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DCPC Board Approves New Intramural Laboratory For Diet And Nutrition; NCAB To Consider It Next

Peter Greenwald called it "one of the landmark steps forward" as the Board of Scientific Counselors of the Div. of Cancer Prevention & Control enthusiastically approved establishing an intramural laboratory for research in diet, nutrition and cancer. The proposal will be considered by the National Cancer Advisory Board May 26, with the final decision up to NCI Director Vincent DeVita and the NCI

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In Brief

Kansas To Provide State Funds For Cancer Center; Meeting On Freestanding Centers In Philadelphia

KANSAS LEGISLATURE has passed legislation providing $190,000 a year for core funding of the cancer center at the Univ. of Kansas in Kansas City. The funds will cover salaries of key center personnel and some operating expenses. **Jane Henney**, former NCI deputy director, is acting director of the center. . . . **FOX CHASE** Cancer Center, CDP Associates and Intercommunity Cancer Centers will host a national symposium this summer to address issues involving freestanding cancer centers. It is scheduled for Philadelphia July 9-10. Discussion topics will include the role of surgeons in FCCs, outpatient treatment reimbursement, HMOs and PPOs in cancer treatment, and new technologies such as digital diagnostics. Contact CDP at 404/391-9872. . . . **BERNARD JANICKI**, deputy director of the Immunology, Allergic & Immunologic Diseases Program of the National Institute of Allergy & Infectious Diseases, has been named director for research at Dana-Farber Cancer Institute. . . . **CHARLES LEMAISTRE**, president of the Univ. of Texas System Cancer Center, has received the 1987 President's Award from the American Lung Assn. for "his many years of courageous effort to alert the public and scientific community about the dangers of smoking" . . . . **STEVEN ROSENBERG**, NCI Surgery Branch chief who has been picking up honors right and left for his development of innovative immunotherapy, will get another this summer from the International Society of Blood Purification, to be presented by King Carl Gustaf of Sweden . . . . **SAMUEL BRODER**, director of NCI's intramural Clinical Oncology Program who has been called "both a general and a private in the war on AIDS," during a discussion on drug development: "Rational drug design is when you find something that works, you then go back and say it was rational."

DCPC Board Agrees With Committee Report On Establishing Nutrition Lab

(Continued from page 1)
Executive Committee, probably during their semiannual retreat in July.

The DCPC Board's action followed presentation of a report by the committee of the Board established last year to look into the merit and feasibility of an intramural lab. Malden Nesheim, director of the Div. of Nutrition Science at Cornell Univ., chaired the committee and presented the report.

"The committee strongly supported the development of such a laboratory as a unifying center of excellence for research in nutrition and cancer prevention and recommended its establishment at NCI," the report says. "It was perceived that the development of a strong, vigorous intramural program in nutrition and cancer research was essential in progress toward the commitment by NCI to explore all relationships between diet and nutrition and cancer and would result in an improved program for cancer prevention and control. The laboratory would also serve to stimulate new research directions among all scientists in the nutrition field."

The committee recommended that the lab be located within DCPC, that it should consist of three sections--basic science, human studies and nutrition epidemiology, "with all sections being closely interactive and housed in one building. The Frederick Cancer Research Facility at Ft. Detrick was considered to be an excellent location."

The report notes that extramural funding for nutrition research in the NCI RO1 grant pool has been level over the 1984, 1985 and 1986 fiscal years, at $35 million, $31 million and $35 million, respectively. The actual number of nutrition projects for those dollars have been 244, 243 and 266 over the same three years. "The investment in nutrition research has amounted to approximately three percent of the total NCI research program dollars. This is relatively modest considering that as much as 35 percent of all cancers may be related to diet and nutrition," the report says.

Nesheim told the Board that the committee felt "there is not enough expertise at NIH to support the number of extramural research initiatives. Many people have been frustrated by RFPs that are not based on nutrition expertise."

Nesheim said the lab eventually would require 60,000 square feet of space and recommended a budget of $5 million in FY 1988.

Board members expressed strong support for the new lab. "It has been very well worked out," Frank Meyskins said. "I'm extremely enthusiastic about it," Mary-Claire King added. "It will be synergistic to relate inhouse and extramural nutrition research."

But Philip Cole and Lloyd Everson had some reservations. Both asked where DCPC would get the money, considering the budget limitations. "What might have to bear a reduction to support this? Cole asked.

"I'm not sure where the money would come from," Greenwald first responded, then later added that "it is built into the bypass budget." It is not, however, built into the President's budget for FY 1988, under which NCI must operate until Congress makes the 1988 appropriation.

"We're dealing with policy, not management," William Darity said. "Where the money comes from is NCI's problem."

"This will be an add on, not a take away," Board Chairman Erwin Bettinghaus said.

"That's easy to say but it does not always work out that way," Cole responded.

Noting that NIH has a Nutrition Coordinating Committee and that nutrition research and training cuts across all NIH institutes, as mentioned in the report, Cole asked if there is "any possibility the intramural laboratory could be NIH wide?"

"No way," Greenwald said. All NIH intramural laboratories are located within single institutes.

The committee offered recommendations on organization of the laboratory.

"Each of the three major sections will require a critical mass in order for the laboratory to be viable and able to attract both first rate young as well as more established investigators and to make a significant national and international contribution to the field. The committee was of the opinion that at full complement each area should involve nine to 15 doctoral level scientists who would be from the nutrition field and also from related disciplines.

"There would be a director of the overall laboratory who would have responsibility for the total laboratory program. She/she must be an individual who has an outstanding research background and has achieved national recognition in the field of nutrition. Each of the

units would be headed by a section chief. . . There would be a number of visiting scientists and postdoctoral fellows. A centralized core facility might be developed from common needs of the sections since this would be economical and provide an integrative function."

The report outlined briefly the mission of the three sections:

Basic Sciences Section--"This facility would explore mechanisms by which food components (nutrient and non-nutrient) may inhibit cancer formation. It should have capabilities for exploring problems at the molecular (gene function and expression), cellular (membrane, cytoplasm) and organ (intermediary metabolism, organ-organ interactions) levels. Cell free, cell culture, isolated organs and nonhuman in vivo animal models would be developed. The laboratory would also attempt to advance analytical methodology for the study of nutrition as it may relate to cancer prevention."

Human Studies Section--"To promote transfer of knowledge from the more basic to the more applied areas of the nutrition-diet cancer connection, the laboratory must have a vigorous program in the area of human-clinical investigation. Only in this way can the quantitative aspects of nutrient and non-nutrient metabolism, or the response of the intact human host, be defined and its significance for cancer development and/or prevention be appreciated. Furthermore, there are many basic issues of nutrient/non-nutrient metabolism that need to be investigated directly in humans; for example, the absorption and metabolism of B-carotene at various intakes and from different food sources. Such human investigations would contribute (a) immediately to an improved and more precise interpretation of epidemiological associations; (b) to the development of improved markers of dietary exposure (i.e., metabolic epidemiology); and (c) to broadening our understanding of the role of diet in human health. Nonhuman studies cannot answer these questions without an interdigitated activity in the area of human metabolism and its response to dietary factors. Animal and other nonhuman models can help to provide information and mechanistic knowledge."

Nutrition Epidemiology Section--"This unit would have a more applied orientation with a heavy nutritional epidemiology component. It would be responsible for conducting research that is needed to support large scale population based studies including:

"1. Developing approaches to assessment of food intake including adequate knowledge of the composition of food. A focused effort on analysis of foods and on acquisition, retrieval and application of food composition data would be an essential component of this unit. Facilities should be established to implement use of data on food composition with modern information systems, concepts and techniques.

"2. Developing of analytical methods that may be useful in assessing dietary compliance and also those that may be useful in assessing risk factors for cancer.

"3. Having the capability for carrying out analytical procedures needed to support large studies and perhaps develop and maintain storage capacity for biological samples for extended periods of time.

"4. Conducting smaller scale studies with human subjects in the clinical research unit or in the outpatient diet facility that is part of the Human Studies Section."

Richard Costlow of DCPC was executive secretary of the committee, with other staff support provided by Ritva Butrum, Carolyn Clifford, Elaine Lanza and Mickey Hanna. Members of the committee, in addition to Nesheim, were Andrew Clifford, Univ. of California (Davis); Vernon Young, MIT; Johanna Dwyer, Tufts and a BSC member; James Gaylor, E.I. du Pont; Daniel Nixon, Emory (soon to join DCPC as director of the Prevention Program); Myron Winick, Columbia; Mark Hegsted, Harvard and a BSC member; and Walter Mertz, U.S. Dept. of Agriculture.

Leukemia Society Now Accepting Grant Applications For 1988

The Leukemia Society of America is accepting applications for 1988 grants to encourage research at both the basic science and clinical levels in the fields of leukemia and related diseases.

Werner Kirsten, chairman of the Grant Review Subcommittee, said the awards are a primary source of salary support for individuals whose work is concentrated in leukemia, the lymphomas, Hodgkin's disease and multiple myeloma. All candidates should hold PhD, MD or equivalent degrees. For information and application forms, contact Research Grant Coordinator, Leukemia Society of America, 733 Third Ave., New York 10017. Deadline for filing applications is Sept.1.

DCPC Board Approves Concepts For Three New Grant Programs

The Board of Scientific Counselors of NCI's Div. of Cancer Prevention & Control has approved the concept of three new research programs which would support up to 12 grants at a total estimated cost of $2.6 million a year. But the Board turned down an ambitious new proposal to establish from four to 20 Cancer Prevention Research Units with an estimated cost of $4 million a year.

Concepts approved for development into requests for applications (RFAs) were evaluation of the impact of early detection; breast cancer detection, management and sequelae in elderly women; and cancer nursing interventions to promote patient self care.

The Board also gave concept approval to three contract supported efforts with a total estimated cost of $2.2 million a year: a new program for phase 1 clinical trials of chemopreventive agents, to be awarded through master agreements; recompetition of an existing master agreement for efficacy studies of chemopreventive agents in animals; and recompetition of a support contract for diet, nutrition and cancer prevention projects.

The Board's Cancer Control Science Program Committee had approved the CPRU concept (**The Cancer Letter**, April 24). It would have established a national long term resource in cancer prevention research aimed at preventing cancer by applying proven or state of the science interventions in the smoking, diet and screening areas.

Criticism from the full Board ranged from the contention that there are not enough trained people available to do that kind of work to the suggestion such efforts in prevention should include diseases in addition to cancer.

"Unless you have on the shelf proven technology at the phase 3 level, CPRUs would have to spend a lot of time developing phase 1 and 2," Paul Engstrom said. The proposal was designed to support phase 4 (studies on effectiveness of proven interventions in communities or defined populations) and phase 5 (implementation studies for widespread adoption of interventions).

"Smoking cessation is the only primary prevention that makes sense," Lewis Kuller said.

Kenneth Warner argued that the concept would not help much in training new people for cancer control research. "I keep going back to that. I don't see the rationale for this."

DCPC Deputy Director Joseph Cullen responded, "Where do we get the stuff to put into phase 4 and 5? We have 47 trials in phase 3 and 4 ending in the next year and a half. We'll get it from there"

"I would rather see more money in training grants for people in prevention and control," Frank Meyskins said.

All Chronic Diseases

"There's a lot of what you want to do out there already," Warner said. "It's just not called cancer. It's called health promotion. We need to train people in prevention and control of chronic disease, including cancer." He noted the coalition of the American Cancer Society and American Lung Assn. to work against smoking. "That has been tremendously effective."

Carlos Caban, acting chief of the Cancer Control Applications Branch who presented the concept, pointed out that the proposal contained specific language encouraging linkage to other diseases.

"The nub of the concern of those opposed to this concept is that there are not enough trained people to do this work," James Holland said.

Philip Cole suggested that the existing Cancer Control Research Units, upon which the CPRU proposal was patterned, "could and should" do prevention application. "I can't accept that we need both."

Neither did a majority of the Board.

Details on approved concepts follow:

Evaluation of impact of early cancer detection: retrospective studies. DCPC anticipates that four two-year grants will be awarded at an estimated total cost of $812,000 each year.

Purpose of this RFA is two fold--to discover existing data in defined population groups which have been exposed to various screening or health maintenance procedures and analyze the data for impact on cancer prognosis; and to identify and evaluate intermediate end points that can be used to assess the benefits of early cancer detection through an analysis of the existing data bases. Consideration needs to be given to possible over diagnosis, lead time and length biases and treatment differences. These studies should aid the evaluation of early detection activities and other research (e.g. chemoprevention) by minimizing the need for long term followup, thus reducing the cost in time and money associated with mortality studies. The goal of this RFA is to identify data sets, end points and be in a position to assess the contributions of early detection intervention.

For the purpose of this concept, early detection is defined as the process of finding precancerous lesions or cancers in their early stages of growth among symp-

tomatic individuals either in a screening mode or in the physicians' office, when appropriate early treatment should lead to increased survival and decreased morbidity and mortality.

For most cancers, early detection, diagnosis and treatment at an early stage of disease may afford a much greater chance of patient survival than at later stages of disease. Results from mass screening for cancers of the breast and cervix indicate that early detection is beneficial and a desired objective. Women with in situ cervical cancer are usually cured if treated. There is significant treatment morbidity associated with the treatment of advanced cancer.

Although a number of end points have been suggested for the assessment of benefit of early cancer detection, except for staging and life table estimation they have not been critically investigated nor tested for their validity and applicability for early detection. These could include an absolute shift in stage of disease at time of diagnosis especially from the most advanced stages, lead and length time estimates, reduction in the incidence of recurrent cancers, increased median survival time, and reduced morbidity. For screening procedures that detect precancerous lesions, the end point is a reduction in incidence of invasive disease. Another example may be the shift toward earlier stages in breast cancer and in occupational groups undergoing surveillance for bladder cancer.

Ideally, end points should be relatively easy to measure, and involve reasonable costs, time and manpower and be highly indicative of disease prognosis. The intermediate endpoints should demonstrate through the analysis of scientific data and ongoing research, the benefits from early detection. These studies may reveal important relationships, for example, between stage of disease and mortality. Data from two breast cancer screening projects, the HIP and the Swedish trial, which showed a decrease in mortality, have also demonstrated a concomitant downshift in stage.

The scope of this RFA is limited to the analyses of existing data in defined populations having information about early detection and diagnosis of cancer with patient followup. Those with data banks located in HMOs, diagnostic centers, screening and hospital clinics, industrial medicine clinics, wellness clinics, comprehensive cancer centers and in other institutions will be encouraged to participate.

The spectrum of approaches can include case control studies, descriptive analysis, descriptive epidemiological surveys, clinical trial data, retrospective reviews, or other types of analysis that the applicants may wish to propose. Applicants will be required to justify the sites selected for study and to describe how the selected end points will be measured and their advantages for the evaluation of early detection. They will also be required to identify and evaluate any biases and treatment difference that might influence the results.

This RFA will not support the collection of additional data. It requests that existing data be analyzed in relation to the possible end points for early detection. Thus, the study is expected to be accomplished in a relatively short period of time. Analysis can include one or more anatomic sites as well as one or more end points.

DCPC Director Peter Greenwald said this project would help find "new ways to make judgments on screening." Kuller referred to the study using sputum cytology for early detection of lung cancer. "They found earlier cases, with more treatable cancers, but the same numbers died. Charles Smart, chief of the Early Detection Branch, challenged the validity of that study.

Smart noted that this concept had twice been turned down by the Board. But Cole responded, "Now that I understand what it is, I can support it. It is a proposal for innovative ideas for evaluating screening methods."

Kuller suggested that randomized studies might be needed, but Holland responded that "there is a whole spectrum of things that can't be done with randomized trials. You can't randomize a lot of things unless you deprive yourself of a lot of information."

The vote to approve was unanimous.

Breast cancer detection, management and sequelae in elderly women. DCPC estimated that three three-year awards will be made with a total cost of $1.26 million a year.

The goal of this research initiative is to improve the results from breast cancer management using available techniques in women over age 65. There are two major objectives of this effort:

1. To identify and analyze factors important in the early identification of potential breast cancers, access to treatment, medical decisions and management of the cancer, sequelae from the interaction of comorbid conditions, and late treatment effects.

2. To analyze and develop interventions which will enhance the access to care and the treatment of these patients while minimizing both early and late complications.

It is expected that the primary targets for the interventions to be developed will be elderly women, for early detection and access to health care; health professionals, for diagnostic workup and management; and patients, families and health professionals for early and late sequelae from the interaction of disease, treatment and comorbidity.

The aging population, the decrease in heart disease, and the special diagnostic and treatment needs of the elderly suggest that the detection and treatment of breast cancer in this population will be a major problem over the next 40 years. There is little solid data by which to guide future decisions.

Although data bases do exist which provide some information, most pertain to minimal management information, with little attention to particular aspects, cancer detection, the diagnostic workup, the algorithms physicians use in management decisions, comorbidity considerations, or the prevention and care of late sequelae. As a result, it is apparent that if useful information is going to be collected in this population, it must be prospective and focused on a set of specific questions in order to yield the development of specific interventions aimed at an appropriate and accessible study population.

Information focusing on specific issues in the elderly would allow the development of interventions, both simple and complex, aimed at the problems uncovered in the first phase. For detection, the patient would be the focus, with particular emphasis on health maintenance behavior including breast self examination and mammography. For diagnosis, attention would be aimed at the health professionals and their use of the physicial examination, mammography, the staging workup, and the biopsy algorithms they use for decisions leading to patient management. For treatment, the focus would be on health professionals and the information base they employ to make decisions. Their selection of treatment with special attention to deviations from acceptable practice (both conservative and radical) for surgery, their use of radiation therapy both with and without surgery, and the use of hormonal and chemotherapy or combinations of treatments and their indications for selection would be explored.

The research initiative itself includes two phases: The first will focus on hypothesis development, data collection and analysis, and pilot testing of poten-

tial interventions. An attempt to assess the important factors complicating and detracting from the successful management of breast cancer in the elderly should receive primary attention. Patient behavior, professional attitude and behavior related to workup and management, and the relationship between the late disease, its earlier treatment, and comorbid interactions are all to be addressed.

In the second phase, the applicant will be expected to test and compare efforts aimed at optimizing early detection, patient workup, decision algorithms for management, and prevention efforts aimed at avoiding late complicating sequelae. These interventions may include educational efforts, systems enhancers, promotion of self care, social support and resource allocation.

Cole asked why breast cancer was selected for this study. "With the increase in age of the population, we will see increases in all cancers."

Rosemary Yancik, assistant director of the Centers & Community Oncology Program, answered, "We wanted to start with breast cancer, and then have another for prostate cancer." Responding to Cole's question on why an RFA should be issued rather than relying on investigators to "do this on their own initiative," Yancik said that there hasn't been much work in this area.

"I've never seen anything like this have any impact," Cole argued.

Yancik disputed that contention. "At the right institution, with leadership, things do change sometimes." She mentioned major changes in breast cancer management in recent years.

Lloyd Everson backed Yancik's position. "There is ample evidence that you can change primary care in breast cancer. It was not too long ago that everyone did radical mastectomies."

There was no opposition to the motion for approval.

Cancer nursing interventions to promote patient self care. DCPC anticipates making up to five three year awards at a total cost of $600,000 the first year, $630,000 the second and $660,000 the third.

The purpose is to encourage and stimulate cancer nursing research which develops and evaluates nursing interventions aimed at facilitating self care capabilities of patients who are receiving cancer therapy. Self care consists of activities done by patients to maintain or improve current health.

Specific objectives are to determine cancer nursing interventions which are effective in promoting patient self care; to detect and address patient chacteristics which facilitate or limit utlization of self care during treatment; to identify patient factors predictive of the utlization of an intervention promoting self care during treatment.

The research projects to be conducted under this intiative will identify nursing intervention approaches, such as structured patient teaching groups, and specific self care practices, such as oral care regimens. The researchers will assess the actual use of the selected self care practices and the associated outcomes, such as oral infections. Evaluation will include the effectiveness of the nursing approach in achieving patient performance of the selected self care activities and an analysis of factors which influence patient participation. This systematic research is needed to guide nursing practice in effective interventions to enhance cancer patient self care.

Among the most notable of recent changes in health care has been the shift to outpatient and home care or the use of minimal care boarding facilities for patients who previously would have received their therapies while hospitalized. This is reflected by a decrease in the average length of hospital stay by two days. A major consequence is that patients no longer receive the continuous nursing care associated with hospitalization, nor do they benefit from nurses teaching them and their families during multiple interactions which occur over several days in the hospital, the traditional method of preparing patients to live with a disease. Staff in outpatient settings are attempting to fill this gap. However, patients have the responsibility to determine what to do to take care of themselves as well as how and when to seek help from professionals. Self care restores self respect for many patients who have been forced into an unwelcome dependency role and view every opportunity for participation in their own treatment as an expression of independence.

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The dollar estimates with each concept review brought before the various boards of scientific counselors 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 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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For patients who are receiving radiation therapy or chemotherapy, the degree to which they take an active role in their own care can have major implications. Specifically, patient self management can help to prevent complications, lessen the duration and intensity of symptoms, promote the desired treatment effects and provide greater independence. Patients must perform specific self care activities depending upon their particular treatment such as:

*Taking leucovorin tablets for rescue several hours after receiving high dose methotrexate.

*Maintaining high fluid intake and altering the usual patterns of urination after receiving cytoxan therapy.

*Avoiding exposure to infection and being aware of its early signs during periods of neutropenia.

In order to meet the cancer control objectives for the Year 2000, it is necessary to have aggressive application of proven therapies. However, a major deterrent to such application is the occurrence of complications which mandate reductions in therapy. Self care activities have the potential to deter or decrease the morbidity associated with treatment and thus allow aggressive therapy. This initiative supports the goals for the Year 2000 by obtaining systematic and cumulative knowledge about self care and its results.

Nursing research has addressed the issues of self care with only occasional inclusion of cancer patients. Evaluation of methods of teaching, acceptance, compliance, and effects on morbidity are not available. There is a pressing need to apply optimum nursing interventions to aid cancer patients in taking responsibility for many of the care activities previously directed by nurses. The long term goal of this initiative is to improve the ability of patients to take care of themselves, receive optimum benefit from medical interventions, and assure the best possible professional instruction and support.

Target population. Participants in this study should share a common entry point, preferably their first course of either radiation therapy or chemo-

therapy. Researchers could include adolescents who can be responsible for their own care as well as adults. Investigators will be expected to identify a target group of patients with a high likelihood of particular problems for which self care content can be focused. Examples of possible patient groups include those who are receiving chemotherapy which will dramatically increase risk of infection; radiation therapy to the pelvic region; multimodality therapy for head and neck cancers.

Nursing interventions. These are defined as those actions or functions organized and implemented by professional registered nurses that are designed to impart to patients specific content and process knowledge related to self care for their disease or treatment. Whenever possible, the researchers are to develop nursing approaches and content within the context of current theories of self care. The investigators are to determine the timing, sequence and duration of the interventions. Examples of possible interventions include goal setting with patients and families for specified achievements; peer group problem solving sessions; practice in strategies for working with specialists in many areas such as physical therapy, nutrition or social service; provision of audiovisual programs which are followed by patients demonstrating an activity.

The interventions are to be given in a treatament setting and coordinated with the patients' therapy schedule. Treatment settings may be a hospital patient care unit, outpatient department, physician office or clinic in which chemotherapy or radiation therapy is provided.

Cole noted that the concept statement was broad enough to permit studies with patients with a variety of cancers, including some with the probability of short life expectancy. "Would the principle be better evaluated if this were more restrictive? You could identify some which impose serious burdens yet have longer life expectency, for instance colon cancer and colostomy. Perhaps do only males or females, since the support networks are different. This might be the subject of two RFAs. I think you should cast the net narrowly, not broadly."

"If you close it too narrowly, you might eliminate some that should be included," Anne Bavier, program director, said.

"Phil's approach might have a better chance of getting through peer review," Board Chairman Erwin Bettinghaus said.

"From the clinical point of view, it is important to key in on a specific problem," Meyskins added. He asked if the National Center for Nursing Research is doing anything along this line.

Bavier said she had discussed the concept with NCNR "and they encouraged us to go ahead. It is important for us to key on cancer. Their mission is broader."

The concept was approved unanimously.

Contract concepts approved by the Board:

Phase 1 clinical trials of new chemopreventive agents. This will be a master agreement with organizations qualified to do these studies. DCPC had estimated a budget of $300,000 a year, but the Board insisted this program would need more and approved $1 million.

The primary goal of a phase 1 clinical trial of a chemopreventive agent is to develop a safety and toxicity profile on the agent so that an appropriate and safe dose for a subsequent phase 3 risk reduction trial can be determined. Whenever necessary, an IND will be obtained by NCI or the investigator prior to the phase 1 trial. It is also necessary to obtain required information so that an application for an IND can be submitted to FDA prior to phase 3 cancer risk reduction trials.

A secondary objective is to obtain pharmacokinetic data on the compound, and on its metabolites, if possible, so that a maximum body of knowledge concerning the distribution, metabolism, excretion, and toxicity of the compound will be available. Such data may enhance the efficacy and safety of that compound in the phase 3 trials to be developed subsequently.

An active preclinical program is already in effect within the Chemoprevention Branch to identify, evaluate the efficacy, and study the toxicology of potentially active compounds in both in vitro and in vivo systems. Presently, 25 agents or regimens are being studied; testing on an additional 25 new compounds, selected by extramural experts, will begin this year. It is anticipated that several of these compounds will be appropriate for phase 1 clinical trials during the next year. Thus, the capability to initiate phase 1 clinical trials is a high priority. The progress of the chemoprevention program will be delayed if the phase 1 clinical trial mechanism is not available for introducing new compounds into phase 3 trials.

Master agreement orders will be issued to all investigators/institutions who are deemed via peer review qualified for carrying out the proposed tasks. The award to investigators/institutions will be for five years. As agents become available, applications will be requested and reviewed, and the best proposal will be selected for funding and implementation. Six to eight new agents will be studied per year; the number of subjects will be determined as necessary for each compound evaluated. All master agreement order holders will be asked to submit a master protocol for phase 1 studies in their technical proposals which details all aspects of the study except those determined by the specific agents.

Protocols must be approved by the funded institution's investigational review board and contain an informed consent form specific for the investigational agent. All specific protocols will also be reviewed by an NCI safety and protocol review group. Each study must have approval in accordance with FDA IND regulations.

Master agreement order holders might be expected to compete for at least one study per year. The investigator will develop and submit a final report on the results of each study. Six to eight task orders will be issued annually for studies on specific agents.

Meyskins observed that "this is a small amount of money for the task," and Greenwald said the Board could increase it. Holland added, "This is something on which the mission of this division rests" and agreed that more money would be needed. Meyskins' motion to approve the concept at a total of $1 million a year was approved without dissent.

Efficacy studies of chemopreventive agents in animal models. This is recompetition of master agreements with 10 laboratories, which expire in July. DCPC hopes to expand to additional labs, at a total estimated cost of $900,000 a year. Awards will be for five years.

The primary objective of these studies is the evaluation of efficacy of various selected chemopreventive agents at several dose levels in animal models. The animal models are chosen for their relevance to the human cancer problem including an emphasis on lung, colon and breast cancer. The emphasis of activity will be to take the initial leads from the published literature, and the results from the chemoprevention in vivo and in vitro screening program and focus on the most promising agents. The data on the selected agents will be expanded by an evaluation of the dose response, bioavailability, spectrum of

target sites, and potential toxicity. Combinations of promising chemopreventive agents and inhibition of initiation as well as promotion will be examined by this contract.

This effort will improve the criteria for the selection of agents for toxicology and potential clinical testing, decreasing toxicology costs and accelerating the rate at which agents are evaluated.

All master agreement order holders will be asked to submit a master protocol (for animal efficacy studies in at least one target organ including lung, colon, mammary, bladder or a model they feel is relevant to the human cancer problem) in their technical proposals which detail all aspects of the study except those determined by the specific chemopreventive agent. A standardized protocol will be developed by DCPC for each target organ model and for each chemopreventive agent including the number of experimental groups and controls, statistically valid group sizes, number of doses of chemopreventive agents, number of doses of the carcinogens, standardized test for purity of the agent, and preparation of the agent in the diet, standardized tests for assay of the agent (in food and in sera), criteria for animal evaluation including source, care monitoring, and pathology evaluation. The investigator will develop and submit monthly reports and a final report on the results of each study.

The concept was approved without dissent.

Research support services for diet, nutrition and cancer prevention projects. This is recompetition of an existing contract now held by Prospect Associates. The award will be for five years at an estimated cost of $315,000 a year.

This project will provide services for evaluation of hypotheses which might result in concepts for new research projects for RFA and RFP initiatives; searches and compilation of materials, some of which may form the basis of division documents on diet, nutrition and cancer issues; organization of information for development of manuscripts, official monographys and science support materials for other contractual liaisons; and development of critical review articles as potential position papers for the diet, nutrition and cancer program.

The research support services are not available within the division because of limitations on the variety of skills required for these activities in the present staff and operational time constraints on present staff. The tasks, requiring a diversity of knowledge and training and short term efforts of specialists and skilled support personnel, can be obtained most efficiently and cost effectively and clearly to the best interests of the government by contract.

The project includes assistance in gathering, analyzing, synthesizing, and integrating information pertinent to preclinical and clinical issues fundamental to human biology, epidemiology, and potential human diet and nutrition intervention trials of high priority to DCPC's goals and objectives. Specific tasks will provide:

*Literataure searches in all National Library of Medicine computer data bases relating to diet, nutrition and cancer science.

*Identification of information source deficiencies in the NLM electronic data bases and in published literature, and searches in data bases outside the US.

*Compilation of abstracts, integration of information retrieved from all sources, and critical analyses of published reports and available technical documents.

*Preparation of documents for analyses by special advisory groups and programmatic reviews.

The tasks are labor intensive. Each will be specified in detail, supervised and monitored closely on an ongoing basis by NCI to ensure accurate and high quality performance and to avoid unnecessary effort, materials and inappropriate procedures.

The concept was approved without dissent.

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-CP-71107-13

Title: Breast and other cancers following x-rays for scoliosis

Deadline: Approximately July 25

The Radiation Epidemiology Branch of the Div. of Cancer Etiology is soliciting proposals from qualified firms to provide the necessary resources to conduct a study on breast and other cancers following x-rays for scoliosis.

A feasibility study of cancer morbidity and mortality among scoliotics was initiated in 1983 at four hospitals in Minneapolis-St. Paul. Objectives of the feasibility study were to determine if medical records were available for persons diagnosed with scoliosis between 1935 and 1965, to evaluate the quality of information contained in the medical records, to develop and pretest a medical record abstract form, to identify and tabulate the radiologic records for all diagnostic x-rays taken during the course of monitoring scoliosis, to estimate the radiation doses to the breast using data from the radiation records or actual films, to trace and locate patients, and to conduct a mail questionnaire survey. The pilot study was carried out with the Scoliosis Research Society.

The objectives of this competition are to obtain managerial, technical, and clerical support services for an expanded epidemiologic followup study of patients treated for scoliosis. In order to obtain sufficient numbers, it will be necessary to enlist subjects from approximately eight different centers across the U.S. Emphasis shall be on breast, leukemia, lung and thyroid cancers.

Contract Specialist: Sharon Miller
RCB Blair Bldg Rm 114
301-427-8888

CORRECTION

The RFP entitled, "Record linkage studies utilizing resources in population based tumor registries" (**The Cancer Letter**, May 8) has been changed from the number listed to **RFP NCI-CP-71106-56**.

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

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