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Clinical Cooperative Groups Asked To Develop Tamoxifen Prevention Trial; CGOPs To Participate

The clinical cooperative groups have been asked by NCI to formulate proposals for participation, with their affiliated academic, Community Clinical Oncology Program, and Cooperative Group Outreach members, in a national tamoxifen chemoprevention trial to test the effectiveness of the agent in preventing breast cancer. The trial also will look at the

(Continued to page 2)

In Brief

896 Nurses Pass Oncology Certification Exam; ACS Awards 375 New Grants Worth $43.8 Million

EIGHT HUNDRED ninety-six registered nurses passed the certification examination administered during the Oncology Nursing Society's annual meeting in Washington in May. Of the 1,005 nurses who sat for the exam, 566 passed the exam for the first time, and 330 of those renewing their certification passed. There are now 7,801 certified oncology nurses. The next exam will be held Sept. 22. . . . **AMERICAN CANCER** Society has awarded 375 new grants to examine various issues in cancer control, and 57 institutional research grants. The grants, totaling more than $43.8 million, were given to scientists at 157 institutions. The society also has created special institutional grants for psychosocial and behavioral research. These will be five-year grants for interdisciplinary study, and are for up to $1 million total. . . . **SIX MEMBERS** of the Div. of Cancer Etiology Board of Scientific Counselors have finished their terms on the board: Board Chairman Hilary Koprowski, Anna Barker, George Casarett, Lawrence Fischer, Moyses Szklo, and Alice Whittemore. . . . **HERBERT KERMAN,** medical director of Halifax Medical Center's Regional Oncology Center, is the first recipient of the Gold Medal of the Florida Radiological Society, given for outstanding contributions by a member of the society. . . . **HAROLD FREEMAN,** chief of surgery at Harlem Hospital and past president of the American Cancer Society, has received the Strang Award for Achievement in Cancer Control from the Preventive Medicine Institute/Strang Clinic, of New York City. . . . **MICHAEL KEATING** has been named associate vice president for patient care in clinical investigations at Univ. of Texas M.D. Anderson Cancer Center. Keating came to the cancer center as a fellow in developmental therapeutics in 1974 and joined the faculty as an assistant professor of medicine four years later. . . . **SYED ZAKI SALAHUDDIN,** a retrovirologist in NCI's Laboratory of Tumor Cell Biology, has resigned following allegations of conflict of interest involving an NCI subcontractor, Pan Data Systems Inc., of Rockville, MD.

Cooperative Groups Asked To Develop Tamoxifen Trial

(Continued from page 1)

impact of tamoxifen on cardiovascular disease, and the National Heart, Lung, & Blood Institute will participate, in funding as well as review and oversight of that portion of the trial.

Another proposal for a tamoxifen prevention trial made by a California organization, presented to the Food & Drug Administration's Oncologic Drugs Advisory Committee last week, was rejected by the committee (see following story, page 4).

The tamoxifen chemoprevention trial (TCT) is an initiative of NCI's Div. of Cancer Prevention & Control. It was brought up last week by DCPC Director Peter Greenwald to cooperative group chairmen during their semiannual meeting at NCI.

Greenwald presented an implementation plan for TCT to the group chairmen. Although it refers primarily to CCOPs as the organizations which will carry out the trials, Greenwald emphasized that CGOPS and other group members would be encouraged to participate. CCOPs are funded by DCPC, while the groups and CGOPs are funded by the Div. of Cancer Treatment. The cooperative groups and cancer centers which serve as research bases for CCOPs are supported for that activity by DCPC.

Implementation Plan for Tamoxifen Chemoprevention Trial in the CCOP Clinical Trials Network

A clinical trial to test the effectiveness of tamoxifen in preventing breast cancer in postmenopausal women (> 50 years) is a high priority of NCI. DCPC currently has cooperative agreements with eight clinical cooperative groups and seven cancer centers to serve as research bases for the CCOP. As a CCOP research base, in addition to ongoing responsibilities in treatment research, these groups are expected to develop and implement cancer prevention and control clinical trials to be used in the CCOP network. University members and outreach affiliates are also encouraged to participate in prevention and control research, thus expanding the available subjects for such studies. The cooperative agreements also allow use of this network to conducted NCI assisted cancer control research. It is through this mechanism that NCI plans to implement the tamoxifen chemoprevention trial.

1. All CCOP research bases and new applicants are being informed of NCI's interest in conducting the TCT and invited to submit a detailed concept for the trial. [The research bases are being recompeted, with proposals due next month].

2. Following current procedures for cancer prevention and control clinical trials, all interested research bases are being asked to submit a detailed concept for the trial. Research bases are encouraged to work together in the development of a single concept and protocol since only one study will be approved. The concept should describe plans for the full trial; recruitment of additional sites (if necessary) for accrual; and preliminary budget estimates over and above the current CCOP and research base cancer control support. Special attention should be given to adequate representation of minorities. If a feasibility/pilot phase is proposed, the concept and budget for that and for the full trial must be included. Concepts will be due Oct. 1, 1990.

3. The TCT should include measurable endpoints for breast cancer and cardiovascular disease as well as overall mortality. The protocol should contain formal statistical rules to be used in making decisions regarding stopping or modifying the trial. Consideration should also be given to the effect of tamoxifen on bone mineral density and osteoporosis. NHLBI will work closely with the research base in defining the cardiovascular endpoints of interest in the final protocol.

4. The concepts will be reviewed by a joint committee of the DCPC Cancer Control Protocol Review Committee and the DCT Cancer Therapy Evaluation Program's Protocol Review Committee, with representation from NHLBI (William Harlan) and other NCI and NIH staff, as required.

5. Based on this review, one research base will be approved to develop the protocol for the TCT. Again, the intergroup mechanism will be encouraged.

6. The final protocol will again be reviewed jointly by the CCPRC with CTEP and NHLBI representatives.

7. The final approved protocol (feasibility/pilot

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Editor: **Jerry D. Boyd**
Associate Editors:
Kirsten B. Goldberg, Patricia Williams

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

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phase) will be implemented with accrual from CCOPs, and members and affiliates of the research base (or all research bases depending on the intergroup status). Additional affiliates (HMOs, screening clinics, etc.) could be recruited by the research base.

8. Quality control, drug toxicity, etc., will be handled as with any large research base clinical trial. The operations and statistical offices of the lead research base will be responsible for data monitoring and analysis, as with any clinical trial.

9. A data and safety monitoring committee will be appointed by the NCI director in consultation with the NHLBI director. This committee will comprise knowledgeable non-NIH persons not involved in trial operations and representatives of NCI and NHLBI staffs. This committee will be charged with oversight of trial design, data quality, assessment of safety and toxicity and unblinded monitoring of endpoints. Recommendations about trial conduct and continuance will be made by the committee to NCI and NHLBI. The following areas of expertise should be represented: clinical oncology, clinical cardiology, pharmacology, clinical trials conduct, biometry, and medical ethics.

10. An alternate design option of interest to NCI would be a factorial design using N-(4-hydroxyphenyl) retinamide (HPR). Laboratory study suggests an independent or synergistic benefit of HPR and tamoxifen in breast cancer prevention. Veronesi, et al, in Milan have in progress a trial using HPR and aimed at preventing contralateral breast cancer.

11. One year after initiation of the trial, or at the end of the feasibility/pilot phase if that is the plan, the investigators will be asked to present a progress report to the DCPC Board of Scientific Counselors, including accrual, quality control and end points monitoring, anticipated progress and time line to completion of the trial, and adherence to budget projection. Continuation of the trial will be contingent on this report.

12. Funding will be handled through the existing dCPC cooperative agreements with CCOPs and research bases. Each CCOP is currently funded for one FTE for cancer control data management. Additional recruitment and data management support may be necessary at the community level depending on accrual.

The research base budgets contain funds for the operations and statistical support for cancer control accrual from CCOPs and members/affiliates, as well as limited funds that are passed through to members/affiliates for cancer control data management. The budget of the lead research base will be supplemented for operations and statistical support for the large additional accrual projected from this study. Funds also will be provided for data management at member/affiliate institutions. Finally, funds will be provided for the additional laboratory tests and procedures necessary to monitor women registered on the study (bone density, electrocardiograms, lipids, antithrombin 3, uterine cancer, and other risks).

CTEP Director Michael Friedman told the group chairmen that "you should discuss this and determine if you want to go independent or work together on this." David Harrington, who heads the Eastern Cooperative Oncology Group's statistical center, said that "this is a nice and unique opportunity for cooperative group chairs to get together and see if they can put together a consortium. There should be a formal meeting to determine if we can go ahead together."

The chairmen agreed to that suggestion, and Ross McIntyre, chairman elect of Cancer & Leukemia Group B, agreed to chair the meeting. It will be held later this summer, probably in New Hampshire where McIntyre is director of the Norris Cotton Cancer Center.

Richard Love, Univ. of Wisconsin, who has been the prime mover behind a tamoxifen prevention trial, told the chairmen that "compliance and recruitment will be a major challenge. The population is well people. We have a window of opportunity now, which will close rapidly. A feasibility study is absolutely critical. A major issue is that we (his colleagues who have participated with him in two NCI sponsored workshops on the issue) clearly believe there should be a new coordinating center for this."

Greenwald did not necessarily agree on the necessity for a feasibility trial or a new coordinating center. He feels that the full trial could be initiated, with review at one year assessing whether it would be feasible to continue. A feasibility study probably would involve about 1,500 women.

Greenwald would not make any estimates on the number of women a full scale trial would require, or of the total cost. "I want to see what the groups come up with themselves," he told **The Cancer Letter.**

Previous discussions led to an estimate that as many as 16,000 women would be required, with two years for accrual and five years of followup. That could cost in the neighborhood of $60 to 65 million.

Proponents have estimated that tamoxifen as a chemopreventive agent could reduce breast cancer incidence by as much as 50 percent.

Greenwald thinks that by using the research bases and their affiliates, with their clinical trials organizations and quality control, data gathering, etc.

already in place, the cost might be less than the estimates.

Andrew Door of CTEP warned that "fast accrual is necessary. We may have cardiovascular and lipid endpoints in hand before complete accrual."

"I'm not sure what is being asked of us," Charles Moertel, chairman of the North Central Cancer Treatment Group, commented. "Are we being served up a protocol and asked to vote? Or are we being asked to participate?"

"This is a chance for the groups to be involved in a major prevention study," Friedman said. "Rick (Ungerleider, chief of the Clinical Investigations Branch) and I have made the point that the groups are too good to limit them to treatment trials, and as resources for only one division of NCI. This is a chance for them to expand their clinical and intellectual activity."

"Where's the cash?" asked Charles Coltman, chairman of the Southwest Oncology Group. "Will this be new money from DCPC, without cannibalizing our other activities?"

McIntyre added the concern that "once launched, this will then be inadequately funded and will tax our resources."

Greenwald said that support for the trial would not be at the expense of other CCOP or cooperative group activities. He added that he could not offer assurance that funding would be adequate, although "I certainly hope it would."

FDA Advisors Oppose Calif. Group's Tamoxifen Study, But Okay The Idea

The FDA Oncology Drugs Advisory Committee, while approving the idea of conducting a randomized study of the effect of tamoxifen in healthy women, recommended against the specific study it was asked to consider last week.

The study, characterized as a "grassroots effort" by the California group that proposed it, was voted down 6-1. The only committee member voting for the study was Harold Harvey, professor of medical oncology at Pennsylvania State Univ.

It is not clear what these recommendations will do to the proposed study, and things may become even less certain in light of the prospect of a similar study to be undertaken by NCI (see story, page 1).

The group said the trial they proposed would involve 14,200 women in the U.S. and an equal number in the USSR and cost $100 million for the U.S. component alone.

"I think the recommendation helps us a great deal," said Terrance McKnight, a Los Angeles attorney who represents the sponsors of the study, adding that the first part of the recommendation constitutes a broad endorsement for FDA staff and the study sponsors to work out details of the protocol.

"One thing that our group brings to the table is our association with the Russians and the publicity involved in that," said McKnight. "The second thing we bring is that we have political support and may bring in outside funds."

The man behind this idea is Phillip Bretz, director of clinical affairs at the Desert Breast Institute of Rancho Mirage, CA.

Over the past year, Bretz and a handful of associates said they spent $75,000 of their own money shuttling between Los Angeles and Washington, Los Angeles and Moscow, and Moscow and Kiev.

According to McKnight, Bretz came up with the idea of a U.S.-Soviet tamoxifen trial after reading an article on the incidence of breast cancer among women living in the proximity of Chernobyl.

That led Bretz to tap Robert Estes, a relative who specializes in trade deals with the USSR, to arrange some meetings at the Soviet Ministry of Health and the All-Union Cancer Institute.

During the meetings, attended by nine U.S. physicians, the Soviets were offered fine needle aspiration and mammography equipment available in the West, provided that the sponsors could arrange the funding. The Soviets would be expected to conduct a study similar to Bretz's, McKnight said.

"We are hoping that we can raise that money privately," said McKnight, who added that he may get reimbursed for his expenses and some of his time if the project is funded.

According to McKnight, last year Bretz asked a neighbor to arrange a meeting with House Minority Leader Robert Michel (R-IL), while he was in Palm Springs for the Bob Hope Golf Classic. The neighbor, former Rep. Thomas Railsback (R-IL), was throwing a party for Michel, McKnight said.

McKnight said the meeting led to introductions to Reps. John Myers (R-IN), Barbara Vucanovich (R-NV) and Mary Rose Oakar (D-OH).

"Mary Rose Oakar told him that we'd like to see it go through peer review," an aide to Oakar told **The Cancer Letter.**

Bretz said the $100 million for the study could come from a combination of federal and private funds. "This is a genuine women's issue," McKnight said. "We need some women's issues beyond abortion."

"This study would probably be one of the most

expensive and complicated clinical cancer trials ever conducted," said an FDA staff summary presented to the Oncology Drugs Advisory Committee.

According to the staff summary:

"Statistical aspects of the study may be more complicated than usual because the study is really a composite of several studies on the effect of tamoxifen on various conditions.

"Sample size for the various conditions may be different. Estimation of sample size requires data on the natural incidence of the condition in the study population and the anticipated effect of tamoxifen.

"Good data on specific populations are not always available. Stopping rules for a favorable or unfavorable effect may be difficult to apply when so many effects are being assessed concurrently.

"Patient compliance and loss to followup may also be a problem in a 10 year study."

Committee member David Ahmann, professor of oncology at Mayo Medical school, called the Bretz study "ill-conceived."

"If we initiate such a trial, we need to have stopping rules, know more about the risks and build in the end points," Ahmann said. "I didn't come here to write a protocol."

"Tamoxifen is a very safe drug," Ahmann said. "However, it has not been used for 10 years in a healthy population. We need to remember that this is a clinical trial involving healthy people and that we don't know the answers."

Harvey, the only committee member to vote for the Bretz plan, said that "Tamoxifen is not clearly unsafe. We can only go with the data. Answers on the long term risks are precisely what we will get from a randomized study."

Committee member Dean Brenner of the Univ. of Michigan School of Medicine, called for additional animal and pilot studies.

"One would have to suggest that this is probably not the time to proceed with such a trial," he said. "We are shifting the rules. We are no longer treating patients. We are treating volunteers."

Craig Henderson, committee chairman and associate professor at Harvard Medical School, said, "It still remains a fact that a number of patients are still using the drug. I think it might be possible to develop a trial for patients who are, in fact, extremists."

Committee member Grace Monaco said trying a variety of doses in otherwise healthy patients could exacerbate toxicity.

"This is very troubling intellectually," she said.

Group Chairmen Propose Four More Trials For High Priority Status

Cooperative group chairmen last week gave their approval to the addition of four more clinical trials to NCI's "High Priority Clinical Trials" list. Their recommendations will be presented to the Div. of Cancer Treatment Board of Scientific Counselors for its concurrence at its October meeting.

High priority designation makes the trials eligible for payment by case accrual, the system implemented by NCI to stimulate accrual.

There currently are 10 trials ongoing with the high priority designation. Two of them probably will close this year, and seven within 18 months.

"There are enough closing in the near future to enable us to consider additional trials," Cancer Therapy Evaluation Program Director Michael Friedman said. "We should keep the number small, but we're in no danger of diluting the system."

The four trials recommended by the chairmen for high priority designation:

* Eastern Cooperative Oncology Group adult acute myelogenous leukemia intensive post remission study.

Patients first receive an induction regimen of idarubicin and cytarabine. Those who do not achieve complete remission go off study. Those with complete remission receive further treatment with idarubicin and cytarabine. Those with histocompatible siblings then receive allogeneic bone marrow transplantation. Those not qualified for allogeneic transplant are randomized to either autologous bone marrow transplant, which includes preparative therapy of busulfan and cyclophosphamide; or consolidation chemotherapy consisting of once course of cytarabine.

* Intergroup rectal adjuvant protocol, developed by Cancer & Leukemia Group B.

Patients with resected adenocarcinoma of the rectum, with no evidence of gross or microscopic residual disease, are randomized to:

--5-FU, followed by radiotherapy plus 5-FU, followed by 5-FU.

--5-FU and leucovorin, followed by radiotherapy plus 5-FU and leucovorin, followed by 5-FU and leucovorin.

--5-FU and levamisole, followed by radiotherapy and 5-FU, followed by 5-FU and levamisole.

--50-FU, leucovorin, and levamisole, followed by radiotherapy, 5-FU, and levamisole, followed by 5-FU, leucovorin, and levamisole.

As replacement for the adjuvant colon cancer study comparing 5-FU and leucovorin to untreated controls, placed on the high priority list last year but

discontinued when the 5-FU/levamisole study turned positive, which forced discontinuation of untreated arms in Dukes C cancer:

* North Central Cancer Treatment Group protocol, in which M.D. Anderson Cancer Center is participating, comparing 5-FU and levamisole with 5-FU, levamisole and leucovorin, with secondary randomization to six vs. 12 months of treatment. The National Cancer Institute of Canada is also participating in this trial.

* Intergroup study (CALGB, ECOG, Southwest Oncology Group), comparing 5-FU and leucovorin with 5-FU, leucovorin and levamisole.

DCE Board Approves Recompetition Of Support Contracts, PA Revision

The Div. of Cancer Etiology Board of Scientific Counselors gave concept approval to recompetition of two support contracts worth more than $2.3 million.

In addition, the board, at its recent meeting approved the revision of a program announcement on cancer epidemiology, and gave concept approval to several noncompetitive projects to be funded through interagecy agreements.

The texts of the concept statements follow:

Supply purified recombinant human viral proteins produced in insect cells. Recompetition of a contract held by Repligen Corp. Proposed first year award $415,000; total $1,308,290 over three years.

Due to the continued spread of HIV and the need for the development of a vaccine to control the spread of AIDS, the Laboratory of Tumor Cell Biology has been investigating several experimental vaccine approaches, ranging from subunit vaccines to insertion of HIV genes into viral carriers such as vaccinia. An important approach is based on the use of recombinant viral proteins, especially envelope produced in insect cells. It is hoped that group specific rather than type specific neutralizing antibody response and/or cytotoxic T cell response can be generated capable of effectively blocking infection by different HIV variants.

This contract was originally awarded in January 1989 to obtain purified recombinant HIV and SIV, gp120, 140 and 160, produced in baculovirus. In the first year the contractor has provided 100 mg of HIV-1 gp160 and 10 mg of gp120 for use as part of a multicomponent vaccine preparation; for analysis of humoral and cellular protective immune response as measured by neutralizing antibodies, ADCC and proliferation assays, and for analysis of gp160 and gp120 interaction with CD4. In the second year of the contract the contractor will produce 30 mg of HIV-2 gp160, 50mg of SIV gp140 and 1mg of HIV-1 tat. It is hoped that the glycoproteins produced in baculovirus would have proper glycosylation and information similar to the native proteins isolated from concentrated virus. This information may be important in provided the conformational epitopes necessary to obtain a broadly cross reactive antibody for neutralization of different HIV variants.

A major objective of the continuation of this contract will be the productions of 5--100mg of HIV of SHIV purified glycoproteins from three different virus strains, and regulatory proteins (5-10mg) for use as part of a multicomponent vaccine preparation, for analysis of humoral and cell mediated immune response and interaction with CD4, immunotherapy and structure function analysis. Polyclonal and monoclonal antibodies against the HIV ans SHIV proteins will be provided by the contractor and will be used for testing their ability to neutralize the infectivity of various laboratory and primary isolates of HIV. Depending on results of these studies, the glycoproteins will be used alone or in conjunction with proteins and/or peptides from other HIV strains to attempt to generate a broadly cross reactive neutralizing antibody response.

Tracing individuals for environmental epidemiologic studies of cancer. Recompetition of contracts held by Equifax Inc., Johns Holdings Co., Tracers, and Policy Management Systems Corp. Proposed first year award $250,000; total $1.05 million over four years.

This concept provides for the recompetition of the master agreement under which experienced tracing firms may qualify to be included in a pool of contractors, which are authorized to bid on master agreement order requests for proposals. Specific tracing tasks involve the location of epidemiologic study subjects designated as "difficult to find." The subjects in this category cannot be located using a variety of standard initial tracing resources such as the National Death Index, Health Care Financing Administration, Veterans Administration, and others.

Nearly every cohort and case-control study conducted within the Epidemiology & Biostatistics Program requires additional tracing to maximize follow-up. The program has been contracting for tracing services since 1980.

The three distinct tracing methods are a) M-1: tracing individuals through credit bureaus, b) M-2: tracing individuals through motor vehicle bureaus, c) M-5: tracing individuals through other sources and resources. Offerors may submit proposals for any combination of tracing methods. A complete technical proposal, reviewed by an outside Initial Technical Evaluation Group, as well as an in house Source Evaluation Group, is required for each method for which an offeror applies. Offerors are included in every pool for which they submitted a technically acceptable proposal, and are subsequently eligible to bid on every master agreement order issued for that method.

Since the inception of the master agreement, a total of 323,093 subjects, representing more than 40 distinct studies, has been submitted for tracing. The total number of subjects traced is as follows: M-1: 86,425 (27 percent), M-2: 107,329 (33 percent), M-4 and M-5 combined: 129,339 (40 percent).

Small grants for cancer epidemiology. This is a revision of a program announcement. This PA was initiated in 1986 and modified in 1988 to increase the funding from $25,000 to $50,000. The purposes remained unchanged, i.e., to support pilot projects, test new techniques, or encourage innovative or high risk research. The eligibility criteria have been expanded, but no further changes is proposed here except to clarify that the mechanism may be used to provide essential resources for an investigator to mount an investigation of an emerging issue. While definitive and costly studies are best supported by other research grants, a small grant can provide resources for such essential preliminary tasks as questionnaire design, preliminary assessment of exposure prevalence and test development including field testing.

An investigator is eligible to apply for a small grant in cancer epidemiology and etiology if the thrust of the project involves Planning a complex epidemiologic investigation, developing or

validating a laboratory or statistical procedure with potential for improving the quality of cancer epidemiologic research, analyzing previously collected data for epidemiologic purposes, such as combining data from multiple studies to examine consistency or strength of observed associations, resolving methodologic problems, such as documenting the accuracy of a customary procedure in preparation for use in epidemiologic research, evaluating the effect of cancer diagnosis and/or treatment on risk factor estimates derived from case-control studies, and obtaining rapid funding for an urgent or time-limited issue relevant to cancer epidemiology. The latter situation may occur, for example, when specific personnel or resources are available for only limited periods of time, or when research is rapidly evolving on topics of great public health importance, such as AIDS.

Also given concept approval were four task orders involving an interagency agreement between NCI and the National Institute of Occupational Safety & Health, and two projects involving interagency agreements with the Dept. of Energy and the Air Force. The titles and proposed funding levels for the NIOSH projects are as follows:

Feasibility assessment for new topics, no added funding. Task order for a feasibility assessment or a study of workers employed in the production of formaldehyde resin and molding compounds, $40,000. Task order for a feasibility assessment for Stoddard solvent, $20,000. Task order for a feasibility assessment for dimethylformamide, $40,000. Task order for a feasibility assessment for a study of workers exposed to ortho-toluidine, $40,000.

The agreement with the Dept. of Energy involves a new contract to estimate cumulative radiation exposures from long term, low level occupational exposures at the Sellafield nuclear fuel reprocessing plant, operated by British Nuclear Fuels Ltd. DOE is providing half of the funding for the study.

The board gave concept approval to an extended evaluation of a study of the mortality of workers at Hill Air Force Base. The Air Force is funding the project.

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-CM-17502-19
Title: Natural products lead-based synthesis
Deadline: Approximately Aug. 27

The Drug Synthesis and Chemistry Branch of the Developmental Therapeutics Program within NCI's Div. of Cancer Treatment is seeking contractors with established expertise in the field of enantio-and stereoselective synthesis of complex molecules to prepare natural products and their derivatives for evaluation as antitumor and AIDS antiviral agents. NCI signs legally binding agreements with some suppliers (often pharmaceutical of chemical companies) which state that all information on compounds donated by those suppliers will be held confidential. The successful offeror may be assigned a confidential compound as a synthesis or modification target. If the contractor were a chemical or pharmaceutical company, it could gain valuable data on confidential new lead compounds. NCI believes that in order to avoid any chance of transmitting privileged data to a competitor, pharmaceutical and chemical companies are excluded from this competitive procurement. The contract period is to be for three years, beginning approximately March 1991.
Contracting Officer: Dorothy Coleman
RCB Executive Plaza South Rm 603
301/496-8620

RFP NCI-CN-05302-03
Title: Surveillance, Epidemiology & End Results expansion
Deadline: Approximately Sept. 13

NCI's Div. of Cancer Prevention & Control is soliciting proposals for an expansion of the Surveillance, Epidemiology & End Results Program (SEER). The thrust of this project is 1) to obtain within the geographic area of coverage, data on all newly diagnosed cases of cancer beginning Jan. 1, 1990 forward, 2) to obtain cancer patient survival data on all cases diagnosed 1990 forward, 3) to monitor trends in the incidence of specific forms of cancer, particularly with respect to demographic and social characteristics of the populations, 4) to assess the completeness and accuracy of all data collected.

It is anticipated that offerors must provide documentation of authority to collect data for their identified coverage area and be required to have a Hispanic population of at least 300,000.
Contracting Officer: Shirley Kyle
RCB Executive Plaza South Rm 635
301/496-8603

Program Announcement

PA-90-17 Multidisciplinary research on solid tumors. NCI through the Organ Systems Coordinating Branch seeks grant applications to conduct multidisciplinary research on human solid tumors. This program announcement encompasses a full range of studies from basic through clinical, including technology research. Applications may focus on one or several solid tumors.

The intent of the announcement is to encourage research on human solid tumors that contribute substantially to cancer incidence, morbidity and mortality. NCI is especially interested in novel ideas and approaches to solid tumors.

In past years, significant progress has been reported for leukemia and lymphoma research, but advances in solid tumor research have not been commensurate. This disparity has been due partly to the lack of suitable models and particularly to the lack of available human tissues. The establishment of the Cooperative Human Tissue Network, supported through the nCI Div. of Cancer Biology, Diagnosis & Centers, now makes human tissues more readily available for research purposes. Thus, an increased emphasis on human solid tumor research becomes feasible.

NCI now seeks to stimulate novel research in the solid tumors, particularly those tumors that account for significant cancer

Expedite routi...

incidence, morbidity and mortality, e.g., lung, colon-rectum, breast, upper aerodigestive, prostate, bladder, pancreas, melanoma, stomach, kidney, ovary, brain.

A major portion of NCI support for research on these tumors has been in applied research, e.g., clinical trials; basic research has received less attention.

In the past, NCI has supported solid tumor research through clinical cooperative trials which have addressed a variety of solid tumors, as wells as through the Organ Systems Program which sought to stimulate multidisciplinary research in selected solid tumor sites. A recent reorganization of the OSP has broadened its responsibility to include research encompassing all solid tumors, with emphasis on those that contribute substantially to cancer incidence, mortality and morbidity and/or have particular significance to minorities and the aged.

This announcement seeks to encourage multidisciplinary research on human solid tumors. Research grant applications utilizing the traditional grant mechanisms, including the RO1 investigator initiated or the PO1 program project grant, are encouraged. Small PO1 program project applications with three to four subprojects, addressing one or more tumor sites, would be particularly relevant. A PO1 application could be multi-institutional, thereby providing multidisciplinary linkages not otherwise available. A full range of research activities including basic, clinical and technology development is within the scope of this announcement.

Examples of research areas include but are not limited to those being explored under the previous organization of the OSP, which utilized standing working groups of expert scientists to identify multidisciplinary research opportunities. For example, the Bladder Cancer Working Group concluded a workshop on "The biology of Bladder Cancer and the Potential Implications" in which opportunities were identified relating to stromal epithelial interactions and oncogene activation, new potential markers in tumorigenesis, tumor growth influence on immunobiology, development of laboratory techniques for predicting chemotherapy and radiation responses, and opportunities for prevention trials.

The Breast Cancer Working Group has addressed interactions between hormonal and cytotoxic adjuvant therapies and the effects of tamoxifen, estrogens and progestins on high risk breast lesions.

The CNS Oncology Working Group was developing ideas for research on targets and mechanisms of CNS radiation damage in order to understand molecular lesions responsible for radiation injury specific to cellular elements and vasculature of the central nervous system.

The Large Bowel Cancer Working Group was developing ideas focused on the transformation and progression of normal colonic epithelium to adenocarcinoma, as well as protocols for conservative treatment of rectal cancer, thereby avoiding permanent colostomy.

The Prostate Cancer Working Group was addressing genetic instability and tumor heterogeneity, the biology of latent cancer and its clinical progression and a re-examination of prostate epidemiology.

The Upper Aerodigestive Cancer Working Group convened a workshop on chemoprevention of upper aerodigestive tract cancers and was developing concepts for related research initiatives. In addition, ideas were being discussed relative to genetic susceptibility to subclinical disease in the head and neck, and a possible viral etiology in the epidemiology of upper aerodigestive cancers.

For further information on any of these working group activities, call the Organ Systems Coordinating Branch (see below). These examples focus on single tumor sites and are not all inclusive. Other tumor sites and other areas are encouraged as well as approaches which study tumors across organ sites.

NCI is especially interested in novel ideas and approaches. Applicants are encouraged to use multidisciplinary approaches for investigating common as well as unique properties and behavior of solid tumors. Human tissues for research purposes are available through the Cooperative Human Tissue Network (for information, contact Dr. Roger Aamodt, 301/496-7147). Prospective applicants could benefit by calling the Organ Systems Coordinating Branch to establish relevant contacts within NCI. If a program project application is considered, preliminary contact should be made to assure adherence to guidelines for program project applications. Grant applications submitted in response to this announcement will be assigned to the relevant divisional programs.

For more information contact Dr. Andrew Chiarodo, Organ Systems Coordinating Branch; Centers, Training & Resources Program, Div. of Cancer Biology, Diagnosis & Centers, NCI, Executive Plaza North Suite 316, Bethesda, MD 20892, phone 301/496-8528.

New Publications

"The Lymphomas: Current Concepts in Pathogenesis and Management, Number 10" in the "Journal of the National Cancer Institute" Monographs series is now available from the Government Printing Office.

The proceedings of a conference held in Washington Sept. 21-23, 1989 discuss the evolution of lymphoma treatment, the current status of diagnosis and therapy, and glimpses at future directions of research and treatment. Highlighted are the areas that need further investigation--an understanding of the genetic events that characterize malignant transformation, optimization of the chemotherapeutic regimens in regard to dose intensity and use of biologically active agents alone or in combination with chemotherapy.

Single copies of the publication are available for $4.50. Credit cards are accepted and checks for orders may be made payable to the Superintendent of Documents and mailed to: Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

"Cancer Causes & Control" is a new journal of studies of cancer in human populations, published by Rapid Communications of Oxford Ltd. The journal will accept articles for publication under the headings of research articles, review, comment, opinion, letters to the editor, and others as appropriate. Submissions may be addressed to Dr. Brian MacMahon, Dept. of Epidemiology, Harvard School of Public Health, 677 Huntington Ave., Boston, MA 02115, fax 617/734-4713.

For further information, contact Rapid Communications, The Old Malthouse, Paradise St., England OX1 1LD, phone 44/865-790447, fax 44/865-244012.