THE CANCER LETTER

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Army Accepting Letters Of Intent For Research In Breast Cancer; Plans Announcement In Sept.

The U.S. Army Medical Research and Development Command has begun to accept letters of intent for proposals for its FY93-94 breast cancer research program.

The Army last week formally announced its intent to solicit propsoals through a Broad Agency Announcement, expected to be issued in September. The letters of intent will help the Army get a better idea of

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In Brief

Gritz Heads New Dept. At M.D. Anderson; NCI Grants Manager Leo Buscher Honored

ELLEN GRITZ, clinical psychologist known for smoking cessation and cancer prevention research, has been named to chair the new Dept. of Behavioral Science at M.D. Anderson Cancer Center. Gritz has served on the faculty of Univ. of California at Los Angeles School of Medicine for 22 years, and directed the Div. of Cancer Control at Jonsson Comprehensive Cancer Center. In 1980, she wrote the behavioral section for the Surgeon General's report on smoking among women. She was recently elected president of the American Society of Preventive Oncology. "I have long admired Dr. Gritz's innovative efforts in smoking prevention and cessation," said M.D. Anderson President **Charles LeMaistre.** "We are enthusiastic about her appointment and anticipate she will enhance our overall cancer prevention effort." . . . **LEO BUSCHER JR.**, NCI grants management officer, was presented the Robert Newton Lifetime Achievement Award by the National Grants Management Assn. for his "strong record of achievements in grants management." . . . **JOSEPH SAUNDERS**, who was acting director of NCI's Office of International Affairs and a long time deputy director of that office in the 1970s, died last month after a heart attack. He was 66. Saunders retired from NCI in 1983 and became executive director of the American Assn. of Immunologists. He retired from that position last year. . . . **NEW GUIDELINES** for institutional National Research Service Awards (T32 training grants) have resulted in some confusion among grantees and applicants, according to Brian Kimes, director of DCBDS's Centers, Training, & Resources Program. A new requirement is that at least 50 percent of the preceptors' support must come from NCI, the American Cancer Society, or other organizations with qualified, peer reviewed cancer related grants, as reported in **The Cancer Letter** April 2. Some have interpreted that requirement to mean that 50 percent must be from NCI, Kimes said.

Army Seeking Letters Of Intent, Nominations For Peer Review Panels

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how many investigators might apply, Army sources said. Congress appropriated $210 million to the Dept. of Defense last year for a breast cancer research program.

The Army also is seeking nominations for its peer review panels.

The Medical R&D Command intends to follow closely the recommendations of the Institute of Medicine (**The Cancer Letter**, May 21). While the program is a few weeks behind schedule, the Command intends to obligate the funds by the Sept. 30, 1994 deadline. The IOM recommended that research proposals be due no later than Oct. 1 for the first round of funding.

A program manager has not been hired; the Army is still interviewing candidates for the job.

Letters Of Intent Due Aug. 16

Letters of intent need only be one page, and are due by Aug. 16. Letters should be addressed to: Commander, U.S. Army Medical Research & Development Command, Attention: Col. Patricia Troumbley, AN, SGRD-ACQ, Fort Detrick, MD 21702-5012, phone 301/619-7219.

According to the Army announcement, funds will be available to support projects in the following areas:

Investigator-initiated research:

▶ What genetic alterations are involved in the origin and progression of breast cancer?

▶ What are the changes in the cellular and molecular functions that account for the development and progression of breast cancer?

▶ How can endogenous and exogenous risk factors for breast cancer be explained at the molecular level?

▶ How can investigators use what is known about the genetic and cellular changes in breast cancer paitents to improve detection, diagnosis, treatment, and ongoing care on the psychosocial and clinical outcomes of breast cancer patients and their families?

▶ How can investigators define and identify techniques for delivering effective and cost-effective health care to all women to prevent, detect, diagnose, treat, and facilitate recovery from breast cancer?

Infrastructure enhancement:

Funds will be available for enlarging or developing shared resources that broadly support breast cancer research. Examples include:

Cancer registries; registries of high-risk women; DNA resources; transgenic mouse husbandry; banks of cell lines and tumor samples; and information systems.

A significant factor for evaluating these proposals will be the applicant's ability to document demand for the proposed infrastructure resource in the breast cancer research community.

Training and recruitment:

Funds will be available for predoctoral, postdoctoral, sabbatical, and career development programs and fellowships to enhance and expand the pool of talented individuals.

Service on a peer review panel.

Individuals may nominate themselves or colleagues to serve on panels to review grant proposals. To avoid conflicts of interest, no reviewer may evaluate a proposal submitted by members of an organization that employs or provides benefits to the reviewer.

Besides the areas noted above, the Army said, "potential applicants are encouraged to consult the IOM report and to consider submitting letters proposing additional approaches to the breast cancer problem."

THE CANCER LETTER

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Capitol Notes

HHS Plan Ties Breast Cancer Screening, Mammography Quality Act

A plan recently released by HHS attempts to tie together two Congressional issues that have been regarded as separate and distinct.

The measures being linked into a "Strategic Plan for the Early Detection and Control of Breast and Cervical Cancer" by HHS are:

► Legislation that would allow the Centers for Disease Control and Prevention to step up its program for screening for breast and cervical cancer among the underserved women.

► The attempts on Capitol Hill to provide adequate funding for a nationwide mammography quality assurance program.

Programs Grossly Underfunded

According to their advocates, the two programs have one thing in common: both have been grossly underfunded.

The CDC program is operating on a $71.3 million budget in FY 1993, but needs about $200 million, its advocates say.

The mammography quality assurance program is, by anyone's standards, even worse off.

Authorized last year, the program received no appropriations until recent weeks, when it was given a $3 million transfer of funds, of which $1 million came from NCI.

Now, according to the strategic plan announced by HHS Secretary Donna Shalala, HHS will regard mammography screening and mammography quality assurance as two sides of the same coin.

The plan's objective, according to Shalala, is to double the ratio of women who follow the NCI guidelines for mammography screening. Currently, about 41 percent of women over 40 follow the guidelines.

The 90-page plan, developed by CDC, NCI and FDA in cooperation with 75 agencies and public groups, includes the following components:

1. Integration and coordination of services to provide better access to screening and close gaps in followup services, including treatment and diagnosis.

2. Public education to ensure that women are aware of the importance of screening and the availability of care.

3. Education of health professionals to ensure effective screening and appropriate followup referrals.

4. Quality assurance for breast cancer screening, to ensure consistent high quality screening throughout the entire process of obtaining, interpreting and reporting mammogram results.

5. Similar quality assurance for cervical cancer screening.

6. Assessing whether the program is successful in increasing the number of women screened, identifying their cancers earlier and reducing fatalities.

Under the CDC program, now in its third year, state health agencies receive funds to develop public health infrastructure for screening and followup.

While its advocates, including the American Cancer Society and the Susan Komen Breast Cancer Foundation, are trying to get the program funded at as much as $200 million, any increase is likely to hinge on the program's reauthorization. The Senate Labor and Human Resources Committee hearing on reauthorization is expected later this week.

It can be said that the mammography quality standards legislation, passed by the 102nd Congress, got off to a bad start. In the final days of the session, Congress pulled out the program's funding.

Though $3 million has been carved out of other agencies to get the program initiated this year, ACS and others are asking for about $13 million for FDA to run the program next year. That money is included in the President's budget proposal and the House appropriations bill.

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Conflict of interest regulations: While there is no guarantee that following three years of drafting and redrafting, NIH will finally complete its conflict of interest rules, it appears that a copy of the long-awaited regulations is about to see the light of day.

Shortly before she left office, former NIH Director Bernadine Healy wrote in a letter to Rep. Ron Wyden (D-OR) that the latest version of the revised draft "is being reviewed informally by NIH, PHS and HHS staff" and that the final version was about to be forwarded to HHS for approval.

If approved, the regulations are expected to include a provision for disclosure of financial interests by investigators, Healy wrote in a recent letter to Wyden.

"Disclosure of financial interests is an essential component of oversight," Healy wrote, responding to questions by Wyden. "The restrictions are directed at circumstances that are considered to be the most questionable practices, circumstances that would clearly compromise the confidence with which the results of the research would be received.

"These restrictions were developed with a theoretical framework that also includes the protection of the objectivity with which the research is conducted and reported and the need to promote the transfer of technology from academia to industry.

"Significant alterations to this component of the proposed regulations are not anticipated."

The financial disclosure provision was the principal the reason the rules were rejected three years ago by then HHS Secretary Louis Sullivan.

Slashing the "regulatory burden" was consistent with the ideology of the former Administration and constituted a direct response to the biotechnology industry's claim that conflict of interest rules would

bar small companies from compensating scientists with stock instead of money.

In her final Capitol Hill appearance as NIH director, Healy was blunt about her frustration with the slow pace of rulemaking.

"I am sorry to report to you that conflict of interest guidelines which have been in development in my agency for several years are not finalized, have not appeared in the Federal Register and have become a tennis ball going back and forth between NIH and the Department," Healy said to Rep. Ron Wyden at a hearing last month.

DCPC Establishes Decision Network To Oversee Chemoprevention Effort

NCI's Div. of Cancer Prevention & Control is making several administrative changes in its Cancer Prevention Research Program to provide greater overview for its expanding research effort in chemoprevention.

The changes, disucussed by DCPC Director Peter Greenwald at the DCPC Board of Scientific Counselors meeting in May, include:

▶ Establishing a "decision network" of four committees to provide administrative overview to the testing of agents for possible study.

▶ Greenwald will serve as acting associate director of the Cancer Prevention Research Program. Winfred Malone has served as acting director since 1991, exceeding the time "generally advisable for such temporary appointments," Greenwald said to the board. A search for a permanent director will continue. Malone continues his position as chief of the Chemoprevention Branch.

▶ A group headed by Gary Kelloff will work with Greenwald on chemoprevention investigational drug development. The group will develop an on-line information system which will include a project plan for each high priority chemoprevention agent, the responsible program director, a schedule of the availability and distribution of agents and drug development time lines for each agent that has reached the point of preclinical toxicology or clinical testing. Tom Marciniak will help to develop the system.

Prioritizing Research

Funding for chemoprevention in NCI has grown from $57 million in 1990 to $84 million in 1992. DCPC has about 36 percent of the total NCI expenditure.

The goal of the decision network, Greenwald said, will be to:

--"Build and maintain cancer chemoprevention as one of our highest research priorities.

--"Make it easier for interested scientists and physicians to take part in the research, for example, by improving communications about new chemopreventive agents and their testing and availability by working with cooperative groups and others to plan for new trials, by working with the pharmaceutical industry and regulatory agencies to plan for new trials."

The decison network committee is made up of DCPC staff, Judith Karp, special assistant to NCI Director Samuel Broder, and David Parkinson and Saul Schepartz of the Div. of Cancer Treatment. Executive secretary is Cynthia Birch Witman, in Deputy Director Edward Sondik's office.

The group will oversee safety and protocol reviews and consider the reports of committees reporting to it. It will report annually to the Board of Scientific Counselors.

Gary Kelloff will chair an agent selection committee. Members have not been finalized, but will include NCI staff as well as ad hoc extramural members. This committee will oversee the development of chemopreventive agents for preclinical studies and for clinical trials, Greenwald said. It will interact with the pharmaceutical industry and oversee agent and dose selection acquisition, formulation and distribution.

The committee would work on biomarkers and their performance characteristics in concert with an end points and biomarkers committee. The selection committee also would oversee Investigational New Drug development for division-sponsored trials and interact with the Food & Drug Administration.

Two other groups would cover chemoprevention, but also would have more broad functions, Greenwald said. These are the end points and biomarkers committee, chaired by Barry Kramer, and a large trials committee chaired by Larry Friedman.

The end points committee would oversee the development and use of surrogate biomarker end points for clinical trials and would work to move biomarkers from the laboratory to clinical testing. The group would track the use of biomarkers in clinical chemoprevention trials with regard to quality control and efficacy.

"Right now there are a myriad of biomarkers," Greenwald said. "As we use them in clinical trials or later on in clinical practice, we need documentation of the performance characteristics of the assays.

"I have trouble now, even reading through some of this field," he continued. "A lot of the papers are not awfully clear about what is theoretical and what is in

clinical practice. We need a system that is more precise at telling us what is working."

The large trials committee, a mix of NCI staff and extramural researchers, would "document and synthesize the lessons learned from past and ongoing trials" and recommend methods for large trials, Greenwald said.

"We would expect them to examine all new proposals for large trials" costing over $1 million a year, he said. These trials would have to be prioritized, which is part of the BSC's function.

The division would develop an annual cycle for the work of these committees, present an annual report to the BSC in January, and would present any concepts to the board in May.

To Begin, Breast Cancer

Since breast cancer has a high priority in NCI, the division plans to start the process by bringing through breast cancer trial information first, Greenwald said.

Chemoprevention agents under study in breast cancer include tamoxifen, 4-HPR, calcium plus vitamin D, several vitamin D analogs, and DFMO.

"A major issue in breast cancer [chemoprevention] studies is how to do biomarker studies," Greenwald said. "Can you get tissue or breast fluid, how do you sample it, is there a standardized way? We are trying to stimulate studies that would look either at histologic lesions which are well established, like lobular carcinoma in situ, ductal carcinoma in situ, or atypical hyperplasia.

"If we could come up with a good way to do this, it would greatly accelerate progress or research toward breast cancer prevention," Greenwald said.

To stimulate the field of biomarker study, DCPC recently released a cooperative agreement for studies of biomarker end points particularly for studies in breast cancer.

Greenwald emphasized that the large chemoprevention trials should carry enough financing to pay for biomarker and mechanisms studies. "We should make a great effort to make sure that we have strong basic and clinical scientists working together on these. I am not sure the way we have set up the trials makes that too easy right now."

Board member Helene Brown asked Greenwald how the prioritization of large trials might work. Greenwald said the chemoprevention trials would come through phase I and phase II, and the division and the board would have to consider the potential impact and likelihood of success. In addition, these trials would be prioritized for funding within NCI as a whole, as is the case with any major funding commitment.

"I don't know any magical way except to systematically discuss them and look at things like potential impact, practicality and likelihood of success," Greenwald said.

Feds Should Improve Recruitment, Retention Of Top Scientists: NAS

The federal government should take additional steps to improve its ability to recruit and retain top-flight researchers, including fully implementing the Federal Employees Pay Comparabilty Act to provide federal agencies with greater flexibility in compensating employees, concludes a report from the National Research Council.

Although federal agencies currently are having little difficulty hiring scientists and engineers, the report warns that the government's competitive advantage in this area, like the just-ending recession that spawned it, is probably only temporary.

Over the next seven years, veteran federal researchers are expected to retire in higher numbers, while at the same time there is reason to believe that fewer young people will enter science and engineering careers.

Thus, when the economy becomes strong again, it is likely that the federal government will once more find itself competing with industry and academia to recruit high-level talent, the report predicts.

The report, "Improving the Recruitment, Retention, and Utilization of Federal Scientists and Engineers," is available from the National Academy Press, phone 202/334-3313 or 800/624-6242, for $24 plus $4 shipping.

The 1990 pay act "could go a long way toward making the federal government more competitive where it needs to be by increasing the flexibility of agencies to pay more in higher-pay geographical areas and higher-pay occupations, and to better performers," the report said.

The report recommends that:

▶ The federal Office of Personnel Mangement should establish an office for personnel policy on scientists and engineers.

▶ Congress and executive branch should work together to make legislative changes in the civil service system that address problems for scientists and engineers beyond pay flexibility issues, such as the situation in which scientists must give up research and take management jobs in order to obtain top pay and benefits. The report calls for a "Senior Research and Development Service" modeled after the government's Senior Executive Service.

ACS Awards $1 Mil. Each To USC, Wisconsin, For Behavioral Research

The American Cancer Society has awarded two $1 million Special Institutional Grants in psychosocial and behavioral cancer research to the Univ. of Wisconsin, Madison, and the Univ. of Southern California.

The two SIGs, which provide support for five years, focus on managing pain in cancer patients and minimizing the burden of cancer in ethnically diverse and socioeconomically disadvantaged populations.

At Univ. of Wisconsin, the SIG under the direction of Charles Cleeland, will be used to establish a Center for Symptom Control in Oncology. The center will be a regional and national resource for interdisciplinary research and training in pain management. Research projects will be developed to determine why socioeconomically disadvantaged and ethnically diverse patients receive less adequate symptom control, to improve health professional practice in pain management, and to increase patients' ability to report pain and other symptom distress.

At USC, the SIG directed by Jean Richardson will establish the American Cancer Society Behavioral and Psychosocial Cancer Research Program. The program is a multidisciplinary effort to identify barriers to, and develop interventions for the early detection and treatment of cancer in ethnically diverse and socioeconomically disadvantaged populations. Stiudies will evaluate delay and stage at cancer diagnosis, compliance and self-care during treatment, and patient-provider interactions.

The society's Board of Directors also recently awarded about $54.9 million in grants to scientists throughout the country. The board approved 218 new grants and renewed 244 for a total of 462 grants.

RFA Available

RFA AI-93-014

Title: **Centers for AIDS research/core support grant**

Letter of Intent Receipt Date: July 23

Application Receipt Date: Sept. 17

The National Institute of Allergy and Infectious Diseases and the National Institute of Mental Health invite the submission of applications for Centers for AIDS Research/Core Support Grants (CFAR/CSGs) from institutions conducting high quality, multidisciplinary AIDS research. The purpose of the CFAR/CSG is to provide administrative and shared research support (Core facilities) to synergistically enhance and coordinate high quality AIDS and AIDS-related research projects requiring resources or services not otherwise readily obtained through traditional, peer-reviewed funding mechanisms.

Applications may be submitted by domestic (not foreign) for-profit and non-profit organizations. Both new applicants and competition renewal applicants are eligible to apply. Minority individuals and women are encouraged to submit as Principal Investigators. Only a single CFAR will be supported at a given institution per funding institute, i.e., one institution may have a CFAR funded by NIAID and one funded by NIMH, but will not have more than one CFAR funded by either institute. An applicant institution must have a continuing Funded Research Base comprising at least $800,000 in annual direct costs of peer-reviewed AIDS or AIDS-related research funded by the institute which will be supporting the CFAR/CSG, either NIAID or NIMH (exclusive of funding for an existing CFAR), or by another NIH Institute, when the CFAR/CSG is awarded (March 1994) and throughout the award period.

CFAR awards will be made under the NIH Center Core Grant (P30) mechanism. Sizes and number of the awards may vary. Total project period may not exceed five years of support. However, recommended support beyond the third year for the CFAR/CSG is subject to determination by the awarding institute that stated goals (milestones) have been sufficiently met.

NIAID has set aside $7.2 million for the initial year's funding. NIAID anticipates making 9 to 11 awards. NIMH has set aside $1.5 million for the initial year's funding and anticipates making two awards. All applications are limited to requests for no more than $750,000 in total costs (direct plus indirect) in the first year. Increases of up to four percent are permitted for allowable recurring costs for each of the subsequent years.

This award will:

--Encourage those activities that will consolidate and focus high quality AIDS and AIDS-related research into coordinated administrative and scientific programmatic structures;

--Promote effective synergistic collaborations and interactions among investigators participating in basic and clinical areas of AIDS research, in large part through the establishment of Core facilities which must include a Clinical Core in addition to Basic Research Cores, a Developmental Core and an Administrative Core. Such interactions should facilitate translation of information obtained in the laboratory to specifically address problems in the clinic, and enhance the possibility of observations in the clinic being translated to the laboratory setting for further investigation;

--Foster development of new research areas in AIDS research by providing support for investigators new to the field, and through the funding of innovative and high quality feasibility studies whose results can form the basis for competitive applications;

--Support administration of the Center, including activities such as seminars and workshops for CFAR members and AIDS investigators in general, education at all levels, including community programs, and fund the leadership responsible for organizing and sustaining the Center's activities.

A CFAR and its Parent Institution will be evaluated in each of the following critical areas, as a prerequisite for successfully competing for a CFAR/CSG award: the interdisciplinary coordination and collaboration, especially between basic and clinical investigators; institutional commitment; qualifications and authority of the CFAR director; organizational capability; and developmental and educational commitment.

Inquiries: Dr. Robert Bassin or Dr. Janet Young, Div. of AIDS, National Institute of Allergy and Infectious Diseases, 6003 Executive Blvd. Room 2B31 (or 2B28), Bethesda, MD 20892, Tel. 301/402-0755, Fax 301/480-5703.