THE CANCER LETTER

Vol. 18 No. 4
Jan. 24, 1992

Price $215 Per Year US, Canada.
$240 Per Year Elsewhere

P.O. Box 15189 Washington, D.C. 20003 Telephone 202-543-7665

Healy Transfers $15 Million From NCI To Fund Cancer Research Around NIH; Another $16M Held

NIH Director Bernadine Healy has transferred $15 million from NCI's fiscal 1992 appropriation to pay for cancer research funded by other NIH institutes. Congress gave Healy the authority to consign to other institutes a portion of $160 million of the NCI budget. Healy also has asked NCI to hold another $16 million in reserve for possible transfer.

(Continued to page 2)

In Brief

Gilbert Fletcher, Father Of Modern Radiotherapy, Dead At 80 In Houston; Built First Cobalt-60 Unit

GILBERT FLETCHER, known worldwide as the father of modern radiotherapy, died Jan. 11 in Houston of heart failure. He was 80. During nearly half a century at M.D. Anderson Cancer Center, Fletcher designed innovative machines and introduced dramatic treatment concepts. In 1990, the American Cancer Society presented Fletcher with its highest award, the Medal of Honor, for "revolutionizing the field of radiotherapy and improving the quality of life" for thousands of cancer patients. Fletcher was chairman of radiotherapy at the center from 1948 to 1981, retiring from administrative duties at age 71. He continued to work over the past decade. Fletcher, with Leonard Grimmett, designed and constructed the first cobalt-60 unit and was the driving force behind development of the original high voltage linear accelerators. Fletcher proposed most of the principles of physics for radiation safety and therapeutic accuracy, and personally trained more than 200 physicians. . . . **IMMUNEX CORP.'S GM-CSF** (trade name Leukine) has been approved by FDA for use in cancer patients whose bone marrow transplants have failed. The drug was approved last March for the acceleration of marrow engraftment following autologous bone marrow trnsplantation. . . . **JOHN GOHAGAN** has been selected branch chief of the Early Detection Branch, Early Detection & Community Oncology Program, of NCI's Div. of Cancer Prevention & Control. Other new DCPC staff include: **Rachel Ballard-Barbash** rejoined DCPC as an epidemiologist in the Applied Research Branch, from the HHS Office of Disease Prevention; **Susan Krebs-Smith,** a nutritionist for the Applied Research Branch; **Gloria Stables,** nutrition specialist in the Diet & Cancer Branch; **James Crowell** joined the Chemoprevention Program as a pharmacologist. The following scientists were promoted to tenure: **Frank Cuttitta, Michael Birrer,** and **Stuart Baker. Claudia Baquet,** Cancer Control Science Program director, received Senior Executive Service Status.

$15 Million Transferred From NCI To Fund NIH Cancer Research

(Continued from page 1)

The $15 million was moved to 11 other NIH components. The largest amounts, $3 million each, went to the National Institute of Diabetes, Digestive & Kidney Diseases and the National Institute of Environmental Health Sciences.

Amounts of $1.5 million each went to the National Heart, Lung & Blood Institute, the National Institute of General Medical Sciences, and the National Institute on Aging. Another $1 million each went to the National Institute of Neurological Disorders & Stroke, the National Institute of Allergy & Infectious Diseases, and the National Eye Institute. Three institutes received $500,000 each: the National Institute of Dental Research, the National Institute of Child Health & Human Development, and the National Institute of Arthritis & Musculoskeletal & Skin Diseases.

The transfer took place with the involvement of the NCI Executive Committee, which reviewed projects proposed in support of cancer research submitted by other NIH institute directors. NCI placed emphasis on those areas highlighted in the FY92 appropriations conference report to make breast, prostate, ovarian, and cervical cancer high priorities. According to the NIH budget office, Healy then conducted a second review and selected additional projects.

Indicative of the projects selected were those in: brain tumor research, grants to study serum markers for benign prostatic hypertrophy and prostatitis, gastric cancer, effects of tamoxifen on heart disease, cell cycle regulation, breast cancer and birth control pill study, longitudinal DES study, aging and cancer, oral cancer, and skin cancer.

If Healy does transfer the full $31 million requested, that would mean that 11 percent of NCI's $277 million budget increase for FY92 would go to other NIH institutes.

Healy also retains the authority to transfer up to 1 percent from any institute's appropriation to another NIH appropriation, but Congress added a provision that those funds are to be used for emergency purposes only. Last year, Healy used this authority to fund the new James Shannon Awards.

$38 Million In Cuts, Transfers

NCI's FY92 appropriation was $1.989 billion, but the Institute's operating budget will probably end up around $1.951 billion, $38 million below the appropriation, NCI executives said last week.

In addition to the $15 million transfer and $16 million reserve for other institutes, there was an across the board Congressionally mandated $1.262 million reduction in travel expenses and $21.475 million reduction in salaries and expenses.

After taking out travel expenses for patients, NCI faces a 20 percent decrease from last year's actual travel expenses, NCI Deputy Director Dan Ihde told the Div. of Cancer Prevention & Control Board of Scientific Counselors last week.

Another unique provision in NCI's FY92 budget is the delay of $223 million which will not be available until the last day of the fiscal year.

"Despite these provisions, the Institute is extremely grateful to the support shown for cancer research during this 1992 budget process," Ihde said. "We can use the additional funds very effectively.

"From the language in the House, Senate and conference reports, we have a clear indication f the priorities and emphasis areas of the Congress," he continued. "Breast cancer, prostate, cervical, ovarian and lung cancer were all identified by Congress as needing special attention."

At the $1.951 billion level, NCI's budget will be broken out as follows:

▶Research project grants will get $100 million of the increase, and 10 percent increase over last year's level. "We will need to fund grants within the rules of the NIH cost containment plan, including tying the average increase of a grant to the biomedical inflator, limiting the average length to four years and fund a specific number of competing grants as assigned by NIH," Ihde said. "I can tell you that the challenge is real, given all of the parameters we need to operate within. It will require a hard look at the mix of the portfolio of our grants to ensure that the most cost effective proposals are funded."

▶Cancer Centers--Over $32 million will go into the centers line, split about evenly between the existing cancer center initiatives and the new SPORE concept

THE CANCER LETTER

Editor: **Kirsten Boyd Goldberg**
Associate Editor: **Lisa M. O'Rourke**
Contributing Editor: Jerry D. Boyd

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

Subscription rate $215 per year North America, $240 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter.

for breast, prostate and lung cancers. This represents a 30 percent increase over last year's level.

►Prevention and control will receive $106 million, a $21 million increase from last year, or 26 percent.

►Cooperative groups will get an additional $17 million for clinical trials, a 28 percent increase.

►National Research Service Awards have been held flat across NIH until Congress passes the NIH reauthorization bills.

►Research contracts will get an addition of $16 million.

►Intramural research would receive a 10 percent increase "including the support of our activities requiring NIH central services," Ihde said.

"What is the take-home message?" Ihde asked. "From our perspective, I'm gratified that support for cancer research appears to have become more of a priority to the American people as seen through the eyes of their elected representatives in Congress. However, it is clear that Congress expects that certain areas be given special attention.

"We have asked the extramural community to help answer this challenge by coming up with new and innovative approaches for certain cancer sites," Ihde said, referring to NCI's universal program announcement released last week (**The Cancer Letter,** Jan. 17). "There is no question that we can and will be able to develop initiatives that will have a positive impact on cancer mortality."

Priorities In Prevention & Control

DCPC Director Peter Greenwald last week outlined for his advisors how his $21 million increase will be spent. The budget increase demonstrated the importance of having concepts and programs in place, ready to be funded, he said.

"We looked at what we could accomplish this year. Since it generally takes 18 months from the time this board approves new concepts to the time investigators have approved grants or contracts to do the work, we obviously had to focus on mechanisms already approved by the board," Greenwald said.

"The Community Clinical Oncology Program was approved by the board in January 1989 with a strong BSC recommendation that we strengthen the prevention trials and control aspects of CCOPs. There also is Congressional language supporting CCOPs. Thus, this year we have allocated about half of our budget increase to CCOPs.

"These monies will be used for the following purposes: stabilize the budget for therapy trials, including those within the minority CCOPs, provide funding for chemoprevention trials initiated by CCOP investigators, fully fund the tamoxifen breast cancer prevention trial including study of the genetic process that underlies malignant transformation in breast cancer, and initiate a prostate cancer prevention trial [with the drug finasteride; see related story this issue]."

In addition, Greenwald said, the chemoprevention budget for preclinical phase 1 and 2 studies has been increased by $4.4 million. This program supports the master contracts the board approved last May. Other increases will go to the Women's Health Trial minority feasibility study, ASSIST, the polyp prevention trial, the Early Detection Network, and the patterns of care studies.

Budgeting 'Worrisome'

Greenwald also noted that a one-time budget increase presents potential problems if the funding level is not continued in future years.

"One factor that makes budgeting worrisome is uncertainty about out years," Greenwald said. "These decisions do create requirements for FY 1993 and later years. We are moving ahead in the belief that these initiatives are crucially important for the success of cancer prevention and control, and thus for the public."

DCPC Advisors Okay 'Omnibus' Prevention And Control PA

Advisors to NCI's Div. of Cancer Prevention & Control last week gave concept approval to an "omnibus" program announcement designed to generate R01 applications in all aspects of cancer prevention and control research.

The DCPC Board of Scientific Counselors unanimously approved the concept. DCPC staff explained that the division wants to use the R01 pool more effectively, and that if more applications are submitted, the review process could be better tailored to cancer prevention and control.

In 1990, 39 applications were submitted for prevention and control, 39 were approved, and five were awarded. In 1989, the numbers were 41 submitted, 38 approved, and four awarded.

Following is the text of the concept statement:

Omnibus cancer prevention and control research. Proposed program announcement; application receipt dates Oct. 1, 1992 and regular dates thereafter.

NCI invites applications for studies covering a broad range of research related to cancer prevention and control. 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 for profit and nonprofit organizations, public or private, units of state or local governments, and agencies of the federal government. Foreign organizations are not eligible, and domestic applications may not include foreign components.

DCPC conducts a broad array of cancer control research and application activities which 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:

▸Chemoprevention: preclinical and clinical studies related to the identification and evaluation of agents 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.

▸Diet and nutrition: role of nutrients, food groups, or other dietary components in cancer incidence. Influence of dietary factors on the modulation of cancer risk markers or intermediate endpoints. 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. Development of reliable analytical techniques for analyses of nutrients and other component in foods and biological fluids. Development of improved dietary assessment instruments and nutrient data bases. Identification of biological markers of dietary exposure and compliance and the role of dietary components on the modulation of early indicators of cancer risk.

▸Screening and early detection of cancer: research to significantly reduce cancer morbidity and morality through early detection including identification of markers of risk, exposure, and premalignant events of progression which can be used to identify subpopulations 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.

▸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.

▸Rehabilitation and pain management: research that focuses on the application of rehabilitative medicine and pain management for cancer patients.

▸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.

▸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.

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

Requests for further information would be directed to the relevant program directors, list as follows:

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

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

Screening and early detection of cancer: Dr. Barnett Kramer, 301/496-8541.

Community oncology and 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.

NCI Plans Trial Of Finasteride In Stage A1 Prostate Cancer

Advisors to NCI's Div. of Cancer Prevention & Control have endorsed a proposed study of the drug finasteride as a preventive agent for prostate cancer.

Finasteride (trade name Proscar, by Merck, Sharp, and Dohme), is a 5-alpha reductase inhibitor, a steroid analog of testosterone, which in clinical trials has reduced levels of dihydrotestosterone and prostate specific antigen in prostate cancer patients.

Merck's studies to date have found the drug well tolerated and active in reducing hormone levels, but have not proven antitumor activity. Therefore, the company turned to NCI for help in devising a study of early-stage patients, according to a company representative.

The proposed study is one aspect of a new emphasis at NCI on prostate cancer, NCI officials said. "While we have frequently discussed the need for expanding our research base in breast cancer, prostate cancer has received one-fifth the funding of breast cancer, and at present we have few options other than hormonal therapy for metastatic disease," Bruce Chabner, director of the Div. of Cancer Treatment, told his advisory board recently. "During the coming year, we intend to place a high priority on new initiatives in this disease."

DCPC Director Peter Greenwald said he wants to "put more emphasis on prevention trials, and do it largely though the CCOP program."

NCI staff last week presented a proposal to the DCPC Board of Scientific Counselors for a double blind randomized trial to test the efficacy of finasteride in preventing the progression of stage A1 prostate cancer.

Standard medical care for this stage is observation for disease progression after the initial transurethral resection.

Approximately 10,000 patients (there are roughly 11,000 estimated cases per year) will be randomized to receive finasteride or placebo and will be followed for at least 10 years. There will be a 90 percent power to detect a 25 percent decrease in new tumors or local recurrence.

The study would be conducted as an intergroup trial through one of the Community Clinical Oncology Program research bases, with participation of CCOPs and minority based CCOPs.

The lifetime risk of developing prostate cancer is 9.6 percent for African-American men and 5.2 percent for white men.

There are also familial patterns of inheritance. Men who have a first degree relative with prostate cancer have an estimated 2.1 to 2.8 times greater risk of developing the disease than the general population. Those with a first degree relative and a grandfather or uncle with prostate cancer have a risk that may be six times greater than the general population.

Finasteride is being used in patients with benign prostatic hypertrophy, and is expected to get FDA review later this year for that use. It is likely that the drug will be commonly used by the end of this decade for BPH, said Otis Brawley of DCPC.

Although the concept of the prevention trial did not require approval of the DCPC board, the board voted unanimously to endorse the trial as it was described by NCI staff.

NCI will solicit letters of intent from institutions wishing participate in the trial, and expects to begin development of the protocol between February and May, involving Merck and participating cooperative groups.

The protocol would require FDA approval. DCPC staff estimated that the protocol could be finalized by this fall. Merck would provide the drug and its distribution to the clinical sites, said Brawley.

AIDS Research

FDA Sanctions Over 360 Studies To Test AIDS, OI Therapies

The Food & Drug Administration has given all potential AIDS drugs a 1AA classification--the highest priority--in the agency's new drug review system. The agency's expedited review of zidovudine (AZT), which became the first approved treatment for AIDS, served as the prototype for the 1AA classification.

FDA has sanctioned more than 360 investigational new drug studies to test drugs that may have potential in treating AIDS and related conditions. At present, IND studies involve about 90 different antiviral or immunomodulating drugs. Many trials are now investigating the use of two or more experimental therapies in combination.

Following is a listing of all potential AIDS therapies undergoing FDA approved clinical testing. Requests for additional information on any of the products should be directed to the sponsor or to the AIDS Clinical Trials Information Service, 1-800-TRIALS-A.

INDs for Experimental Antiviral Agents

GLQ223--GeneLabs Inc., Redwood City, CA (415) 369-9500.

SC48334--G.D. Searle & Co., Chicago, IL, (312) 982-8651.

DHEA--Elan Corp., Atlanta, GA, 404/534-8239.

Ribavirin--Viratek/ICN Pharmaceuticals, Costa Mesa, Calif. (800) 556-1937.

DDC--Hoffmann-La Roche Inc., Nutley, N.J. (201) 235-5000. National Cancer Institute, (301) 496-6631.

AL 721--National Institute of Allergy & Infectious Diseases, (301) 496-5717.

Dextran Sulfate (UA001)--Ueno Fine Chemicals Industry Ltd., New York, N.Y. (202) 452-8666. NIAID, (301) 496-5717. National Jewish Center for Immunology & Respiratory Diseases, Denver, Colo. (303) 388-4461.

R-beta-ser interferon--Triton Biosciences, Alameda, Calif. (415) 769-5200.

D4T (didehydrodeoxythymidine)--Bristol Myers, Wallingford, Conn. (203) 284-6000.

AZDU (azidouridine)--Triton Biosciences, Almeda, Calif. (415) 769-5200.

VaxSyn HIV-1--MicroGeneSys Inc., Meriden, Con. (203) 686-0800.

DTC (Imuthiol)--Connaught Labs, Swiftwater, Pa. (717) 839-7187.

Thymopentin--Immunobiology Research Inst., Annandale, N.J. (201) 730-1799.

Peptide-T--National Institute of Mental Health, (301) 443-4515. Reed, McFadden, Toronto, Canada, (416) 941-9739.

Isoprinosine--Newport Pharmaceuticals, Newport Beach, Calif. (714) 642-7511.

Alpha interferon--Hoffmann-La Roche Inc., Nutley, N.J. (201) 235-5000. Schering-Plough Corp., Kenilworth, N.J. (201) 558-4000.

Oral alpha interferon--Interferon Science, New Brunwick, N.J. (201) 249-3250.

Gamma interferon--Genentech Inc., San Francisco, Calif. (415) 266-1000.

CD4 protein--Genentech Inc., San Francisco, Calif. (415) 266-1614. Biogen Inc., Cambridge, Mass. (617) 864-8900.

AS-101--NPDC-AS101 Inc., New Brunswick, N.J. (908) 249-3232.

CD4-IgG--Genentech Inc., San Francisco, Calif. (415) 266-1614.

Interleukin-2--Hoffmann-La Roche Inc., Nutley, N.J. (201) 235-5000.

r-GM-CSF--Sandoz Pharmaceuticals Corp., East Hanover, N.J. (201) 386-7500. Schering-Plough Corp. Kenilworth, N.J. (201) 558-4000.

r-G-CSF--Amgen, Thousand Oaks, Calif. (805) 499-5725.

Salk HIV immunogen--Immunization Products Limited, Seattle, WA (619) 587-1407.

Soluble CD4-PE 40 (Pseudomonas Exotoxin A)--Upjohn Co., Kalamazoo, MI. (616) 323-4696.

New Drug Approvals

Last October, FDA approved dideoxyinosine (DDI) for treating patients at advanced stages of infection with the AIDS virus. DDI is approved for use in adult and pediatric AIDS patients who are intolerant to or whose health has significantly deteriorated while on zidovudine.

Also last fall, FDA approved foscarnet for the treatment of AIDS patients with cytomegalovirus (CMV) retinitis. On January 3, FDA approved epoetin alfa, a genetically engineered form of the protein erythropoietin to treat the anemia that some patients with AIDS or patients at earlier stages of infection with the AIDS virus experience while taking zidovudine. Epoetin alfa is marketed by Amgen Inc. of Thousand Oaks, CA, under the trade name Epogen and by Ortho Pharmaceutical Corp. of Raritan, NJ, under the trade name Procrit.

Last June, FDA authorized release of ddC under a treatment IND. DDC is being made available to patients with AIDS and advanced ARC who fail to benefit from or are unable to tolerate treatment with AZT.

Last November, FDA authorized pre-approval availability of 566C80, for treatment of pneumocystis carinii pneumonia. The drug will be made available under a treatment IND protocol that will grant access to the drug to physicians treating patients with PCP who cannot tolerate treatment with trimethoprim-sulfa.

There are a number of drugs which are either already approved or are being developed for opportunistic infections and cancers associated with AIDS. Ganciclovir is approved to treat AIDS patients with sight-threatening CMV retinitis, and aerosolized pentamidine is now commercially available for use in preventing the occurrence and recurrence of PCP.

Two recombinant human alpha interferons have also been approved for the treatment of Kaposi's sarcoma. The injectable form of pentamidine has been approved for the treatment of PCP.

In addition, fluconazole has been approved for the treatment of candidiasis and cryptoccocal meningitis.

Experimental Anti-Infective Agents

Trimetrexate--National Institute of Allergy & Infectious Diseases, (301) 496-5717.

Aerosol pentamidine--Fisons Corp., Bedford, Mass. (617) 275-1000. LyphoMed, Rosemont Park, Ill. (312) 390-6500. NIAID (301) 496-5717.

Ansamycin--Adria Laboratories, Dublin, Ohio (614) 764-8100.

Piritrexim--Burroughs Wellcome Co., Research Triangle Park, NC (919) 248-3000.

Immune globulin IG-IV--Sandoz Pharmaceuticals Corp., East Hanover, NJ, (201) 386-7500. Alpha Therapeutics, Los Angeles, Calif. (213) 227-7526. Miles Inc., West Haven, Conn. (203) 937-2205.

Nystatin--Squibb Corp., Princeton, N.J. (609) 921-4650.

Clofazimine--San Francisco General Hospital, San Francisco, Calif. (415) 821-5531.

Sandostatin--Sandoz Research Institute, East Hanover, N.J. (201) 386-7500.

Diclazuril--Janssen Pharmaceutica, Piscataway, N.J. (201) 524-9591.

Dapsone--Jacobus Pharmaceutics, Princeton, N.J. (609) 921-7447.

Clindamycin--Mark Jacobson, MD, San Francisco, CA.

Pyrimethamine--Burroughs Wellcome, (919) 248-3000.

Itraconazole--Janssen Pharmaceutica (201) 524-9591.

FIAC and FIAU--O'Classen Pharmaceutical, San Rafael, Calif. (415) 258-4550.

Experimental Immunomodulating Agents

Lmphoblastoid interferon--Burroughs Wellcome (919) 248-3000.

Cryptosporidium immune colostrum--Immucell Corp., Portland, ME (207) 878-2770.

Experimental Anti-Neoplastic Agents

Piritrexim isethionate--Burroughs Wellcome, (919) 248-3000.

Doxorubicin--National Institute of Allergy & Infectious Diseases, (301) 496-5717.

Tumor necrosis factor--Genentech Inc., (415) 266-1000.

Menogaril--National Cancer Institute, (301) 496-6641.

M-BACOD (with Retrovir)--National Institute of Allergy & Infectious Diseases, (301) 496-5717.

Vaccines In Development

R-GP-160--Immuno AG, New York, N.Y. (212) 951-5430.

GP120--Genentech Inc., S. San Francisco, CA (415) 266-1614.

RG-83894--Immunization Products, Ltd. San Diego, Calif. (619) 431-7080.

GP120--Chiron, Emeryville, CA, and CIBA-GEIGY, Basel, Switzerland, 011-4161-696-5961.

VaxSyn HIV-1 (gp160)--MicroGeneSys, Meriden, CT (203) 686-0800.

Vax Syn HIV-1 (rp24)--MicroGeneSys.

GP120--Chiron Corp., Emeryville, Calif.

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-21051-25

Title: Cancer Risk in women with augmentation mammaplasty

Deadline: Approximately March 16

NCI's Environmental Studies Section, Environmental Epidemiology Branch, is seeking a contractor to perform the above named project. This contract will support NCI in performing a retrospective cohort study of women having undergone augmentation mammaplasty. Plans are to assemble a cohort from a variety of different surgery practices of approximately 12,000 women having undergone such operations during the period 1960 to 1985 (median follow-up of 10 years is sought) and to abstract patients' medical records for pertinent identifiers, operation details and other historical factors. Also to be assembled will be a comparison cohort from the same plastic surgery practices as the breast augmentation patients of approximately 4,000 women with other types of plastic surgery, who will serve as a comparison cohort.

Both cohorts will be traced over time and will be sent questionnaires to elicit details on risk factors for a variety of diseases and medical events subsequent to their operations. Any breast biopsies or occurrences of cancer will be validated by retrieval of appropriate medical records.

The contractor must be capable of assisting NCI in assembling the required cohorts, which will require contact with a number of plastic surgery practices and professional organizations. In addition, the contractor shall be responsible for developing abstract forms and questionnaires to be used in the project, tracing women over time, performing telephone interviews for non-responders to the mailed questionnaires, obtaining death certificates for deceased subjects, validating occurrences of subsequent medical events, developing coding schemes for collected data, computerizing collected data and assisting with deriving expected values of subsequent event (both from the internal cohort and external standards) for epidemiologic analyses of long-term events among the cohort of interest.

The contractor must be sensitive to the unique privacy issues involved with this project and assure extreme confidentiality of the data collected. The total estimated level-of-effort to be provided for a four-year period is 79,040 direct labor hours. Award is anticipated by Sept. 30, 1992.

Contracting officer: Nancy Coleman
RCB Executive Plaza South Rm 620
301/496-8611

RFP NCI-CP-21008-21

Title: Continuation of followup on participants in the breast cancer detection demonstration project

Deadline: Approximately March 16

NCI's Environmental Epidemiology Branch, Div. of Cancer Etiology and the Cancer Prevention Studies Branch, Div. of Cancer Prevention and Control, are jointly seeking a contractor for a proposed study which is a continuation of a follow-up study on a sample of 64,185 of the 280,000 women who previously participated in a five-year multicenter breast screening program--the Breast Cancer Detection Demonstration Project (BCDDP)--conducted during 1973-1980. Currently, approximately 58,371 women are known to be alive.

The above sample of women was chosen to include all women who had a breast cancer diagnosed while they were in the screening project (4,275), all who had a biopsy or aspiration that was determined to be benign (25,115), all who had a surgical evaluation recommended by the project but did not undergo biopsy (9,629) and a sample of those who had neither surgery nor a recommendation for further evaluation (25,166).

The value to DCE and DCPC in continuing to follow the cohort lies in the opportunity to address prospectively a number of hypotheses in cancer etiology having direct relevance to prevention strategies, taking advantage of the substantial amount of relevant data and materials already collected on this population of women. Continuation of the follow-up will allow accrual of additional cases of breast cancer and other diseases, thus increasing the overall power of the study. It will also be essential to effectively utilize the risk factor data that were collected only in the last questionnaire.

Under this proposed follow up the contractor shall conduct further follow-up on a cohort consisting of the approximately 58,371 remaining women from the BCDDP. The average age of the cohort in 1990 was 65 years. The study is expected to last three years.

A summation of the specific activities to be performed by the contractor include: a) establishing and maintaining a centralized office in which documents associated with this study can be stored and from which mail and telephone interviews can be conducted, b) modify existing mail and telephone questionnaires (may include content as well as format), c) provide personnel to conduct follow-up activities, d) obtain the following information for each participant: (1) vital status information on cohort members, (2) responses to one mailed questionnaire from living study subjects during the three-year study period, (3) e.g., copies of pathology reports, hospital discharge summaries and operative reports for colon polyps, all cancers and breast procedures reported since the last interview in 1987/89, (4) copies of death certificates for all deceased subjects since the last interview (approximately 5,700 deaths are expected), e) at the direction of NCI, the contractor shall: (1) randomly select a sample of approximately 200 participants for purposes of checking the reproducibility of the dietary and physical activity information obtained from the 1987/89 interview, (2) obtain eight 24-hour recalls from a sample of approximately 200 subjects for purposes of validating the diet information, (3) select a sample of approximately 200 participants who reported recent use of hormone replacement therapy in the 1987/89 interview for the purpose of validating self-reported use of estrogens and estrogens

combined with progestins, (4) validate cancer status of subjects, match a sample of approximately 2,000 women with and without new cancer diagnoses to a population-based cancer registry to confirm status, f) have a trained nosologist code medical and death certificate data, using specified International Classification of Disease (ICD) codes, g) review and edit all collected and coded information, prepare all data for keypunching and develop and modify coding schemes as needed, h) code, keypunch and verify all data from items d), e) and f), above, i) establish and maintain control procedures to ensure standardization and a high level of quality of data collection and processing, including: (1) a written log or record book of all decisions affection study design, conduct or analysis, (2) field manual with instructions easily understood, (3) training of personnel prior to the start of the study in the use of data collection (including telephone interviews) and coding techniques, (4) monitor the performance of the field activities, and (5) verify accuracy of coding and keypunching data, j) develop a ready-access, patient oriented storage system for information and materials collected on cohort members during previous phases of the BCDDP, k) develop computer programs to check all data for range, skip and consistency errors and 1) produce and provide to NCI the data tapes of edited information collected on the study participants.

The estimated total level-of-effort for the three-year period of performance is 50,976 direct labor hours. Award of this project is anticipated by August 1, 1992.

Contract specialist: Barbara Shadrick
RCB Executive Plaza South Rm 620
301/496-8611

RFP NIAID-DIADS-92-15

Title: Evaluation of immune based therapies for AIDS using animal models

Deadline: Approximately March 20

The Developmental Therapeutics Branch, Basic Research & Development Program, Div. of AIDS, National Institute of Allergy & Infectious Diseases, has a requirement for the evaluation of immune based therapies for AIDS using animal models. This procurement consists of two parts that seek testing capabilities for immune based therapies that target different types of immune deficiencies seen in HIV infection and AIDS.

Part A of this procurement will provide for the evaluation of immune based therapies in an established small animal model, alone or in combination with other therapies, for their capacity to augment host defense mechanisms or otherwise ameliorate immune dysfunction characteristic of HIV infection. Emphasis will be placed on aspects of immune based therapies, i.e., mechanisms of action, optimal scheduling, identification of quantifiable parameters related to in vivo efficacy, potential for positive or negative interaction between immune based and antiretroviral therapies, and the potential of immune based therapies to upregulate virus expression. An established and validated animal model is requires for Part A.

Part B of this procurement will provide for development, validation, and testing of a model in which an immunodeficient animal is reconstituted with a source of human multipotent stem cells that can re-establish the immune system and that may also be genetically modified to resist subsequent infection with HIV-1.

The offeror shall, at the time of proposal, have identified an animal system to be developed and validated and a source of human multipotent stem cells. These capabilities are required by the Div. of AIDS in its efforts to develop immune based therapies for human subjects infected with HIV-1. There will be separate work statements and competitive ranges established for each part.

Offerors may respond to one or more parts. It is anticipated that one or more awards will be made for Part A and one award will be made for Part B. If more than one award is made for Part A, the government reserves the right to make only one award per animal model.

This project will take approximately five years to complete. A cost reimbursement type contract is anticipated.

Requests for the RFP may be directed in writing to Cyndie Cotter, Contract Management Branch, National Institute of Allergy & Infectious Diseases, Solar Bldg. Room 3C-07, 6003 Executive Blvd., Bethesda, MD 20892. Supply two self-addressed labels.

RFA Available

RFA CA-92-07

Title: Domestic animal models for retrovirus associated human cancers

Letter of Intent Receipt Date: Feb. 28

Application Receipt Date: April 28

Retroviruses isolated from mammalian species have the potential to provide valuable basic information on the etiology and mechanism(s) of cancer induction by viruses and to serve as models for evaluating antiviral agents prior to human clinical trials. The occurrence of neoplastic sequelae in retrovirus-infected animals supports the view that these viruses may be directly or indirectly involved in the etiology of malignancies. The identification and development of suitable animal models of viral neoplasia may aid in investigations of the mechanisms of cancer initiation and progression, ultimately providing a better understanding of the role of viruses in the etiology of human cancer.

The Congress, in both FY90 and FY92, has expressed its interest in retroviral infections in large domestic animals as excellent models for retroviral-induced diseases in humans such as leukemia, lymphosarcoma, and AIDS.

Non-profit and for-profit, domestic and foreign, organizations and institutions, governments and their agencies are eligible to apply. Applications from minority individuals and women are encouraged.

Support of this program will be through the NIH individual research grant (R01). This RFA is a one-time solicitation. Approximately $1,750,000 in total costs per year for four years will be committed. Five to seven awards will be made. The total project period may not exceed four years. The earliest feasible start date for the initial awards will be September 1992.

The objectives of the RFA are to encourage basic research on retroviral pathogenesis in domestic livestock animals. These studies will aid in understanding the properties of viruses and features of the host and its response that determine disease progression from initial virus infection to neoplastic sequelae. For the purposes of this RFA, domestic animals include cows, horses, sheep, goats, and pigs; specifically excluded are retroviruses of dogs, cats, primates, and avian species. Collaborative efforts between scientists with complementary areas of research expertise will be encouraged.

The areas of proposed investigation include: (1) investigations of the oncogenic mechanisms in domestic livestock retroviruses; (2) investigation of cancer etiology and viral pathogenesis from initial infection through the development of pre-neoplastic lesions and neoplastic sequelae with retroviruses of domestic livestock; (3) the role of RNA and DNA viral co-factors in cancer etiology animal models and definition of virus- and co-factor-host interactions and immune function alterations in the host that dispose the host to neoplastic processes; 4) investigations to assess the role of the host immune system and host genetic factors in the control and limitation of virus replication, and the susceptibility or resistance of animals to oncogenic processes;

and (5) studies on the expression and regulation of viral and/or associated host cell genes in pre-neoplastic lesions and malignant tissues from retrovirus-infected domestic livestock animals.

Inquiries and letters of intent should be directed to Dr. Kenneth Cremer, Program Director, AIDS Virus Studies, Biological Carcinogenesis Branch, Div. of Cancer Etiology, National Cancer Institute, Executive Plaza North, Room 540, Bethesda, MD 20892, phone 301/496-6085.

Program Announcements

PA-92-26

Title: NCI/MARC summer training supplement

Application Receipt Date: Feb. 1

The Comprehensive Minority Biomedical Program (CMBP) of the Div. of Extramural Activities, NCI, invites interested grantee institutions that have Minority Access to Research Careers (MARC) grants to apply for CMBP support of MARC scholars interested in obtaining laboratory research experience at NCI.

NCI, through a co-funding arrangement with the MARC program of the National Institute of General Medical Sciences (NIGMS) provides support for research training to minority individuals and institutions, and conference grant support to further address and enhance the mission of the National Cancer Program. The NCI/MARC Summer Training Program is an extension of the co-funding process.

All domestic institutions with active MARC research training grants are eligible to apply. A MARC honors training grant (T34) to the academic institution requesting support for a student will be administratively supplemented.

The supplement will provide the following: 1) A subsistence of $300 per week ($3,000 for a maximum ten-week period), and 2) round-trip transportation (from MARC student's academic institution to NIH and return to student's institution). Indirect costs may be awarded to the institution for up to a maximum of eight percent of direct costs.

The purpose of this award is to increase research training opportunities in the NCI for underrepresented minority scholars and to increase the number of minority scholars entering cancer related research careers through the influence of short-term laboratory training at NCI.

Applications in response to this announcement will be considered by NCI staff; final selection for laboratory experience will be made by the relevant laboratory directors. Selection will be made on the following criteria:

--Strength of the interest in pursuing a laboratory experience in the biomedical sciences based on the statement from the student;

--The strength of the letters of recommendation;

--Cumulative grade point average (2.75 or more based on 4.0 maximum).

In lieu of submitting a form PHS 398, the Principal Investigator must submit a letter, countersigned by an authorizing official of the grantee institution, requesting support of a student for short term laboratory training at NCI.

This letter shall constitute an application and must include or be accompanied by the following:

--A statement from the student that describes his/her research interests and career objectives and a brief resume;

--Two letters of recommendation;

--A current official college/university transcript;

--The student's selection of three NCI laboratory choices prioritized by level of interest;

--The title of the announcement;

--A copy of the face page of the active MARC grant including the grant number and period of award; and

--A description of the personnel to which the student shall report his/her NCI laboratory experience.

A list of NCI laboratory choices will be available to all applicants through the CMBP office. Application packages must be received by the CMBP no later than Feb. 1. The 10-week training period may be between May 1 and August 1992, inclusive. Under this announcement funding is available for this period only.

More than one supplemental application may be submitted by each grantee institution.

Submit applications and direct inquiries to: Program Director, Comprehensive Minority Biomedical Program, Div. of Extramural Activities, National Cancer Institute, 9000 Rockville Pike, Building 31 Room 10A04, Bethesda MD 20892, phone 301/496-7344.

PA-92-32

Title: Minority school faculty development award

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

The Comprehensive Minority Biomedical Research Program, Div. of Extramural Activities, NCI, invites academic health centers and other health professional schools that employ, educate, or serve a preponderance of minority faculty, staff, trainees, and communities to submit applications for support of activities directed at the development of faculty investigators at minority schools in areas relevant to cancer. The intent of the award is to provide the awardee with increased access to research opportunities through collaborative arrangements with outstanding cancer research scientists, usually at institutions within a 100 mile radius of the applicant organization.

A minority school is defined as a medical or nonmedical college, university, or equivalent school in which students of minority ethnic groups, including African Americans, Hispanics, American Indians, and Asian or Pacific Islanders, comprise a significant proportion of the school enrollment and that has a commitment to the special encouragement of minority faculty, students, and investigators.

Candidates for this award are minority school faculty members who: 1) are citizens of the United States, noncitizen nationals or permanent residents at the time of application; (2) have a M.D., Ph.D., or equivalent degree, in a biomedical or behavioral science; 3) wish to receive specialized training in cancer research;and (4) have the background and potential to become an independent biomedical investigator. A minimum of 50 percent effort annually must be committed to the award.

Applicants may not apply for, or accept, other PHS research grant support or its equivalent at the time of Minority School Faculty Development Award application, nor may they apply concurrently for any other type of academic award. However, applicants may apply for and accept research grant support subsequent to award of the Minority School Faculty Development Award.

Each candidate must also identify and complete arrangements with a mentor, at a preferably nearby (within reasonable commuting distance), majority or minority institution who is recognized as an accomplished independently funded investigator in the research area proposed and who will provide guidance for the awardee's development and research plan. Plans for obtaining an intensive research experience must be developed with the mentor.

The commitment of the mentor and his/her institution to year round (i.e., summer and academic year) exposure to research must be evidenced by a letter of support from each to be included in the application. A commitment from the mentor's department chair must be included in the application. Support of this program will be through the NIH Academic/teacher award

(K07). Awards may be requested for a period of three to five years. Allowable costs include:

--The salary of the applicant up to a maximum base salary of $50,000 per year and related fringe benefits.

--Costs for further optional preparation of the applicant in additional clinical or basic research methodologies (this aspect of the program is not to exceed the equivalent of one academic year total over the duration of the award).

--Domestic travel expenses for the awardee to attend professional meetings, training courses, and an annual two-day awardee meeting in Bethesda, MD.

--Partial salary support up to $40,000 per year for one additional faculty or staff researcher as a direct participant in research-related activities or services.

--Up to $10,000 per year in supplies for research activities.

--Indirect costs not to exceed a maximum of 8 percent of direct costs, exclusive of tuition fees, if any.

--The total award may not exceed $100,000 in direct costs per year.

--Equipment: Specialized research equipment essential to the proposed program. In accordance with PHS policy, title to such equipment will vest with the grantee institution.

--Supplies: Consumable supplies essential to the proposed program.

--Tuition and Fees: If essential to the awardee's individual research development program.

--Other: Personnel, publication costs, computer costs, and other costs necessary for the research program.

Inquiries may be directed to: Dr. Lemuel Evans, Div. of Extramural Activities, Comprehensive Minority Biomedical Program, NCI Bldg. 31 Room 10A04, Bethesda, MD 20892, phone 301/496-7344, fax 301/402-0062.

PA-92-33

Title: Minority oncology leadership academic award

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

The Comprehensive Minority Biomedical Program, Div. of Extramural Activities, National Cancer Institute (NCI), invites academic health centers and other professional schools that employ, educate, or serve a preponderance of minority faculty, staff, trainees, and communities to submit applications for support of an individual to pursue leadership activities in the development of research and training programs in clinically oriented cancer research (defined as including population research; surgical medical, or radiation oncology; cancer prevention and control; epidemiology and biostatistics; nutrition; clinical pharmacology and clinical trials; behavioral medicine; and related areas of cancer research).

The purpose of this initiative is to address underrepresentation of minority groups in research projects as investigators and subjects in research projects involving human populations. One method of addressing this problem is to broaden the experience of the faculty at minority health professional schools that serve these populations in the initiation and participation in cancer research.

In doing so, the pool of clinical biomedical investigators in all aspects of cancer research will be increased, and trainees will become more cognizant of research opportunities in oncology and related disciplines. These institutions represent a unique concentration of minority faculty, trainees, and patients to address the needs outlined above.

To be eligible, candidates must:

--Have an appropriate clinical academic appointment at a minority health professional school at the time the award is activated. The candidate must be a citizen, a non-citizen national of the U.S., or have been lawfully admitted to the U.S. for permanent residence.

--Have appropriate documented research experience and background in a clinical oncology specialty and/or cancer research.

--Specify a program for enhancement of personal research skills as needed, and for the conduct of research in one or more areas cited in this announcement. Proposed research must be described in sufficient detail for reviewers to evaluate the likelihood of success of this element of the plan. All sources of support proposed for this activity must be indicated.

--Present a program for developing or improving clinical cancer research and training capabilities at the grantee institution.

--Commit a minimum of 60 percent total time and effort to the research and development aspects of the program.

--Agree to report annually on the status of the program and to meet annually to exchange information with NCI staff and other awardees.

--Specify a plan for evaluating the effect of this award on the candidate and institution.

Support of this program will be through the National Institutes of Health academic/teacher award K07.

Allowable costs include:

--A portion of the salary of the faculty leader up to a maximum of $50,000 per year and related fringe benefits.

--Costs for further optional preparation of the faculty leader in additional clinical or basic research methodologies (this aspect of the program is not to exceed the equivalent of one academic year total over the duration of the award).

--Domestic travel expenses for the awardee to attend professional meetings, training courses, and an annual two-day awardee meeting in Bethesda, MD.

--Partial salary support up to $40,000 per year for one additional faculty or staff researcher as a direct participant in research related activities or services.

--Indirect costs not to exceed a maximum of eight percent of direct costs, exclusive of tuition fees, if any.

--The total award may not exceed $100,000 in direct costs per year.

Inquiries may be directed to: Dr. Lemuel Evans, Div. of Extramural Activities, Comprehensive Minority Biomedical Program, NCI Bldg. 31 Room 10A04, Bethesda, MD 20892, phone 301/496-7344, fax 301/402-0062.

NCI Contract Awards

Title: Feral mouse breeding colony

Contractor: Hazelton Washington Inc., Vienna, VA; $347,348.

Title: Managing your child's eating problems during cancer treatments

Contractor: Carter Printing, Richmond, VA; $39,200.

NIH Plans Conference On Aging

The Christopher Columbus Medical Sciences Committee of NIH, in conjunction with several NIH institutes, the Food & Drug Administration, and the Italian National Research Council, has organized an international conference on "Aging: The Quality of Life," to be held at the Omni Shoreham Hotel, Washington, D.C., Feb. 10-12. For information, contact Suzanne Kuntz, 202/639-4524.