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Centers Program Debate Turns Into Full Review Of All Issues; Massive Survey, Hearings Planned

What started out as a debate over where management of the Cancer Centers Program would be located within NCI has led to a full scale, all out, all encompassing review of every issue related to centers which will include a survey of

(Continued to page 2)

In Brief

Elizabeth Miller Dies; Mihich Named Associate Director At RPMI; AACR Calls For Abstracts

ELIZABETH MILLER, who with her husband James formed a research team at the Univ. of Wisconsin's McArdle Laboratory that won world wide acclaim for research in carcinogenesis, died Oct. 14 of kidney cancer. She was 67. The Millers shared the Bristol-Myers award one year, among their many honors, and she served a term as member of the President's Cancer Panel. A memorial service will be held Oct. 25, 1 p.m., at the Wisconsin Center in Madison. . . . **ENRICO MIHICH**, director of Grace Drug Institute at Roswell Park Memorial Institute, has been appointed associate director for sponsored programs, RPMI Director Thomas Tomasi announced. The appointment will take effect Jan. 1. Mihich, current president of the American Assn. for Cancer Research, will facilitate development and coordination of programs with agencies and corporations outside RPMI. He will continue as director of Grace. . . . **AACR HAS** issued the first call for abstracts for its 79th annual meeting May 25-28 in New Orleans. Scientific sessions and commercial exhibits will be held at the New Orleans Convention Center. As usual, the annual meeting will be held jointly with that of the American Society of Clinical Oncology, scheduled for May 22-24, and the traditional joint AACR/ASCO session will be held May 25. Deadline for abstracts is Dec. 8. Abstract forms and further information may be obtained from the AACR Office, Temple Univ. School of Medicine, West Bldg Rm 301, Philadelphia, PA 19140, phone 215/221-4565. Questions regarding abstract preparation should be directed to 215/221-4720. . . **CORRECTION:** It is the 29th annual Postgraduate Institute for Pathologists in Clinical Cytopathology at Johns Hopkins, not clinical pathology as reported in **The Cancer Letter** Sept. 25 meetings column. The Home Study Course A will extend from February through April, the in residence course B from April 25-May 6. Contact John Frost, MD, 604 Pathology Bldg, Johns Hopkins Hospital, Baltimore, MD 21205.

NCI, NCAB To Conduct Full Review Of Centers Program; Survey Planned

(Continued from page 1)
everyone who might have an opinion on what centers should be, or even if they should exist at all.

The discontent expressed during the past year by cancer center representatives over what they perceived as inadequate priority given the program in its present location, the Div. of Cancer Prevention & Control, has been discussed by the DCPC Board of Scientific Counselors and the National Cancer Advisory Board. Options suggested by NCI Director Vincent DeVita include establishing a new division for centers and other non-cancer control programs within DCPC; moving the centers program into his office; leaving it where it is.

No clear consensus was reached on any of those suggestions, and the matter was turned over to the NCAB's Centers Committee, chaired by John Durant, president of Fox Chase Cancer Center.

DeVita also revived the matter of comprehensive cancer center recognition. During the 1970s, stimulated by language in the National Cancer Act of 1971, NCI "recognized" (as opposed to "designated") 21 centers as comprehensive. Recognition followed review by the NCAB to determine how well the center met the 10 characteristics established by the NCAB as criteria for comprehensiveness.

Comprehensive recognition did not carry with it any monetary awards, but it was highly prized anyway for the prestige, bragging rights and potential aid in recruiting scientists, patients and donors. By the end of the 1970s, however, many center executives had come to believe that it was more trouble than it was worth, and that NCI placed too many demands on the comprehensive centers which were not backed up with money. No center had sought comprehensive recognition in the 1980s, and NCI was content to let that aspect of the cancer program languish.

Sydney Salmon, director of the Univ. of Arizona Cancer Center, brought that interlude to an end with his request for comprehensive recognition. DeVita then asked the NCAB to reconsider its list of characteristics, and that, with the other issues, was turned over to Durant's committee.

Meeting prior to the recent NCAB meeting, Durant's committee considered this list of issues which he had drawn up, with the language designed to be "evocative and provacative," he said. These were offered as a basis for a questionnaire to be sent to institutions and individuals with an interest in the Cancer Centers Program:

I. Reevaluate the concept of cancer centers in the context of today's research climate.

A. What is the greatest contribution of cancer centers to today's research climate?

B. What tangible advances since 1971 are attributable to the Centers Program that probably would not have occurred without it?

C. How important is the core grant to the basic research effort or could it be improved upon?

D. Are there issues extraneous to NCI policy that inhibit the function of centers, e.g., other federal government, state and local policies?

E. Does your institution believe that being a "center" gives it some kind of competitive advantage?

F. Does your institution believe that being a "comprehensive center" gives it some additional competitive advantage?

II. The meaning and special characteristics of comprehensiveness.

A. What criteria define comprehensiveness? Are comprehensive centers distinguishable from clinical cancer centers?

B. Should a periodic redesignation process for comprehensiveness for all centers be developed? If so, how?

C. Do comprehensive centers have a responsibility for addressing avoidable mortality in their geographic areas?

D. What mechanism can you propose to integrate cancer prevention and control research into cancer centers?

E. Should comprehensive and clinical centers be expected to respond, according to their capabilities, to national initiatives?

F. What is the mechanism of participation by which priority goals for NCI can be implemented?

G. Should a forum be established for the consideration of intercenter technology transfer, e.g., high priority clinical trials? If so, why? If not, why not?

H. Should the clinical activities and output of centers be coupled to medical practice in their geographic region?

III. The logistics of the centers program.

A. What is an adequate number of cancer centers and how is the number determined?

B. What is the proper geographic distribution of of centers?

C. What is the proper mixture of the different types of centers--comprehensive, clinical, basic science, consortium?

D. What should be the role of consortium core grants in relationship to core grants for individual centers within a region?

E. The original models for cancer centers described in the National Cancer Act were free standing cancer centers. What are the special characteristics of the free standing centers? Should incentives be provided to enable some centers located in universities to become free standing?

F. Should cancer centers have academic and educational missions which require affiliation with a medical school (medical and graduate students)?

IV. Funding and management issues for the Cancer Centers Program.

A. What is the best organizational location for the centers program within NCI?

B. What kind of mechanism should be established to promote communication between center directors and NCI staff in order to evaluate the feasibility of broad initiatives? What kind of mechanism should be established to fund these initiatives?

C. The basic science centers budget will hereafter be identified separately in the centers line of the NCI budget to clarify the differences between support for centers with clinical capabilities and those without such capabilities. Should the basic science centers also be moved to another NCI division such as the Div. of Cancer Biology & Diagnosis?

D. Given the limited role of basic science centers in the clinical application of the results of basic research, are their activities more appropriately funded through inclusion of support for core facilities in PO1 grants?

E. Are there other instruments which could be used for support of centers?

F. In order to allow the funding of new cancer centers to expand the centers program within a finite budget, should there be a time limit such as 10 years for receipt of core funding support from NCI with the expectation that the center will develop other funding sources during that period?

G. Some institutions desire recognition as cancer centers as a means to develop support for their programs. Should there be a mechanism for recognition of an institution as an NCI cancer center without funding? If so, how should such programs be reviewed and what should be expected of them?

"These questions were meant to stimulate responses," Durant told the committee. He added that he planned to ask the full Board for approval to solicit that type of information "from the constituency."

That constituency will include all institutions with current core grants, all NCI grantees, members of the Assn. of American Cancer Institutes, and members of various cancer related professional societies. The total could reach 15-20,000.

"There are words here that make university folks uneasy," Board member Roswell Boutwell said. "Avoidable mortality and response to national initiatives carry with them the prospect of directed research, which is contrary to the ethos of NCI. We don"t want to see centers misconstrued as public health agencies."

Boutwell added, "The language [in the issues presented by Durant] is delicously provacative."

"Basic scientists say that center core grants are not needed," DeVita said. "When you ask center directors, they say the only role of the core grant is to support basic research."

Boutwell said he could not see the relevance to basic science of the question asking if comprehensive centers are distinguishable from clinical cancer centers.

"There is no way a basic science center can be comprehensive [without adding a clinical component]," DeVita responded. "So matters relating to comprehensiveness are not relevant to basic science centers."

DeVita continued, "We have 20 clinical centers (those with NCI center core grants) which are indistinguishable from comprehensive centers. We were ignoring the distinction until Syd Salmon precipitated this. So now we need to have another look."

Durant said that there is no deadline for consideration of Salmon's request for comprehensive recognition which would preclude reconsideration of the comprehensive characteristics. "Syd won't launch an attack on Building 1 (NIH headquarters) or Building 31 (which includes NCI headquarters) if we don't get this out right away. That means we can take longer if we need to, and do it right."

On the issue of requiring centers to address avoidable mortality in their commu-

nities, DeVita said that Los Angeles County has 700 deaths a year from cervical cancer, all of which are avoidable. The county includes two comprehensive centers, another clinical center, and two NCI funded Community Clinical Oncology Programs.

"I asked the centers who had responsibility [to do something about that avoidable mortality]," DeVita said. "They answered, 'Our job is doing research.'"

DeVita told the committee that the issue of comprehensive characteristics has to be resolved, and that if the NCAB does not do it, NCI staff will. "The comprehensive criteria never satisfied everyone. The issues of centers playing national roles, networks, clinical trials, avoidable mortality, prevention, have never been addressed."

NCI wants a complete evaluation of the centers program, DeVita said. "We need it, particularly with reauthorization coming up." Congress will consider renewal of the National Cancer Act next year.

Durant suggested that at least two workshops would be required, one on centers evaluation, determination of their worth, comprehensive characteristics, and another on the question of logistics and administration.

"It's important to let all grantees know a review of centers is going on, and that they can take part in it," DeVita said.

Brian Kimes, associate director and head of the Extramural Research Program in the Div. of Cancer Biology & Diagnosis, said, "I haven't heard a good definition of what a center is."

"The definition of a cancer center is that it is an institution with a center core grant," DeVita said.

"That's the bureaucratic definition," Durant said. "You can look in the newspaper and see all kinds of organizations calling themselves cancer centers."

Later, in discussions at the meeting of the full NCAB, Durant said, "If we don't come out strong [on definition of a comprehensive cancer center], every little hospital that wants to declare itself comprehensive will do so."

"The horse is already out of that barn," Board member Victor Braren said.

Braren questioned the practicality of sending the questionnaires to so many persons.

"Most of them won't respond, but if they do, we might learn something," DeVita said. "We don't want to leave anyone out."

Senate Passes Appropriations Bill; Gramm-Rudman Cuts Threaten Total

The Senate passed the Labor-HHS-Education appropriations bill last week, with modest additions for AIDS research above that recommended by the Appropriations Committee. The total for NCI was left essentially unchanged, $1.527 billion.

The House and Senate are only about $10 million apart on NCI's budget for the fiscal year which started Oct. 1; the conference to resolve differences in the two bills had not yet been scheduled by press time.

It appears that NCI will receive an increase of about $120 million over 1987, if the final bill is approved by Congress and the President. However, the spectre of Gramm-Rudman-Hollings once again hovers over the Cancer Program, all other biomedical research and many other government activities.

The current projection is that the government will fall $23 billion short of meeting the GRH deficit reduction target, unless Congress and the President can agree on a mix of reductions and tax increases to achieve the goal. Both houses are developing modest tax increase bills, which coupled with various budget cuts would do the job. President Reagan has said he will veto any tax increase, and it does not appear Congress will be able to override.

Failure to reach the deficit target will trigger an automatic across the board cut that would amount to about eight percent. Applied to NCI, that would wipe out the increase over last year's spending, probably resulting in reductions in most grants from peer review approved levels. It also could mean some competing center grants would not be funded, clinical trials would be cut back, and drug development severely limited, including anti-AIDS drugs.

In debate on the Senate floor, Sen. Howell Hefflin (D-AL) elicited from Lawton Chiles, chairman of the Labor-HHS-Education Appropriations Subcommittee, assurances that the bill included the $118 million needed for funding 60 percent of approved center core grants, including several new centers, at their peer reviewed levels. Language to that effect was included in the committee report on the bill.

No similar language was in the report on the House bill. If a specific agreement on that point is not reached in the conference, NCI does not have to comply.

DCT Board Approves Recompetition Of Six Contracts, Increase In Another

The Div. of Cancer Treatment Board of Scientific Counselors gave concept approval to the recompetition of five Developmental Therapeutics Program contracts at its recent meeting. Estimated annual costs for the five totaled more than $2.5 million.

The Board also approved recompetition of a Clinical Oncology Program contract, estimated to cost a half million dollars a year, and approved a substantial increase in another ongoing contract.

The concepts, which will be developed into competitive RFPs, are:

Surveillance and selection of promising natural products. Recompetition of a contract held by the Univ. of Illinois. Three years, estimated annual cost, $136,000.

Over 5,000 natural products structures from microbial, plant and animal sources are reported in the literature each year. A significant percent of these compounds represents novel structure types which could provide new leads for development of antitumor agents. This is particularly important in the natural products area, since natural products provide highly unusual chemical structures which represent entirely new classes of compounds for anticancer screening. To conduct such a search with a limited staff could cover only a small fraction of the available literature. It is clear that a more extensive search program by an institution properly staffed and adequately equipped is necessary for adequate literature coverage.

This is a competitive contract involving surveillance of literature in the natural products area for new and novel compounds which may have potential activity as chemotherapeutic agents against human cancers. The contractor searches through periodicals and provides the Natural Products Branch with listings of new chemical structures found in plants, animals and microorganisms; abstracts and reprints of pertinent articles; and lists of many biological properties of these compounds, including antitumor activities, thus providing DTP staff with information that is necessary for selecting and acquiring new and promising compounds that may show anticancer activities. The literature available to the contractor is extensive and comprehensive and the coverage of the field has been excellent.

A continuation of this project is essential for a continuous supply of new agents for testing against tumors. This contract has been extremely valuable to the acquisition program of the Natural Products Branch. No significant changes in the scope of work of this effort are anticipated.

DCT Director Bruce Chabner pointed out that none of the work under this contract involves potential AIDS drugs; that effort is carried out under a different contract and supported by earmarked AIDS money.

Large scale isolation of antitumor agents from natural sources. Recompetition of a master agreement. John Meade, DTP deputy director, told the Board that "until recently this was a one contractor arrangement," that contractor being Polysciences Inc. Master agreements will be awarded for five years, with individual tasks to be competed among those determined qualified. Estimated annual cost, $500,000.

The major objectives of this contract are to isolate highly purified bulk drugs from plants and animal materials in large quantities sufficient to meet NCI needs for compounds in clinical trials and advanced preclinical development and to develop suitable processes for large scale isolations.

During the 19 months from the inception of this contract in January, 1986, through August, 1987, the following tasks have been accomplished: (1) solvent partitions and preliminary chromatography of 128 kg of the primary extract of Phyllanthus acuminatus to isolate phyllanthoside for preclinical development; extraction, solvent separation and chromatography on 11,400 pounds of Taxus brevifolia bark to produce taxol for clinical trials.

The contractors will be required to supply NCI with highly purified compounds isolated from plant and marine animal sources. The major task will be to produce bulk drugs for clinical trials and for advanced developmental work including pharmacuetics and toxicology in quantities from several grams to several kilograms depending on the potency of the compounds and NCI needs. Each major assignment will require workup from several hundred pounds up to 20,000 pounds of plants or animal material. A continuing major project will be the isolation and purification of taxol for ongoing clinical trials, and the isolation and purification of phyllanthoside for preclinical development will be completed. As the screening of samples from the ongoing plant and marine organisms collection programs in the new cell line panels progresses, it is anticipated that a number of projects involving large scale isolation of active lead compounds will be required.

Pilot plant assignments will be regularly reviewed and will be subject to change depending on the priority needs of the DTP program for bulk drugs from plant or marine organism sources. In addition to preparing bulk drugs for clinical and advanced preclinical use, contracts will also be required to perform extractions and partial purification of leads in those cases where large amounts of raw material need to be processed to obtain enough of the active fraction for final chemical isolation and identification of the active constituents.

Quality control and model development in rodents and tumor cell lines. Early recompetition of a contract now held by Southern Research Institute. The new five year contract will start Feb. 1, 1989, with an estimated annual cost of $900,000.

This contract was initiated to develop and evaluate protocols for usage in the old in vivo oriented tumor screen and panel program. More recently, protocols have been developed for in vivo testing of actives from the disease oriented in vitro screening program. One of the requirements of tumor lines selected for the in vitro screen is that they be tumorigenic. Consequently, a significant effort has been exerted to implant candidate cell lines in athymic mice subcutaneously and by other routes to evaluate in vivo growth. A number of long passage lines have been dropped because of failure to grow in vivo.

In conjunction with tumorigenic studies, we have developed models and established protocols for compound evaluation for the in vitro screen. One of the most interesting studies has involved the development of a microencapsulation assay which allows for an early evaluation of activity with candidate compounds from the in vitro screen. This contract has played a most important role in developing this model. About 15

protocols have been developed for the subrenal capsule model. These protocols were primarily for lung tumor cell lines but also included brain, prostate, colon and breast. Following recommendations for an ad hoc committee of world experts we are developing protocols for subcutaneous in vivo testing. Protocols are completed or almost finished on nine human tumor lines with this model.

It is imperative that an in vivo tumor system counterpart be available for testing active leads developed through the in vitro screening of compounds in human tumor cell lines. Initial efforts in this area have reinforced the feeling that no single tumor model will be universally adaptable to all in vivo needs, but that multiple models must be developed. It is expected that model selection will be based on a number of factors including target organ, characteristics of correlating in vitro cell lines, pharmacological considerations, etc. Since all the large scale in vivo screening contracts are being phased out, this contract represents DTP's only off site resource for model development and drug testing for verification of protocols.

DTP Director Michael Boyd said that "we have no option other than extramural" to do "this nuts and bolts work."

Board member John Mendelsohn said, "What bothers us is that we are still arguing about the effectiveness of the in vitro screen, then you want to develop a system to move [compounds found active in vitro] into animals."

"We have no leads out of the in vitro screen to evaluate so far," Boyd said. "But we must have a capability in place to evaluate them when we do."

"One of the major questions pharmacologists have raised is that in vitro doesn't tell you what in vivo will about metabolism, etc.," Chabner said. "They have insisted that at least one in vivo testing system is needed."

Boyd noted that an RFA for anticancer drug model development groups has been issued. "I'm sure those groups will address some of these issues."

"I would strongly suggest development of a metastatic model," Board member Robert Jackson said.

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The dollar estimates with each concept brought before the various boards of scientific counselors or other advisory groups are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended as guides for board members to help in determining the value of the projects in relation to the resources available to the entire program or division. In the case of RFAs, the amounts cited are the maximum that will be set aside to fund those particular grants, the final amount depending on NCI's budget and program priorities. Responses should be based on workscope and description of goals and methods included in the RFPs (contracts) or RFAs (grants and cooperative agreements). Availability of the RFPs and RFAs will be announced when NCI is ready to release them.

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Preclinical pharmacology investigations of antitumor agents. Recompetition of contracts now held by Ohio State Univ., Mayo Foundation and Southern Research Institute. Total annual cost of the new three year awards is estimated at $715,000.

In recent years the Blood Level Working Group of NCI has shown that knowledge of the preclinical pharmacokinetics of drugs can, among other things, help to establish starting doses and reduce the number of escalations used in early clinical trials. These contracts are designed to acquire such preclinical pharmacological data on new drugs. They provide data on the most appropriate method of analysis to be used in subsequent toxicology and clinical studies of a drug. They collect data in several species (mice, rat, dog) concering pharmacokinetics, plasma protein drug binding, drug metabolism, drug stability and bioavailability. These data have been used to model drug behavior in vivo and are useful in planning clinical use of the agents.

In addition these data are used in reports to FDA as part of NCI's IND filings for new antitumor agents. Summaries of data from specific reports are discussed with and provided to phase 1 investigators through cooperative efforts with the Cancer Therapy Evaluation Program of DCT.

The three operational contracts involve a total level of effort of 10.5 staff years per year. During the past one and a half years, each contractor has presented reports on three to five drugs. Some of the drugs investigated recently include nafidimide, flavone acetic acid, buthionine sulfoximine, L-histidinol, pyrazine diazohydroxide and 1,7-heptanediol sulfamate. These reports have been used to make decisions on drug development within the program, to support new IND filings, to provide methods of analysis of drugs for clinical trial, to establish starting doses and schedules, and to support modifications of current phase 1 trials. Data from these reports have been provided to support planning of toxicology and to CTEP to support planning of new phase 1 studies.

It is anticipated that the project work will continue as described above. These kind of data are playing an increasingly important role in decisions concerning drug development as more drugs are initially screened in the in vitro human cell line system.

Preparation of radiolabeled materials. Recompetition of a contract held by Research Triangle Institute. Cost of the new five year contract is estimated at $350,000 a year.

This service project is devoted to the procurement, either by synthesis or from commercial sources, of radiolabeled materials needed and requested by various areas of DCT. The compounds scheduled for preparation are not available from commercial sources and involve a wide variety of structures. Materials that are available commercially are also obtained by the contractor, checked for purity, and repurified if necessary. The contractor also handles the storage and distribution at the direction of the project officer, and performs the necessary analytical work for labeled materials. The materials are used primarily in preclinical pharmacological and toxicological studies, mechanism of action studies and clinical investigations. All requests for labeled materials are reviewed by proper authorities prior to assignment to the contractors.

During the past year, 10 labeled compounds were prepared, and 90 shipments of labeled substances were made. A wide variety of labeled compounds were prepared including ^{14}C labeled flavone acetic acid, ipomeanol, pyrazine diazohydroxide, ^{3}H-labeled dideoxyadenosine, dideoxycytidine and tetraplatin.

This resource project will continue to be used for the preparation of radiolabeled compounds not readily available from commercial sources. A wide variety of compounds of varying structures will be prepared and the amount of radioactivity will vary in quantity and specific activity according to the intended use and in accord with safe handling procedures.

The project will also provide for obtaining radiolabeled materials from commercial sources. Materials so obtained will be checked for radiopurity and homogeneity.

All materials, whether prepared or purchased, will be assigned by the project officer upon request from

other areas of NCI. The project also provides for the storage and distribution of the labeled materials. All materials will be dispensed at the direction of the project officer. All materials will be checked for purity prior to shipment and repurified, if necessary, before shipment.

Provision, maintenance and transfer of tumored lab animal models for investigation. Recompetition of a contract now held by Hazleton Laboratories. The new five year contract will cost an estimated $504,000 a year.

This contract is designed to serve all laboratories headed by senior investigators in the Surgery, Pediatric, Medicine, NCI-Navy Medical Oncology and Radiation Oncology branches of the Clinical Oncology Prorgram. The present contract provides for housing and maintenance of 7,900 mice, 500 rats and 30 rabbits.

Because of increased needs within the various COP branches, in particular expansion of preclinical AIDS research, the present workscope should be revised. A request for increasing the number of animals to 10,000 mice, 700 rats and 60 rabbits in a new contract is proposed.

Clinical data management. Additional funding for a contract being performed by the Orkand Corp. for the Clinical Oncology Program.

The present contract, which is costing about $440,000 a year, will be increased by an additional $191,000 in FY 1988, $275,000 in 1989 and $287,000 in 1990. This increased workscope will allow for more timely, complete and accurate data collection and data management, as well as more responsive reporting to external monitoring organizations. It will also result in an enhanced opportunity for research nurses to be able to provide needed patient monitoring as required by protocols, since the nurses will be freed from certain routine data collection and forms completion duties as a result of this increase.

Outside reviewers and COP branch chiefs agreed increased data management support was needed in view of continued commitment to phase 1 and 2 studies, including expansion of AIDS drug testing.

RFAs Available

RFA 87-CA-37

Title: Cancer prevention and control research small grants program

Application receipt date: Dec. 10

The Div. of Cancer Prevention & Control of NCI invites small grants research applications in a program designed to facilitate growth of a nationwide cohort of scientists with a high level of research expertise in human cancer control intervention research.

New as well as experienced investigators in relevant fields and disciplines (e.g. disease prevention and control, medicine, public health, health promotion, epidemiology, social work, nursing research, nutrition, health policy, health services research and behavioral sciences) may apply for small grants to test ideas or do pilot studies.

This RFA is a modified reissuance of an RFA which resulted in 56 awards. It will be reissued annually for four more years with up to 30 awards per year if funds are available.

Cancer control program areas appropriate for research grants include human intervention research in the following areas:

*Prevention (chemoprevention, diet and nutrition and early detection).

*Health promotion sciences (modifying personal, social and lifestyle and health care system factors which contribute to cancer prevention and control).

*Smoking prevention and cessation.

*Cancer control operations research and evaluation.

*Applied epidemiology (using epidemiologic methods to determine the association between exposure to an intervention and its impact on disease).

*Planning, epidemiologic and survey studies aimed at developing cancer control interventions.

*Applications research in modifying, feasibility testing, and adopting proven, state of the art intervention programs and strategies from other research projects in state and local health agencies or other community settings. Also adaption of state and local health agency data bases for cancer control planning and evaluation.

*Community oncology (improving the application of patient management and continuing care research advances into community settings).

It is important that a long term human cancer control hypothesis and supporting scientific justification must be presented, although the specific study proposed may attempt to obtain preliminary data and/or do pilot studies in support of a future more detailed phase 3-4 study.

Total costs, direct and indirect, may not exceed $35,000. Duration of support is one year but may be longer (up to two years) if the $35,000 limit is no exceeded for the entire project.

For program information, consultation and complete copies of the RFA, contact Carlos Caban, PhD, Program Director for Cancer Control Research, Cancer Control Applications Branch, DCPC, NCI, Blair Bldg Rm 4A01, Bethesda, MD 20892, phone 301/427-8735.

RFA 88-CA-01

Title: Cooperative agreements for prevention clinical trials utilizing intermediate endpoints and their modulation by chemopreventive agents

Application receipt date: Dec. 10

DCPC invites applications for cooperative agreements to support clinical trials which are directed toward examining the role of various chemopreventive agents and/or diet in the prevention of cancer. This is a followup to earlier RFAs which had requested grants, and then later, cooperative agreement proposals in this area.

The major objective of this RFA is to encourage cancer chemoprevention clinical trials which utilize biochemical and biological markers to identify populations at risk and/or to provide intermediate endpoints that may predict later reduction in cancer incidence rates.

These studies may be developed in phases, including a pilot phase, which could later proceed to a full scale intervention. The main emphasis should be on small, efficient studies aimed at improving future research designs of chemoprevention trials, providing biologic understanding of what is happening in the trials, or providing better, more quantitative and more efficient endpoints for these trials. After successful completion of the pilot phase (i.e., demonstrated modulation of marker endpoints by the intervention), subsequent studies can include phase 3 clinical trials involving the designated agent, the utilization of the monitoring test system and a cancer incidence or mortality endpoint may be implemented.

Investigators may apply at this time for the pilot phase, or submit an application for both phases. However, if the application is for the pilot phase only, the proposed study must be relevant to a clinical application and utilize a chemopreventive agent, marker test system, and study population which could later be the subject of a full scale, double blind, randomized, risk reduction clinical trial.

Applicants funded under this RFA will be supported through the cooperative agreement mechanism. NCI has

set aside $1.8 million for first year funding of four to five awards.

For further information and complete copies of the RFA, contact Andrew Vargosko, PhD, or Marjorie Perloff, MD, Chemoprevention Branch, DCPC, NCI, Blair Bldg Rm 616, Bethesda, MD 20892, phone 301/427-8680.

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 Blair building room number shown, National Cancer Institute, NIH, Bethesda MD 20892. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring MD, but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-87238-16

Title: Cultivation of marine anaerobic bacteria
Deadline: Approximately Dec. 5

The Div. of Cancer Treatment is seeking a contractor to furnish and operate a microbiological and small extraction laboratory to isolate various groups of anaerobic bacteria from the marine environment.

The specific objectives of this probject are to collect source samples; isolate various species of marine anaerobic bacteria; determine their taxonomic identify; and grow them under conditions suitable to produce at least 100 mg of whole culture extracts.

The principal investigator should be trained in microbiology at the PhD level or equivalent, with at least three to five years experience in research with marine anaerobic bacteria and in their taxonomy. The successful offeror will be expected to provide and grow approximately 250 isolates of marine anaerobic bacteria over a period of three years.

Contracting Officer: Patricia Shifflett
RCB Blair Bldg Rm 216
301/427-8737

RFP NCI-CM-87239-16

Title: Cultivation of marine protozoa
Deadline: Approximately Dec. 5

The Div. of Cancer Treatment is seeking a contractor to furnish and operate a microbiological and small extraction laboratory to isolate various groups of protozoa from the marine environment.

The specific objectives of this project are to collect source samples; isolate various species of marine protozoa; determine their taxonomic identity; and grow them under conditions suitable to produce at least 100 mg of whole culture extracts from each culture used for this contract.

The principal investigator should be trained in microbiology at the PhD level or equivalent, with at least three to five years experience in research with marine protozoa and in their taxonomy. The successful offeror will be expected to provide and growth approximately 600 isolates of marine protozoa over a period of three years.

Contracting Officer: Patricia Shifflett
RCB Blair Bldg Rm 216
301/427-8737

NCI CONTRACT AWARDS

Title: Biomedical computing--design and implementation
Contractor: Information Management Services Inc., $1,737,086

Title: Resource for procurement of human tissues from donors with an epidemiological profile
Contractor: Georgetown Univ., $323,567

Title: Phase 1b clinical trial of immunotherapy with interleukin-2 alone or in combination with adoptive transfer of cytotoxic cells
Contractors: UCLA, $303,634; Cleveland Clinic Foundation, $331,959; Jefferson Medical College, $243,752; Ohio State Univ., $639,949; Univ. of Pittsburgh, $531,847; Univ. of Wisconsin, $630,008.

Title: Early detection of extravasation of intravenous cytotoxic drugs
Contractor: Microwave Medical Systems Inc., $500,000

Title: Record linkage study of leukemia following radiotherapy for uterine corpus cancer
Contractors: Danish Cancer Registry, $132,238; Univ. of Southern California, $72,974; Ontario Cancer Treatment & Research Foundation, $19,941; Univ. of Iowa, $29,047; Connecticut Dept. of Health, $58,586

Title: Development of improved techniques for the cloning of human tumor cells in tissue culture systems
Contractor: Hipple Cancer Research Corp., $494,749

Title: Assay for predicting methotrexate sensitivity in human breast cancer
Contractor: Aeron Biotechnology Inc., $499,952

Title: Clinical trial of monoclonal antibody in combination with interferon or interleukin-2
Contractors: Univ. of Alabama (Birmingham), $237,704; Mt. Sinai School of Medicine, $229,210; Univ. of Southern California, $201,782; M.D. Anderson Hospital, $172,545

Title: Phase 1b clinical trial of monoclonal antibodies to evaluate the role of dose and schedule of administration of the biological effect of antibodies and development of host immune responses to antibody and tumor
Contractors: Memorial Hospital, $325,782; Univ. of Pittsburgh, $308,512; Univ. of Wisconsin, $221,893

Title: Tracing through other sources and resources to determine the vital stataus and current address of members of a New York City trade union
Contractor: Hooper Holmes, Basking Ridge, NJ, $99,403

Title: Support services for genetic factors in persons at high risk of cancer--genetic markers for linkage analysis
Contractor: Integrated Genetics Inc., $1,805,933

Title: Preclinical toxicology/ chemopreventive agents
Contractor: International Research & Development Corp., four master agreement orders for $177,048; $177,048; $188,161; and $179,958

Title: SBIR phase 2, development of a portable and extended version of modeling laboratory
Contractor: Civilized Software Inc., $500,000

The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams

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