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Intergroup 5-FU/Levamisole Study Positive Enough Now To End Untreated Control Arms

The intergroup study which tested 5-fluorouracil and levamisole for the adjuvant therapy of colon cancer has now been determined by study participants as offering a survival advantage in favor of the combination so significant that further use of control arms without adjuvant treatment for that disease may be considered unethical. As a result, the intergroup study testing the combination of 5-FU with leucovorin has closed entry into its control arm.

(Continued to page 2)

In Brief

Senate Markup Adds $22 Mil. To NCI Budget; Roper Formally Named NCI Deputy Director

SENATE LABOR, HHS, Education Appropriations Subcommittee approved a FY 1990 budget for NCI of $1.668 billion, $15.8 million above the House subcommittee's markup and $22 million above the President's request. The Senate version adds $4 million for pediatric AIDS research, $34 million for the NCI supercomputer, $500,000 for rural cancer statistics, and $12.5 million authorization of matching funds for Armand Hammer's STOP Cancer program, which raised $12.5 million from private sources for cancer research. The Senate bill also addresses the Institute of Medicine recommendations and indicates that the subcommittee added sufficient funds to permit the Cancer Centers Program to remain its present size. The exact funding for the centers program was not stated. . . . **MARYANN ROPER** has been formally appointed NCI deputy director after having been acting deputy director since October 1987. . . . **CYNTHIA MILLER** has been appointed director of the Oncology Nursing Certification Corp. In the new position, she is responsible for the overall management of the ONCC. Miller has been director of education for the Oncology Nursing Society since 1986. Bridget Culhane, formerly with Presbyterian-University Hospital in Pittsburgh, was appointed to replace Miller as education director. ONS also announced the appointment of Brenda Nevidjon of Virginia Mason Medical Center in Seattle as editor of "ONS News." She succeeds Karen Hassey. . . . **FIRMS RESPONDING** to the RFP issued by the American Society of Clinical Oncology for staffing of a Washington, D.C., office (**The Cancer Letter,** Aug. 11) may send proposals to Karen Antman, Dana-Farber Cancer Institute, 44 Binney St., Boston, MA 02115, phone 617/732-3339, FAX 617/735-8579. Deadline is Sept. 20.

Untreated Control Arm Closed On Intergroup 5-FU/Levamisole Study

(Continued from page 1)

The 5-FU/levamisole results represent the first major improvement in the chemotherapy of Duke's B-2 colon cancer. It could have an important effect on cancer mortality rates, since colon cancer is the second leading cancer killer in the United States. About 55,000 Americans will be diagnosed with Duke's C colon cancer this year, and only about 40 percent of them will survive five years without effective treatment.

The North Central Cancer Treatment Group, chaired by Charles Moertel of the Mayo Comprehensive Cancer Center, conducted an earlier trial of 5-FU and levamisole which found, as reported at the American Society of Clinical Oncology meeting two years ago, that a significant disease free survival advantage occurred in the combination arm for Duke's C patients, and a lesser advantage for Duke's B patients. At that time, there was an advantage in overall survival but it was not statistically significant.

Earlier this year, an update of the NCCTG study found that overall survival in the treated arm had improved to statistical significance. Moertel was criticized for not making that information known publicly, and NCI Director Samuel Broder was urged by some to issue a clinical alert (**The Cancer Letter**, June 9). Broder declined to do that, and Moertel did submit the update to the "Journal of Clinical Oncology" which has scheduled it for publication in October.

When the first results of the NCCTG study became known, NCI's Cancer Therapy Evaluation Program approved a larger intergroup study to confirm those results. Accrual was completed last year, but no results had been announced by the time of the controversy over the NCCTG update. However, leaks from the study indicated that important and possibly significant improvements in recurrence and survival rates were being observed. That added pressure on Moertel to go public with that data, too, but he refused, contending that the study's principal investigators had unanimously agreed there was nothing in the observations at that time to warrant any such action.

NCI Director Samuel Broder told the National Cancer Advisory Board this week that "there is a high probability" NCI will issue a clinical alert on the 5-FU/Levamisole results within a month. "Language is being prepared by staff" for the alert, he said.

Further adding to the pressure on Moertel was the intergroup study of 5-FU with leucovorin which contains a control arm with no further therapy after surgery. That study opened last January and had only started accruing patients. Moertel insisted it would have been a needless waste of time and resources to close out the untreated arm on the basis of the NCCTG results, and that the intergroup levamisole study had not yet produced sufficient results to close it. He promised an analysis of the intergroup 5-FU/levamisole study later. That analysis, or at least a preliminary analysis, was made Sept. 1. No announcement was made, and no figures were available. **The Cancer Letter** learned, however, that study investigators agreed results were positive enough to force closure of the control arm in the 5-FU/leucovorin trial.

Moertel confirmed that action last week. He told **The Cancer Letter** that he believed enough patients now had been entered on the control arm of the leucovorin study to permit analysis of comparative results. Other arms in the study will remain open, except for the NCCTG protocol which was testing interferon. Other groups are comparing high and low dose leucovorin in the 5-FU combinations.

The intergroup leucovorin study had been designated a high priority clinical trial by NCI, with the concurrence of the Board of Scientific Counselors of the Div. of Cancer Treatment, and the chairmen of the cooperative groups. CTEP Director Michael Friedman, although not confirming that the control arm had in fact been closed, said that if it were, DCT would take another look at the study to determine if it still rated high

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priority status. Moertel had listed the prospect of early closure as one of the justifications for high priority designation.

(The DCT board approved by mail vote the recommendations for new high priority designations approved by the cooperative group chairmen in June. Those are: National Surgical Adjuvant Breast & Bowel Project protocol B18; NSABP protocol B21; Southwest Oncology Group protocol 8897, Radiation Therapy Oncology Group phase 3 study in unresectable nonsmall cell lung cancer; Eastern Cooperative Oncology Group/intergroup protocol for small cell lung cancer, and the intergroup leucovorin study 0089.)

Moertel has developed a well deserved reputation over the years for being critical of many claims for improved results from new therapies being tested. He has been no less strict in applying his standards for demonstration of improvements to his own studies.

Moertel suspected last spring that the intergroup study would turn positive, and he suggested to NCI and the Food & Drug Administration that they should consider placing levamisole on Group C status, which would permit its distribution free to any qualified physician requesting it, "in case the intergroup study turns positive," he said then. That was done in July. After the improving prospects for levamisole were reported in **The Cancer Letter** (and picked up and widely reported by the "Washington Post" and the wire services), NCI was deluged with requests for the drug, which has not been approved by FDA for marketing. A new drug application probably will be submitted to FDA after the complete analysis of the intergroup study is published. Moertel said he hoped that would be soon, but cautioned that a careful analysis was being carried out which probably would require several more weeks.

Use of levamisole to enhance 5-FU's effect was Moertel's idea, but he was reluctant to take any credit for it. "This was a community physician effort. Credit should go to the group, and to those who advocated the concept that community oncologists could participate in research clinical trials. This trial was done with high quality science. If it weren't, it could not have been replicated in a large confirmatory study. It is satisfying that a major advance can be initiated and carried out with high quality science, by a group of community physicians."

NCCTG is headquartered at Mayo but consists primarily of community oncologists the upper Midwestern states. Many of the participants in the study were NCCTG's Community Clinical Oncology Program members.

Cancer Centers Program Will Move To DCBD; Division Will Be Renamed

NCI will move the Cancer Centers Program into the Div. of Cancer Biology & Diagnosis, which will be renamed to have the word "centers" in its title, NCI Director Samuel Broder announced this week.

The move is in response to several years of discontent expressed by cancer center directors over what they perceived as lack of visibility for the program within NCI. Centers directors lobbied to move the program out of the Div. of Cancer Prevention & Control, where it has resided since 1983.

Those concerns were echoed earlier this year by a report on the cancer centers program by the Institute of Medicine.

A new branch will be created in DCBD, the Centers, Training & Resources Branch, headed by Brian Kimes, associate director for extramural programs, beginning Nov. 1, when he returns from serving as acting director of the NIH Office of Scientific Integrity Review.

Besides the Cancer Centers Program, the new branch will consist of the Organ Systems Program, headed by Andrew Chiarodo, the Cancer Training Branch, headed by Vincent Cairoli, and the Research & Facilities Branch, headed by Donald Fox.

"This will take advantage of DCBD Director Alan Rabson's extensive experience and corporate memory in cancer research," Broder told the National Cancer Advisory Board this week. Kimes, he added, "is one of the best science administrators in the country."

"A vigorous, independent and diverse cancer centers program is essential to the success of the National Cancer Program," Broder continued. "It is my intention that the centers program be represented at NCI by creative administrators who know how to assist centers and can provide the services they need.

"The centers program is of personal interest to me as I believe it has been to all NCI directors," Broder said.

"My office will continue its specific involvement in the planning, policy and implementation phases and budgetary elements of the program, irrespective of any other factor."

NCI will add four more staff positions, or full time equivalents (FTEs), to the Cancer Centers Program, and will add one FTE to

Kimes's office. That will bring the total number of FTEs for the branch up from 19 to 24. The total budget of the Centers, Training & Resources Branch will be $1.69 million.

"I have given a great deal of thought to the location of the centers within NCI," Broder told the NCAB's Committee on Cancer Centers this week. "A change of location has been requested by virtually all parties."

Broder said he considered moving the centers program into his office, which many center directors had advocated as a way to increase the visibility of the program. But Broder opposed that move, listing some drawbacks: the need to create a "staff structure" within his office to run the program, and the lack of traditional oversight from a Board of Scientific Counselors.

However, advocates of such a move have noted that the NCAB acts as the "BSC" for the office of the director and its elements.

"We would have had to charter a council of some type to act as oversight for the program," Broder said. "It would not have had standard, administrative processes." He said these processes are especially important for grants review and administration.

As a result of the move, the DCBD Board of Scientific Counselors will be expanded to include three more representatives from cancer centers. Presently, Vittorio Defendi of New York Univ. is the only DCBD Board member who represents a cancer center.

Broder assured the committee and the NCAB that "my office has an exceedingly strong interest in cancer centers."

The NCAB centers committee in May recommended that NCI create a new division for the centers program. Broder said he saw that proposal, also supported by the American Association of Cancer Institutes, as even more problematic than placing the program in his office. A new division would have required authorization by NIH, which may not have been easily or quickly obtained.

Another option was to place the program in the Div. of Cancer Treatment, but NCI sources said they feared basic scientists in the division's extramural programs would have seen the centers program as a threat.

Sources at NCI said that in meetings of the Executive Committee at which options for the centers program were discussed, Rabson emerged as the strongest advocate of cancer centers.

Until 1980, the centers program was located in a division with the other extramural grant programs of NCI. That year, the centers program was combined with parts of the former Div. of Cancer Control & Rehabilitation to form a new Div. of Resources, Centers & Community Activities.

In 1983, a prevention program was added to that division, which was then renamed the Div. of Cancer Prevention & Control. The centers program was placed in a newly created Centers & Community Oncology Program.

The IOM report noted that, "The reorganizations had the effect of reducing the program to an organizational level that is not commensurate with its size or key relationships with the other research grants the program is designed to support and enhance by providing an interdisciplinary environment and shared resources."

The IOM report (**The Cancer Letter,** April 28) stopped short of recommending where to relocate the centers program.

Then-Director Vincent DeVita, acknowledging the center directors' discontent over the perceived lack of access to the highest decision making levels, had decided to move the program from DCPC into his office. He was waiting for the NCAB Committee on Cancer Centers to come up with its recommendations but the proposal was moot when he decided to leave NCI for Memorial Sloan-Kettering.

Sydney Salmon, director of the Arizona Cancer Center, spoke before the NCAB on the issue. He noted that in the 1980s, the centers program was perceived as having some problems: the apparent "downgrading" of the program by NCI, the loss of budgetary growth in relation to other grant mechanisms, and the decline in the absolute number of NCI funded cancer centers.

"I really want to complement Dr. Broder and the staff at NCI for the vigorous response to the Institute of Medicine report," Salmon said. "I think that it appears to me that this is likely to reverse the trend from the 1980s."

Board member Enrico Mihich asked Broder whether the budget for the new branch is enough. "Nothing would be worse for Dr. Kimes than to be strangled by budget problems," he said.

"Very few reasonable requests by Dr. Kimes would be disapproved," Broder said.

Broder told the NCAB centers committee that he thought part of the problem with the centers program has been the lack of funding.

"If we had the bypass budget, I think the centers program people would be happy to be anonymous," he said.

However, John Durant, chairman of the centers committee, framed the problem in another way. "There is some perception that the lack of funding and resources came as a result of the lack of visibility," he said.

NCAB Centers Committee approved the move to DCBD and at Broder's suggestion, requested that Kimes provide the NCAB with a progress report by December 1990.

"It's a reasonable proposition and it is not written in stone, it can be changed," Durant said.

Mihich also endorsed the move, saying, "My sense it that this is a pilot project that might evolve into more independence for cancer centers in the future."

"One Time Offer" of Comprehensiveness

The centers committee also endorsed a proposal by Broder, as a way to phase in the new guidelines for NCI designation as a comprehensive cancer center, to offer currently funded cancer centers the opportunity to apply for administrative designation as a comprehensive cancer center until the next time their grant comes up for review.

The administrative action would be available for two years. The designation would be made by the NCI Director, the Executive Committee and the NCAB on the basis of the guidelines approved by the NCAB earlier this year. It would be a one-time mechanism.

Broder said it did not seem fair to make centers wait two to four years, in some cases, to apply for the comprehensive designation.

The Arizona Cancer Center, for example, which just had its core grant renewed in September, would have had to wait four years before it could apply for comprehensive designation. (Arizona's director, Salmon, was the impetus behind the NCAB's extensive review of the comprehensive designation. He requested comprehensive designation two years ago, when the designation had virtually lost its meaning.)

In applying for the short term administrative designation, a cancer center would have to agree to apply for comprehensive status the next time its grant is reviewed. Then, Broder said, if the center fails in the peer review, it must stop using the title "comprehensive" immediately.

Another reason for the action would be to ease the strain on the peer review process. If every cancer center that wanted the comprehensive designation were to go through peer review now, the process would be delayed. Broder said the Div. of Extramural Activities is "already having trouble" getting through the review of 18 cancer centers. About half of the cancer centers have been reviewed, Fox told the centers committee. In addition, three of the five centers that were in "phase out status"--those that would lose their core grant--have submitted amended applications and will be re-reviewed. Those are Ohio State Univ., Northern California Cancer Center and Roswell Park Memorial Institute.

Eighth Criteria

Broder also proposed, and the centers committee supported somewhat reluctantly, an eighth criteria for designation as a comprehensive cancer center. The NCAB had approved seven. Broder's proposed addition was as follows:

"It is essential that a comprehensive cancer center should define the community it serves and maintain productive outreach efforts in that community. A comprehensive cancer center should take steps to identify cancers of high frequency within the community it serves and carry out appropriate cancer prevention and control activities for such cancers. In addition, comprehensive cancer centers should conduct programs of cancer prevention and control activities relevant to the needs of populations within the community with disproportionate cancer incidence and death rates (eg. minorities, people over age 65, etc.)."

Broder argued that the wording was essential to show that the centers program was carrying out the legislative intent of the National Cancer Act, and he implied that it might be useful during hearings for the 1991 budget next spring.

"I think every existing comprehensive cancer center can pass this test," Broder said. "And any comprehensive center that can't, we have to ask what is happening."

He said the language is not intended to be punitive. "My view is, most cancer centers are going to say lung and breast cancer are the highest in my community."

Mihich noted that the idea was fine in principle. "But how will it be implemented?"

Broder said a cancer center's strength should come from "how it is viewed in the community. If a community thinks it will be grievously harmed by the loss of its cancer center, I can't help but think this will work for the good."

Board Chairman David Korn said, "We want to be very careful not to overpoliticize centers. I don't think cancer centers are post

offices and sewage projects that members of Congress are entitled to. I don't want something independent of merit review that will eat up the institute's budget."

Broder said he agreed and that the idea "is a risk." But he assured the committee that adherence to the eighth criteria by comprehensive centers would be peer reviewed.

Broder asked Salmon whether Arizona would have difficulty meeting this requirement. Salmon said the center would have "no trouble."

But Jerome Yates of Roswell Park was wary of the criteria. He said it presented the danger that "bureaucrats" could attempt to force centers to divert some of their core grant funds to doing "public service" projects.

Broder disagreed. "You can't have language that will defend you from having bad people do bad things. If you are being told to use core grant money that way, I'd like to know about it."

Durant suggested adding the words "within the funding available to it" after the "outreach efforts" and asked for a motion to approve the eighth criteria. Korn made the motion, but could not get a second for about a minute. Board member Roswell Boutwell finally seconded the motion, and three committee members, Korn, Durant and Boutwell, voted in favor of it. Mihich abstained.

Later, Durant told **The Cancer Letter** that the eighth criteria is, in his view, "principally a political consideration to assure Congress that (centers) are doing what we're supposed to be doing."

At the full board meeting later, board member Erwin Bettinghaus said it is possible that with the outreach criteria, some centers with tight budgets will decide not to become comprehensive. He asked Broder whether he or the staff had considered earmarking funds specifically for comprehensive cancer centers.

Broder turned the question to Rabson. "Have you or Dr. Kimes considered that?"

Rabson answered, "That has been discussed, but it is too early to make any announcement such as that."

Korn said he was concerned that any cancer center "can slap the title 'comprehensive' on its name." He asked whether NCI could copyright a symbol.

"I was thinking of having my picture on the logo," Broder quipped.

Office of Cancer Communications Associate Director Paul Van Nevel said his office is developing a copyrighted symbol that NCI designated comprehensive cancer centers would be authorized to use.

Five Year Plan

NCI Deputy Director Maryann Roper, who is chairing an ad hoc committee to develop a five year plan for the centers program, told the board that the committee will develop a plan by next February. She invited the board to submit any comments to the committee.

ONS Issues Call For Applications For Research Grants, Scholarships

The Oncology Nursing Society and the Oncology Nursing Foundation have issued a call for applications for a series of research grants, undergraduate and graduate scholarships, a public education grant and a career development award.

The awards and criteria are as follows:

<>ONS/Smith Kline & French Research Award to promote oncology research on nausea and vomiting management. The principal investigator must be an ONS member actively involved in cancer patient care, education or research. Application deadline is Dec. 1.

<>Foundation/Bristol-Myers Oncology Div. Community Health Research Grant to encourage new investigators and nursing research in community based health agencies, including community hospitals, physician offices and nursing homes, among others. Application deadline is Dec. 1.

<>Foundation/Bristol-Myers Oncology Div. Research Grant to stimulate quality research in oncology nursing to improve cancer patient care. Applicants must be RNs actively involved in some aspect of cancer patient care, education or research. Dec. 1 deadline.

<>Foundation/Lederle Laboratories Research Grant to stimulate research in oncology nursing into quality of life issues related to persons and their families experiencing cancer. Applicant must be an RN involved in some aspect of cancer patient care, education or research. Deadline Dec. 1.

<>Foundation/Purdue Frederick Research Grant to promote oncology nursing in pain assessment and management. Dec. 1 deadline.

<>A series of Graduate scholarships offered with support from Burroughs Wellcome and Adria Laboratories, to improve oncology nursing by assisting nurses in furthering their education. Candidate must be enrolled (full or part time) in a graduate nursing degree program in a National League for Nursing accredited School of Nursing. Deadline Jan. 15.

<>A series of undergraduate scholarships offered through the support of Lederle Laboratories. The scholarships are to improve oncology nursing by assisting registered nurses in furthering their education. The candidate must be enrolled in an undergraduate nursing degree program in a NLN accredited School of Nursing and must have a current RN license. Deadline Jan. 15.

<>Foundation/Lederle Laboratories Cancer Public Education Request for Proposal to enhance public knowledge and awareness of cancer prevention, detection and treatment modalities. Proposal deadline Jan. 15.

<>Foundation/Pearl Moore Cancer Development Awards supported by Anthony J. Jannetti Inc. to reward two staff nurses for meritorious practice by providing financial assistance to attend continuing education programs that will further the nurses' professional goals. The nominee must be employed as a staff nurse, must possess or be pursuing a bachelor of science in nursing, and have two or more years experience in oncology nursing practice. Nominations ONS chapters. Deadline Jan. 15.

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-CN-95198-69
Title: Clinical evaluation of fruit and vegetable based experimental food supplements
Availability of Announcement: Oct. 10

NCI seeks proposals for master agreements to provide clinical evaluation of fruit and vegetable based experimental food supplements according to the following task areas:

Task I: Dietary modulation of human drug metabolism by phytochemical constituents in fruits and vegetables. Requires conduct of acute human metabolism studies on healthy people that are chronically consuming experimental diets fortified with fruit and vegetable phytochemicals, cold storage of blood, saliva, urine, etc., collected from study participants and split-sample analyses of experimental foods.

Task II: Dietary modulation of arachidonic acid metabolism by phytochemical constituents in fruit and vegetables. Requires conduct of human studies focused on measuring the modulatory influence of fruit and vegetable phytochemicals on circulating metabolites in biological fluids.

Task III: Dietary modulation of endogenous steroid metabolism by phytochemical constituents in fruits and vegetables.

Offerors can submit proposals for either or all of the above tasks. Each task will be evaluated separately, and one pool of master agreement holders will be awarded. All master agreement holders will be able to compete for master agreement orders issued during a five-year period of performance.

Up to two master agreement orders will be awarded for each task area per year.

Contracting Officer: Vernon Rainey
Executive Plaza South, Rm 635
301/496-8603

RFP NCI-CM-07321-27
Title: Synthesis of radiosensitizing agents
Deadline: Nov. 21

NCI's Radiotherapy Development Branch, Radiation Research Program, in the Div. of Cancer Treatment, is seeking organizations with the capability to design, synthesize and characterize new and novel hypoxic and aerobic radiosensitizers. DNA targeted drugs and drugs activated by low Ph and/or hypoxia constitute areas of interest. The project also requires designated in vitro data on synthesized compounds and data regarding the in vivo efficacy of designated radiosensitizers with significant in vitro activity.

As a mandatory requirement, at time of best and final offer, the offeror must be accredited or equivalent ad be capable of maintaining a conventional rodent colony of at least 400 mice. The offeror must also have radiation capability suitable for irradiating mice and cell cultures. Physical and chemical analytical equipment, polarographic or pulse radiolysis capability to measure electron affinities and determine physiochemical parameters of chemicals that would be synthesized is also required.

It is anticipated that an incrementally funded contract will be awarded for a period of three years beginning on or about June 1, 1990. This project is a recompetition of the work being done under Contract No. NO1-CM-73708 by SRI International, Menlo Park, CA.

Contract Specialist: Johnny Jordan
RCB Executive Plaza South Rm 603
301/496-8620

RFP-NCI-CO-94380-34
Title: Technical support services for the Div. of Extramural Activities and the Grants Administration Branch of NCI
Availability of RFP: Approximately Oct. 16
This is a 100% small-business set aside

NCI's Div. of Extramural Activities is soliciting proposals for a five year period for services which will be definitized by task orders issued during the period of performance. The task orders will be issued under the following four areas:

1. National Cancer Advisory Board and President's Cancer Panel Support;
2. Quick turnaround assistance;
3. Ad hoc technical assistance, and
4. task order development and administration.

Offerors must demonstrate their ability to meet with the project officer in Bethesda, MD, and then provide certain deliverables, such as slides or charts, to Bethesda, MD within 24 hours. Offerors may have a maximum of 500 employees.

RFP will be available on or about Oct. 16, 1989. Requests should be addressed to:
Contract Specialist: Elizabeth J. Abbott
Executive Plaza South, Rm 635
301/496-8603.

RFP NCI-CN-95201-69
Title: Special studies facilitating the flow of preclinical leads into clinical practice
Availability of RFP: Approximately Oct. 10

NCI is issuing the RFP for master agreements to provide the above referenced studies, according to the following task areas:

Task I: Evaluation of lipids and lipoprotein in fluids and tissues of laboratory animals consuming fruit and vegetable products.

Task II: Evaluation of antiestrogenic activity hormone receptor function and steroid hormone levels and metabolism in laboratory animals consuming fruit and vegetable products.

Task III: Modulation of arochidonic acid metabolism by fruit and vegetable products.

Task IV: Evaluation of modulatory activity of fruit and vegetable products on key regulatory enzymes, antioxidant defenses, and cyclic nucleotide levels in laboratory animals.

Offerors may submit proposals for either or all of the above

tasks. Each task will be evaluated separately, and one pool of master agreement holders will be able to compete for master agreement orders issued during a five year period of performance. It is estimated that two to four MAs will be awarded for each task area per year.
Contracting Officer: Vernon Rainey
Executive Plaza South, Rm 635
301/496-8603

RFP NCI-CN-95199-69
Title: Methods development for phytochemical compliance markers in designer foods
Availability of RFP: Approximately Oct. 10

NCI is soliciting proposals for master agreements to provide the above referenced studies in the following task areas:

Task I: Provide analysis of phytochemical compliance markers in experimental foods including shelf-life stability studies, identifying sources for food material, validating analytical methodology and participate in split-sample analysis, etc.

Task II: Provide analysis of phytochemical compliance markers in human biological fluids. This requires accrual of 25 healthy individuals for the study, verification of compliance markers in experimental foods and for the determination of compliance markers in biological fluids of humans consuming experimental foods. Assist NCI in filing of an IND with FDA.

Offerors may submit proposals for either or both of the above tasks. Each task will be evaluated separately, with one pool of master agreement holders to be awarded, during the five year period of performance.

It is estimated that up to five MA orders will be awarded for Task I per year, and three for Task II per year.
Contracting Officer: Vernon Rainey
Executive Plaza South, Rm 635
301/496-8603

RFP NCI-CM-07320-19
Title: Storage and distribution of clinical drugs
Availability of RFP: Approximately Sept. 26
Deadline: Approximately Oct. 14

The Developmental Therapeutics Program of the Div. of Cancer Treatment is seeking a contractor to store and distribute formulated clinical drug products and keep adequate records of such distribution in support of the clinical programs of DCT.

The project will involve receiving drugs from various sources, storage of the products under specified conditions, inventory, repackaging and subsequent shipment to NCI authorized investigators in the U.S. and abroad. A computerized data processing system will be required for various recordkeeping and repository functions.

The contractor selected for award must meet at least the following minimum requirement: Possess an EPA toxic waste generator permit and the necessary local and state permits for generation and transportation of toxic waste drugs. All personnel must be bonded prior to performing on this contract. The contract period is to be five years, beginning approximately Aug. 15, 1990.

Incumbent contractor is ERC BioServices Corp., Rockville MD.
Contract Specialist: Zetherine Gore
Executive Plaza South, Rm 603
301/496-8620

RFAs Available

89-CA-17
Title: National Cooperative Natural Products Drug Discovery Groups
Application Receipt Date: Dec. 11, 1989
Letter of Intent Date: Oct. 27, 1989

In FY 1983 and 1984, NCI requested applications for National Cooperative Drug Discovery Groups (NCDDG) whose goal was the discovery of improved cancer treatment on the basis of novel mechanism of drug action. In 1986 the program requested applications focused on exploitation of specific and unique characteristics of lung and colon cancer. The NCDDG approach to anticancer treatment discovery was broadened further in August 1987 by RFAs inviting applications for the creation and evaluation of both general mechanism of action based and specific disease-oriented anticancer treatments as well as for the development of innovative preclinical models for determining antitumor selectivity. Natural Products Drug Discovery Groups (NPDDGs) were added in 1988 to enhance discovery of novel drug chemotypes.

This RFA is for the funding of NPDDGs to stimulate the selection and isolation, on a rational basis, of new potential anticancer treatments from natural sources and to evaluate them in preclinical models designed to select those with the most favorable prognosis for clinical usefulness. An NPDDG may be made up of scientists in academic, non-profit research, and commercial organizations. Awards will be made as cooperative agreements.

Multiple awards for project periods of up to five years and anticipated, and $3 million has been set aside for the initial year's funding.

Copies of the complete RFA and additional information may be obtained from Matthew Suffness, PhD, Program Coordinator, NPDDGs, NCI, DCT, Executive Plaza North, Suite 832, NIH, Bethesda, MD 20892.

RFA 89-CA-18
Title: Mechanisms of Protease Inhibitor Anticarcinogenesis
Application Receipt Date: Dec. 1, 1989
Letter of Intent Receipt Date: Nov. 1, 1989

For many years evidence has accumulated that protease inhibitors can suppress both transformation in cell culture and tumorigenesis in animals. Transformation suppression has been shown in several different in vitro systems employing a variety of inducing agents. Some interpret these results to mean that different carcinogens induce similar carcinogenic processes involving at least one critical cellular proteolytic enzyme which is susceptible to protease inhibitor suppression. Some evidence exists that protease inhibitors which inhibit the protease chymotrypsin are the most effective in suppression of malignant transformation.

In vivo studies also have shown or suggested that several types of protease inhibitors can suppress tumorigenesis in animals induced by a variety of carcinogens, in a number of organ systems, and in several species.

Epidemiologic data from population studies have shown that vegetarians and populations consuming large amounts of vegetables have lower tumor risks for a number of organ sites. Many vegetables contain protease inhibitors which could contributed to the lowered incidences observed.

The intended research would encompass both in vitro and in vivo systems, and would be confined to investigations employing known, well characterized models of carcinogenesis/transformation, or to biological systems in which elucidation of basic protease inhibitor mechanisms of action would be expected to contribute to understandings important for anticarcinogenesis. Examples of studies are (1) investigations on the identification and characterization of the target molecules significant to the anticarcinogenic action of protease inhibitors; (2) studies on protease inhibitor suppression of oncogene expression in appropriate model systems; (3) investigations on the role of protease inhibitors in suppression of activated oxygen species employing model systems of significance to anticarcinogenesis; and (4) possible preventive interactions, as well as possible side effect producing interactions, of protease inhibitors directly or indirectly with host immune or endocrinological systems, including possible interactions with autocrine or paracrine systems of control involving growth factors.

This RFA is a one-time solicitation, and will use the NIH R01 program. Approximately $750,000 in total costs per year for five years will be committed to fund applications, dependent on the receipt of sufficient applications of high scientific merit. Non-profit and for-profit, and foreign as well as domestic institutions are eligible to apply.

Copies of the complete RFA and additional information may be obtained from Dr. Carl E. Smith, Program Director, Biological & Chemical Prevention, NCI, DCE, Executive Plaza North, Rm 700, NIH, Bethesda, MD 20892, telephone 301/496-4141.