywhere in the world--a single, flat yearly fee. Payment of this fee will make available to a member any or all of the products/services provided through this contract. The contractor shall provide to members the following products/services: 1) information about and assistance with the ICIC databases, 2) information on the availability of the ICIC databases and assistance in selecting and initiating service with an ICIC licensed vendor, 3) limited access time to the ICIC databases from any licensed vendor, 4) information on and direct access, through the Membership Service 800 telephone number, to CancerFax and PDQ search service for health professionals, 5) information on and a reservation service for PDQ and Cancerlit training from any participating ICIC licensed database vendor and PDQ and/or Cancerlit training sponsored by NCI, 6) information about and single copies of or single subscriptions to any or all ICIC publications, 7) information on and direct 800 number telephone access (routed electronically from the contractor by contractor customer service personnel) to technical expertise in the ICIC for certain types of technical questions related to ICIC products/services, such as assistance with PDQ search strategies, 8) information on and/or referral to non-ICIC cancer information products/services, such as NCI grants, NCI training, scientific research at NIH, etc.

The contractor shall provide nonmembers with access to: 1) mechanisms for joining the service, 2) general information on and referral to sources for ICIC information products/services outside the Membership Service, such as the non 800 number for CancerFax, the Cancer Information Service 800 number for PDQ searches for health professionals, and the Government Printing Office Sales Program and Depository Library Program for publications, 3) information on and/or referral to non-ICIC cancer information products/services, such as NCI grants, NCI training, scientific research at NIH, etc., 4) information on an direct 800 number telephone access (routed electronically from the contractor by contractor customer service personnel) to technical expertise in the ICIC for certain types to technical questions related to ICIC products/services (such as assistance with PDQ search strategies).

Mandatory criteria: Offeror shall demonstrate the ability to meet the requirements of the Quality Assurance Through Attributes Program (GPO Publication 310.1). A three year award of this project is anticipated by October 1993.

Interested companies may submit an original and two copies of a capability statement specific to this project no later than 2 p.m. EST on Nov. 16. A preproposal conference is anticipated.

Contract officer: Charles Jackson
RCB Executive Plaza South Rm 620
301/496-8611

RFP NCI-CN-25502-51

Title: Evaluation of the effect of a fat modified diet on hormones during adolescence
Deadline: Approximately Nov. 13

NCI's Div. of Cancer Prevention & Control is conducting a study to evaluate the effect of a fat-modified diet on hormones during

childhood and adolescence. The study is being performed ancillary to the Diet Intervention Study in Children (DISC), a randomized clinical trial sponsored by the Div. of Epidemiology and Clinical Applications, National Heart, Lung and Blood Institute (NHLBI). The objectives of DISC are to determine whether a fat-modified diet during childhood and adolescence will lower LDL-cholesterol and to assess the feasibility and safety of this diet. The objectives of the NCI ancillary study are to evaluate the effect of this fat-modified diet on sex hormones and to correlate characteristics of children and adolescents, such as age, Tanner stage, anthropometry, diet, and physical activity, with sex hormone levels.

This solicitation seeks a contractor to store serum specimens collected for DISC, develop and issue an RFP for a laboratory to perform serum hormone assays, evaluate the offerors' proposals, award a subcontract to the best qualified laboratory offering the best buy for the Government, and monitor the laboratory to ensure high quality work and fulfillment of contractual obligations.

Contract specialist: Christine Ptak
RCB Executive Plaza South Rm 635
301/496-8603

RFP NIH-NIAID-DAIDS-93-13

Title: Antigenic variation of HIV-1 and related lentiviruses

Deadline: Approximately Dec. 22

The Vaccine Research and Development Branch, Basic Research and Development Program, Div. of AIDS, National Institute of Allergy and Infectious Diseases has a requirement for a contractor to receive and process virus-infected, human-derived samples on a large scale basis and to isolate, expand and immunologically characterize HIV-1 and related lentiviruses from these samples. The selected contractor will be responsible for: 1) performing virus isolation, expansion, and characterization from samples supplied to the Contractor; 2) performing specific immunological assays for HIV and related lentiviruses; 3) classifying all virus isolates received into antigenic subgroups based upon serological/immunological assays; 4) securing, receiving, cataloging, processing, and storing samples from both domestic and international sites, and distributing samples to other investigators; 5) providing inventory and a Database Management System; 6) providing facilities and resources; 7) reporting progress according to reporting requirements; 8) meeting with the Project Officer; 9) obtaining clearance for publication; and 10) implementing an orderly transition to a successor Contractor. One contract will be awarded.

Requests for the RFP may be directed in writing to: Chief, Contract Management Branch, National Institute of Allergy and Infectious Diseases, Solar Building, Room 3C07, Bethesda, MD 20892; fax: 301/402-0972. Provide three self-addressed mailing labels.

RFAs Available

RFA CA-92-28

Title: **Clinical trials of cancer therapy with biological response modifiers**

Letter of Intent Receipt Date: Oct. 30

Application Receipt Date: Dec. 22

The Biological Response Modifiers Program in NCI's Div. of Cancer Treatment invites applications to establish cooperative agreements for Clinical Trials of Cancer Therapy with Biological Response Modifiers (CATBRMs), for the development of novel approaches to such therapy.

Groups constituted according to the guidelines given in the RFA are eligible to apply. Applying groups may include members from academic, non-profit, and for-profit institutions. Domestic and foreign organizations and institutions (non-profit or for-profit) are eligible. Governments and their agencies are also eligible. Applications from women and members of minority groups are encouraged.

Awards will be made as cooperative agreements (U01). Substantial NCI programmatic involvement with the recipient during performance of the planned activity is anticipated. Applicants will be responsible for the planning, direction, and execution of the proposed project. This RFA is a reissuance of RFA CA-92-01. Applicants who did not apply to the first announcement, or who applied but did not receive an award, are encouraged to respond to this RFA. However, this reissued RFA is a one-time solicitation.

NCI plans to make up to six awards for project periods up to four years, and has set aside $1.5 million total costs for the initial year's funding. Applicants may request no more than four years of support. The earliest possible starting date for the initial annual period will be July 1, 1993.

Cooperative Agreements will be established to support Clinical Study Groups for Cancer Therapy with Biological Response Modifiers (CATBRMs), for the design and execution of novel clinical trials with biological response modifiers (BRMs). CATBRM groups will be peer-reviewed groups of highly experienced clinical and preclinical investigators who have the unique technical capabilities to study new agents in early clinical trials and to address hypothesis-driven issues of mechanisms of action. The "Research Goals and Scope" of the RFA will require a novel plan for clinical study of a given new agent or agents, adequately supported by prior preclinical, and if available, clinical, results. The application must describe how its objectives are in accord with the applicant's own interests and experience. The applicant must provide evidence of access to the agent(s) proposed for study. A detailed protocol for an initial clinical trial must also be included. The NCI will facilitate the institution of a peer-reviewed, investigator-initiated trial, participating according to Terms of Cooperation outlined in the RFA.

Each CATBRM study group will be composed of: a Principal Investigator; one or more laboratory programs, each headed by a Program Leader, with the demonstrated expertise to design and carry out assays for the appropriate monitoring of patients on the study; one or more clinical programs, each headed by a Program Leader, with demonstrated expertise in conducting clinical trials of BRMs; and the NCI Program Director.

Letters of intent are to be sent to: Dr. Jon Holmlund, Biological Resources Branch, Biological Response Modifiers Program, NCI-FCRDC, Bldg 1052, Room 253, Frederick, MD 21702-1201; phone 301/846-1098, fax: 301/846-5429.

RFA AI-92-08

Title: **Papillomavirus in vitro cell culture systems**

Letter of Intent Receipt Date: Nov. 6

Application Receipt Date: Dec. 10

The Antiviral Research Branch of the Div. of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases (NIAID), invites Cooperative Agreement applications from organizational entities willing to participate, with the assistance of the NIAID, in furthering innovative in vitro approaches to the study of papillomavirus infections and their therapeutic control. The research goals of this solicitation are to stimulate the use of in vitro papillomavirus replication systems for research on (1) the events of papillomavirus replication and pathogenesis; and (2) the antiviral potential of experimental therapeutic agents.

Applications may be submitted by domestic and foreign for-profit and non- profit organizations, public and private. Applications from minority individuals and women are encouraged.

The funding mechanism to be used is the cooperative agreement (U01). The cooperative agreement differs from the traditional research grant in that there will be substantial programmatic involvement of NIAID staff above and beyond the levels required for traditional program management of grants.

It is expected that at least one application will be funded for

a four-year period, contingent upon the receipt of a sufficient number of meritorious applications. It is expected that the total direct costs for the first year for successful applications will be around $175,000. However, individual awards may be higher or lower.

Papillomavirus infection is a rapidly increasingly serious clinical problem in the U.S. and around the world. None of the currently available therapies has acceptable efficacy. The failure to develop a safe and effective therapy for these infections is due, in part, to the inability to replicate virus in vitro. In the past few years, several research groups have developed in vitro systems in which many of the events of papillomavirus replication have been reported to occur. The availability of these systems provides an unparalleled opportunity to investigate the mechanisms of papillomavirus replication and pathogenesis at a molecular level. This basic research may also result in the identification of viral genes which are promising targets for therapeutic intervention. In addition, these systems should provide a means to evaluate the potential anti-papillomavirus activity of experimental agents and provide a rational basis for selecting agents whose activity warrants further study in the animal models. The proposed systems may utilize either a human papillomavirus (HPV) or an animal papillomavirus as a model of HPV infection.

Letter of intent may be directed to: Dr. Olivia Preble, Chief, Microbiology and Immunology Review Section, Scientific Review Branch, National Institute of Allergy and Infectious Diseases, Solar Building, Room 4C20, 6003 Executive Blvd., Rockville, MD 20892. Direct requests for the RFA and inquiries on programmatic issues to: Dr. Catherine Laughlin, Chief, Antiviral Research Branch, Div. of Microbiology and Infectious Diseases, NIAID, Solar Building, Room 3A-22, 6003 Executive Boulevard, Rockville, MD 20852; phone 301/496-8285.

RFA AI-92-13
Title: **Women and Infants Transmission Study (WITS II)**
Letter of Intent Receipt Date: Oct. 26
Application Receipt Date: Jan. 14

The Vaccine Trials and Epidemiology Branch of the Div. of AIDS of the National Institute of Allergy and Infectious Diseases announces the availability of an RFA for funding the continuation of the Women and Infants Transmission Study (WITS). The purpose of this RFA is a competitive renewal of WITS I, a multi-site epidemiologic cohort study of HIV infected pregnant women and their offspring. New sites not participating in WITS I are encouraged to apply, as are current WITS I sites. Specific aims are: (1) to assess the effects of pregnancy on HIV disease progression, (2) determine maternal cofactors related to maternal-infant transmission and timing of transmission, (3) assess early diagnostic techniques to identify HIV-infected fetuses and infants, (4) evaluate the natural history of HIV infection among infants during an era of antiretroviral and other therapeutic modalities, and (5) assess the feasibility of future vaccine trials in this population.

Applications may be submitted by domestic non-profit and for-profit research institutions; public and private organizations, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged.

Applicants funded will be supported through NIH Cooperative Agreements (U01). This RFA solicitation represents a onetime competition for a four year award.

Approximately $5,000,000 will be available for funding the total costs for the initial year of awards made pursuant to this RFA. NIAID anticipates making four to eight awards. The earliest anticipated award date will be July 1993.

The growing magnitude of the HIV epidemic among women of childbearing age and their infants is becoming apparent in many areas of the U.S. The percentages of AIDS cases among women and children are increasing more rapidly than for any other risk groups. In the 1990s, the AIDS epidemic will continue to attack African American and Hispanic women and children in disproportionately high numbers. To date, more than 80 percent of pediatric AIDS cases have been caused by maternal-infant transmission. Moreover, virtually all new cases of pediatric HIV infection in infants and children will be due to maternal-infant transmission.

In the face of this growing epidemic among women and their offspring, there are a number of critical and unanswered questions related to HIV infection during pregnancy and maternal-infant transmission. These include the impact of pregnancy on the health of HIV-infected women, mechanisms and timing of vertical HIV transmission, rates of maternal-infant transmission (overall and among different subpopulations of at-risk pregnant women), as well as understanding cofactors related to HIV transmission.

The Women and Infants Transmission Study II will be a focused continuation of the current Women and Infants Transmission Study (WITS I), which began in 1988. WITS II will continue and expand this prospective natural history cohort study of HIV positive pregnant women and their offspring. It will rely heavily on the core protocols in place for WITS I, but will also encourage new projects that may shed light on our understanding of maternal-infant HIV transmission and early diagnosis of fetal or infant HIV infection. New applicants should mention to the NIAID contact person that they are new applicants, and they will receive a summary of the WITS I protocol, which is necessary in preparing a response to this RFA.

Inquiries may be directed to Dr. Mary Glenn Fowler, Vaccine Trials and Epidemiology Branch, Div. of AIDS, NIAID, 6003 Executive Blvd, Room 2A24, Bethesda, MD 20892; phone 301/496-6177, fax 301/402-1506 or 301/480-5703.

NCI Contract Awards

Title: Support contract for the public health agency initiative
Contractor: MayaTech Corp., Silver Spring, MD; $1,500,000.

Title: Early detection research network MAO No. 2--Cellular and molecular studies
Contractors: Univ. of Alabama at Birmingham, $773,394; Univ. of Pittsburgh, $1,015,162.

Title: Surveillance, Epidemiology & End Results expansion
Contractors: Univ. of Southern California, $13,103,642; Northern California Cancer Center, $3,362,685.

Title: Prostate, Lung, Colorectal and Ovarian cancer screening trial--study coordination and data management center
Contractor: Westat Inc., Rockville, MD; $9,942,878.

Title: PLCO cancer screening trial--laboratory
Contractor: Univ. of California, Los Angeles, $1,337,719.

Title: PLCO cancer screening trial--screening centers
Contractors: Univ. of Pittsburgh, $4,621,861; Henry Ford Hospital, Detroit, $10,382,790; Univ. of Minnesota, $10,279,827; Univ. of Colorado Health Sciences Center, $7,601,468; Marshfield Medical Research & Education Foundation, Wisconsin, $4,999,919; Straub Pacific Health Foundation, Honolulu, $7,313,236; Washington Univ. School of Medicine, $7,104,576; Georgetown Univ., $4,817,191; Maimonides Medical Center, Brooklyn, $7,507,110; Univ. of Utah, $4,919,142.