THE CANCER LETTER

Vol. 10 No. 19
May 11, 1984

Subscription $150 year North America
$175 year elsewhere

P.O. Box 2370 Reston, Virginia 22090 Telephone 703-620-4646

NEW MECHANISM—CANCER CONTROL COOPERATIVE GROUPS—UNDER CONSIDERATION BY NCI FOR REGIONAL ACTIVITIES

Cancer Control Cooperative Groups. That is the concept that NCI staff and advisers have come up with in the planning effort aimed at encouraging cancer centers and other organizations to develop coordinated regional approaches to cancer control. The Cancer Control

(Continued to page 2)

In Brief

LUCIUS SINKS NEW CANCER CENTERS BRANCH CHIEF; MARY SEARS, ONE OF ASCO FOUNDERS, TO RETIRE

LUCIUS SINKS will leave Tufts Univ. to become chief of the Cancer Centers Branch in the Div. of Cancer Prevention & Control at NCI, effective June 1. Sinks previously was at Roswell Park Memorial Institute, has been extensively involved in pediatric clinical trials, development of high dose methotrexate therapy, other chemotherapy studies. The Centers Branch has not had a permanent chief since it was transferred out of the old Div. of Research Resources & Centers in 1978. Jerome Yates, director of DCPC's Centers & Community Oncology Program, has been acting branch chief since the division adopted its present organizational scheme.... **MARY SEARS,** executive secretary of DCPC's Board of Scientific Counselors, will retire from NCI June 1. She previously had headed the Treatment Projects Section of the Breast Cancer Task Force, and before that participated in clinical studies at M.D. Anderson amd the Univ. of Rochester. She has been at NCI since 1973. Sears was one of the founders of the American Society of Clinical Oncology.... **GARY JACOBSEN,** former medical director of the Oregon Comprehensive Cancer Center Program, has joined the American Cancer Society as national vice president for service and rehabilitation, Arthur Holleb, senior vice president for medical affairs, announced. Jacobsen will oversee programs that support cancer patients and their families. He succeeds Diane Fink, who assumed the position of national vice president for professional education upon the retirement earlier this year of Nicolas Bottiglieri.... **SIX MEMBERS** of the DCPC Board of Scientific Counselors ended their terms with last week's meeting: Chairman Lester Breslow, Charles Cobau, Leonard Derogatis, Harry Eagle, Loretta Itri, and Doris Wilkinson. Their replacements have not yet been named.... **ENRICO FIRMI** awards were presented this week to Alexander Hollaender, formerly of Oak Ridge National Laboratory, and John Lawrence, Univ. of California (Berkeley) for their work which laid the foundations for understanding the effects of radiation on biological systems and the application of that knowledge to medical treatment. The awards included gold medals and $25,000 to each.

DCPC BOARD TO GET CANCER CONTROL GROUP PLAN IN OCTOBER, YATES SAYS

(Continued from page 1)

Working Group of the Centers Planning Committee last week agreed to proceed with development of the cooperative group approach, focusing on cancer centers and other organizations that might have regional capabilities in cancer prevention and management.

Jerome Yates, director of the Centers & Community Oncology Program in NCI's Div. of Cancer Prevention & Control, said his staff and that of the Div. of Cancer Treatment will explore mechanics of group development. The Cancer Control Working Group will meet during the summer to consider staff recommendations for guidelines. Yates said he intends to present details of the program for concept approval to the division's Board of Scientific Counselors at its meeting in October.

The Centers Planning Committee, which includes members of the Board of Scientific Counselors, NCI staff, and cancer center representatives, has been meeting to address specific issues related to the role of centers in reducing the incidence, morbidity and mortality from cancer in their respective regions, and to make detailed recommendations. The Cancer Control Working Group is chaired by Robert Day, director of the Hutchinson Comprehensive Cancer Center and a member of the DCPC Board.

The Working Group in its discussions last week did not delve into the mechanics of cancer control cooperative groups—how they would be organized, funded, and operated; what would be their missions and goals; how many would be supported and how much money would NCI allocate for it.

The program is essentially envisioned as a regional one, presumably with cancer centers as the lead agencies in most regions. Yates told **The Cancer Letter** that one approach might be for a group of centers in a large city or a region to organize into a cooperative group, focus on two or three cancer control activities, and perhaps involve other agencies. The lead agency does not necessarily have to be a center, he said. "I can envision cancer control activities being run from a CCOP, if the interest and expertise is there. It could be a health department."

Yates said he was determined that development of the guidelines for the "Cancer Control Cooperative Group Program" would not turn into the two year long nationwide hassle which preceded adoption of the Community Clinical Oncology Program guidelines.

Yates told the Board of Scientific Counselors last week that he gets a "feeling of deja vu" when he talks about groups organizing for cancer control activities in their communities or regions, referring to the disappointing Community Based Cancer Control Program developed and supported by NCI in the mid-1970s. "Money alone doesn't solve the issue," Yates said. "The theory was that you could crank up a big machine and affect morbidity and mortality. But that was done without assurances that the people were there who could do the job. There was a lot of naivity then. If there is one thing to learn from that, it is that you need management. There was not much of substance left after the programs were closed."

The CBCCP was an ambitious cancer control effort in which six communities were funded (others had planning contracts but did not make it to implementation) to organize into efforts to reduce morbidity and mortality from specific cancers. The five year effort cost in the neighborhood of $50 million.

DCPC Director Peter Greenwald said he did not feel any "deja vu" over Cancer Control Cooperative Groups. "It would be wrong to say what we are describing is the same thing all over again. They (the CBCCP institutions) were constrained from really looking in depth at what it would take to have an impact. Most developed activities that were dependent on NCI money. Some useful things did come out of it."

"A lot of talented people worked very hard on that," Day said. "We want to know why it didn't work."

"The institution needs a strong infrastructure of cancer control," Greenwald said. "It needs a strong research arm. The question is how to get the resources there so that in the long run it will have strong programs in cancer detection, prevention, and education that will be part of the establishment and will continue."

Curtis Mettlin, director of cancer control and epidemiology at Roswell Park Memorial Institute, presented a statement at the working group meeting which suggested the role of cancer centers in cancer control:

"Cancer centers are a diverse group of institutions that, by definition, have certain common features and certain common potentials for contributing to the national cancer control effort. While the actual implementation of a given cancer control activity will differ from one type of center to another, the underlying roles of the center in the process may be defined. Enumeration of these roles may be useful in identifying the types of programs that can assist centers in best fulfilling their obligations in cancer control in the coming years.

"1. Cancer centers serve as institutional settings for the conduct of cancer control research. Where centers have a critical mass of public health

oriented researchers, the inherent access to research resources such as computer facilities, biostatistical expertise, and large numbers of participants in clinical and educational programs make centers logical settings for the conduct of basic research on cancer control issues.

"2. Cancer centers are point sources for the diffusion of emergent cancer technologies. Because centers are often the sites of the development and initial testing of new means of prevention, diagnosis, treatment and rehabilitation, they often represent the best point from which the diffusion to broader settings may be initiated. The clinicians and scientists most knowledgeable about the limits and potential applications of new approaches to disease control may be those who were most directly involved in the technology development process.

"3. Cancer centers may serve as conduits for the diffusion of emerging concepts developed in other settings. Through ongoing educational and training programs, through regional, national, and international visiting physician and scientist programs and through their communications resources, cancer centers serve as media for information transfer and exchange. In addition, through typically well established ties to the community and resources such as cancer information services, the cancer center can serve as a visible and effective source of information to the general public as well as defined target audiences.

"4. Cancer centers may serve as the settings for development of exemplar programs in cancer control. Many centers are, in essence, research and development organizations. Because of this, they have resources and the administrative commitment needed to establish programs for which there are few preexisting models. In addition, the shared resources that often are available to devote to program development broaden the sharing of the risks of attempting something not previously proven successful. Once the problems and the means of overcoming them have been identified, other institutions, less adapted to innovation, may more readily accept novel programs.

"5. Cancer centers may serve as foci for the integration of regional cancer control programming. The academic, research, clinical, and community networks in which cancer centers operate represent established means for the development of regionally integrated approaches to cancer control. The centers' singular interest on the cancer problem is a particular asset because cancer centers often are viewed within their service areas as the most reasonable setting for this coordination function."

Greenwald told the Board of Scientific Counselors that "it is our intention that our partnership with cancer centers and the networking of centers with other community groups respond not only to the needs of the scientific community and the universities, but to the broader needs of the nation. While there is considerable overlap, these are not necessarily identical. We look to the cancer centers to help us to address the major problems of morbidity and mortality in their regions, including the frequently higher cancer rates in minority populations. We look to centers to help achieve a cancer control cohesion and coordination throughout their regions, and to assure an integration of basic with clinical and control research and with health practices.

"Some center directors showed an understandable worry that we are going to ask them to do a job with no additional resources," Greenwald continued. "That is not our intention. It is our intention to seek additional funds to cover these new initiatives whether they be part of the centers program, or in the cancer control budget per se, or in training or other program areas. Defining the methods through which centers can help to reach national goals will help us do this."

NCI Director Vincent DeVita also assured cancer centers that they will not be asked to expand cancer control activities without more money.

"We do not intend for centers to assume additional burdens without additional money," DeVita told the DCPC Board. One of the objectives of the Centers Planning Committee and the parallel effort of the President's Cancer Panel in its series of meetings around the country is to determine if the number of centers and their geographic distribution are adequate, DeVita said. "We need to determine what can be done to meet the mandate of the National Cancer Act, within regions, with present technology... We have identified gaps in Birmingham and Southern California (at Panel meetings there) which need attention. We can't solve a problem until we identify it."

DeVita came under some fire following the Los Angeles meeting of the Panel for putting the centers there on the spot by pointing to mortality rates in the region higher than the national average and asking what the centers are doing about it, without previous notice that he was going to do that. He has since written to center directors advising them of the Panel's plans and NCI's concerns. Greenwald said he feels center directors are inclined toward accepting those assurances.

DeVita said the Panel plans to visit next San Francisco, in September, and Seattle this year, and Hawaii, Wisconsin, Mayo, and possibly Chicago next year, probably in that order.

"One issue, that of changing the guidelines for cancer centers, relates to the question, do we have enough centers," DeVita said. "The suspicion is no,

we need more. A subset of that is do we need to develop centers to meet national problems, such as the failure of some minorities to keep up with the reductions in incidence and mortality we are seeing with white Americans."

DeVita said he is considering a proposal to make available a planning grant to a consortium of the historical black medical colleges, to determine if a mechanism can be developed to enable them to compete for cancer center core grants.

DeVita said he wanted to add "my Harry Eagle comment," nodding to the member of the Board of Scientific Counselors and outspoken defender of basic research. "Are we going to pay for these programs by taking money away from basic research?" The answer, DeVita said, has always been no. "I've said many times that basic research is our number one priority, but I feel that we also must pay attention to the fruitful application to the clinic of the results coming from basic research."

DeVita cited some figures to demonstrate NCI's commitment to basic research:

Since 1976, the percentage of the total NCI budget allocated to basic research (as represented by RO1 and PO1 grants) increased from 27.6 percent to 45.1 percent. During the same time, intramural research, which DeVita said is primarily basic research, increased from 11.8 to 16.8 percent; centers, from 6.3 to 7.1 percent; clinical cooperative groups, from 4.2 to 4.3 percent; cancer control, decreased from 7.4 to 5.8 percent; and R&D contracts, from 29 to 11.8 percent. Clinical trials, including treatment and prevention, were spread among the other categories but split out, they went from 9.7 percent of the NCI budget in 1976 to 14.6 in 1985. The 1985 figures are based on the President's budget request and are not final.

"I've been told by the ASCO Board that since I've spent most of my career in clinical research, I'm bending over backwards to support basic research," DeVita said. "I'm not operating independently. I'm not bent over backwards. I'm twisted like a pretzel."

DCPC BOARD APPROVES CONCEPTS OF SIX NEW RFAs TOTALING $9.3 MILLION A YEAR

The Board of Scientific Counselors of NCI's Div. of Cancer Prevention & Control last week gave concept approval to six new grant and cooperative agreement supported projects totaling an estimated $9.3 million in first year awards.

The projects, which will be detailed in RFAs to be released in the following months, include research on smoking cessation and cancer communications, a $4 million a year prevention clinical trials effort, cooperative agreements for technical support for cancer control efforts by state and local health agencies, and dietary fiber research.

Contract concepts approved included recompetition of the nationwide Cancer Information Service, formerly a very controversial program which barely slipped by the Board when it was up for concept approval three years ago.

The Board also gave concept approval to a new fellowship program for cancer nurse research, and approved a controversial program for prevention of primary liver cancer with hepatitis B vaccine in Africa.

Concepts approved by the Board were:

Title: Smoking cessation and prevention opportunities within the women's health care continuum. Estimated total budget, $1.5 million per year for five five year grants.

The goal will be to determine long term effects of interventions carried out within the women's health care continuum to reduce the prevalence of cigarette smoking among women. Women as a group utilize health care systems significantly more than do men and are more likely to utilize facilities in a logical progression of repeated visits. The continuum includes regular obstetric, gynecologic, and pediatric care with women moving back and forth within this continuum.

Objectives will be to develop and evaluate intervention strategies within the women's health care continuum (obstetrician, gynecologist, nurse practitioner, pediatrician, family practitioner) to reduce the prevalence of cigarette smoking among women; and to develop and evaluate assessment procedures for determining the long term effectiveness of smoking cessation interventions within the women's health care continuum.

Survey data suggest that women are aware of the risks of smoking. However, smoking among women continues unabated. Therefore, other means of intervening in the smoking processes of women are needed. Since women are more likely than men to visit a health care professional during a given year and yet less likely to receive advice from health professionals concerning smoking, and since the advice of these individuals, particularly physicians, has been shown to be effective in reducing smoking, it is proposed that interventions be undertaken to utilize fully the health care continuum that most women utilize.

Such studies should operate within the existing health care framework, i.e., should not require smoking only visits to physicians/nurses by women or require additional staff, since neither of these would likely be generalizable. Rather, the studies proposed should focus on opportunities for intervention that make use of the health care practices in which women are involved. For example, there should be a transfer of smoking advice from a woman's obstetrician/gynecologist to her child's pediatrician since it is during the postnatal period that many women who stopped smoking during pregnancy are most likely to begin smoking again. The pediatrician and, later, the family practitioner and

staff can become valuable intervenors in women's smoking behavior if they are seen as a health care team operating on a continuum rather than as separate, noncommunicating entities. As such, studies focusing on HMOs and primary health care teams, as well as high risk subgroups of women (e.g., young adults, heavy smokers) will be encouraged.

Thomas Glynn is project officer.

Title: Smoking prevention and cessation among women. Estimated annual budget, $1.5 million, five awards, five years. Funding mechanism, grants.

The goal is to determine the long term effect of interventions designed to prevent the incidence and/or reduce the prevalence of cigarette smoking among women. Objectives are to develop and evaluate intervention strategies to prevent or reduce cigarette smoking among women and to develop and evaluate assessment procedures for determining the long term effectiveness of smoking interventions among women.

Since 1964, there has been only a five percent decline im women's smoking prevalence rates compared to a 14 percent decline among men. Data suggest that women may be less successful in stopping smoking through formal programs than men and that problems of cessation maintenance may be especially acute for women. Yet, since the peak of prevalence of smoking among women lags 10 years behind that of men, the opportunity now exists for the prevention of the significant incidence of smoking related cancers seen among men. Prevention of these cancers will be an essential part of NCI's year 2000 goals, and smoking interventions among women will need to be carefully designed, not only to be responsive to smoking patterns unique to women, but also to reflect the multiple and increasingly complex roles women now play in society.

Current smoking patterns among women differ in important ways from those of men. Treatment and maintenance outcome also differ, that there are important smoking related sociological differences between men and women. These interventions should include strategies for responding to some of the social, cultural, psychological, and economic factors that differentially impinge upon women's lives and have been found to influence their smoking behavior. Emphasis will be placed on problem areas and/or settings where previous activities or current data suggest that a combined male-female focus is less effective for women or where women exhibit a unique smoking pattern or problem in prevention/cessation. For example, the problem of weight gain in maintaining cessation, smoking as a means of stress reduction, and greater use of low tar/nicotine cigarettes are all more common among women but have not benefited from the development of the type of large scale, focused interventions proposed here. Finally, interventions aimed at high risk subgroups (e.g., nurses, adolescents) and presently lower risk subgroups (e.g., Hispanic and Asian females) will be encouraged.

Glynn is the project officer.

Title: Cancer communications systems research. Estimated annual budget, $200,000 first year, $300,000 second, $500,000 third. Five to 10 awards funded by cooperative agreements.

The goal is to identify, develop, implement, and evaluate cancer communications research projects targeted at specific audiences and utilizing the resources of the Cancer Communications System. These research projects shall include innovative ways to reach specific target groups with cancer information and an assessment of its impact on their knowledge, attitudes, and/or practices. Projects may be designed to assess the impact of the CCS on cancer incidence, morbidity, and mortality. All research shall have the long term objective of contributing to the NCI goal of reducing cancer mortality rates by 50 percent by the year 2000. Contributing toward this goal would not preclude the development of research projects related to cancer prevention.

Since 1976, the Cancer Communications Network has been funded by NCI to disseminate accurate, up to date information about cancer to the general public, cancer patients and their families and health professionals. This information has been disseminated through the Cancer Information Service, which is a telephone information service, and through educational and informational activities carried out in specific areas of service. Over the years, the CCN has been established as a resource, both locally and to NCI. Individuals who are trained and experienced in cancer information dissemination staff the regional offices of the program. The expertise currently exists in these offices to market and promote cancer information.

In addition, a huge data base is available, both locally and nationally, to use as a research resource. This data base consists of information from two primary sources. A centralized reporting form is used to document all inquiries to the CIS. This form includes information on caller demographics, site and nature of the inquiry, behavioral suggestions made, and the method by which the caller found out about the program. Data from this call record form are available both regionally and nationally. In addition, a survey of CIS users is ongoing. This survey provides information on the health behavior of CIS users as well as their perceptions of the program.

The CCN program has been modified based on the recommendations of an advisory committee and is now being reissued as a contract.

One of the program objectives of the CCS is to serve as a resource for the development and/or implementation of peer reviewed studies for cancer communications research. Limited research has been done in the area of cancer communications research. The extent to which cancer communications can affect the knowledge, attitudes, and practices of individuals is an area which allows for much further investigation. Using the resources available through the CCS, it will be possible for investigators to initiate research that can meet measurable objectives.

Investigators should propose cancer communications research projects which utilize the resources of the CCS (e.g., CIS data, staff expertise, other educational/informational activities). Research

topics can emanate from the CCS or from independent investigators. Each project should contain the elements listed below:

a. A problem analysis. What is the specific question being addressed by this research project? Why is it a useful and important problem to study? Why has the specific target group been chosen for this project?

b. Specific goals and measurable objectives for the project.

c. A project description, including the research plan, methodology, and evaluation.

d. A qualified staff which is capable of planning, implementing and evaluating the research project.

e. Organizational, administrative and institutional procedures, commitments and support.

Some examples of CCSR projects might include, but not be limited to, the following:

*A comparison of CCS users and nonusers in areas such as information seeking and/or health behavior.

*Studies on the diffusion of cancer information by CCS users.

*Studies on the link between cancer knowledge and cancer related behavior.

*The effect of followup reminders on the health action of CCS users.

*Studies on the use of CCS volunteers as community opinion leaders.

*Studies on effective transfer of cancer information through networks of community organizations and the resulting impact on health behavior.

Offerors may also propose new data collection activities for the CCS and/or design studies comparing public knowledge, attitudes and/or behaviors by region, ethnicity, rural vs. urban, etc. Utilization of CCS resources may involve a single office, a region of the country, or the entire CCS network.

Judith Stein is the program director.

Title: Cancer control technical development in health agencies. Estimated total cost per year, $1,260,000 for three five year awards funded by cooperative agreements.

Objectives are:

A. To improve the cancer control scientific and technical expertise available to state and local health agencies for planning, implementing, and evaluating cancer prevention and control programs.

B. To determine the feasibility of utilizing health agencies with expanded cancer control capabilities to stimulate the development of coalitions to promote cancer control programs in accordance with cancer control science and the year 2000 cancer control objectives.

C. To evaluate whether enhancement of technical capabilities can stimulate major improvements and expansion of existing cancer control programs by health departments; and establishment of new, self sustaining cancer prevention and control programs and coalitions.

This project proposes to enable health agencies at state and local levels to plan, implement and evaluate cancer control programs by improving expertise and through the establishment of working relations with other organizations that have expertise related to cancer control. NCI support will provide for access to technical and scientific expertise and program planning and evaluation. Health agencies will provide the funds for operating and providing the cancer control programs. Applicants will be required to have access to the following expertise:

*Risk factor control--smoking prevention and cessation; dietary modification and control; occupational/environmental containment; secondary prevention through earlier detection.

*Scientific and program management expertise--needs assessment, including establishment of a baseline of existing cancer control programs and identification of cancer control opportunities in accordance with the year 2000 objectives; determination of appropriate cancer control methods according to cancer control science; experience in the conduct of community intervention studies with reference to the application of cancer/chronic disease control methods, including statistical and epidemiological resources; approaches in coalition building and networking required to mobilize available resources for cancer control; methods and approaches to stimulate community interest in cancer control, including social and communications sciences.

*Education and training expertise--capabilities in training health agency personnel in cancer control sciences and relevant public health disciplines.

Applicants will also be required to initially, propose interventions in at least one of the following areas: smoking (cessation and/or prevention); diet (fat or fiber); early detection (breast mammography/physical exam and/or cervical); and expand to other areas as capabilities develop; demonstrate the availability of local resources to implement programs; indicate relationships with major NCI supported programs (e.g., centers, CCOPs, SEER).

NCI and health agencies will cooperate in defining specific objectives and expectations for each year of award; determining specific intervention objectives and priorities as new cancer control research results emerge; establishing protocols for specific interventions; developing methods to track cancer control programs.

Knut Ringen is the project officer.

In Board discussion of this proposal, Erwin Bettinghaus said the Board committee's discusion consisted of "three to four hours of argument. There was never any question of the value of NCI helping state agencies with technical support. My objection was that I didn't think we should set up a power broker. This program is to advise state agencies that NCI help is available, and by the way, if we help you, you must help other agencies in our state or region."

"I would suggest we eliminate the number this is limited to," Robert Day said. "If they are in place with the skills, and can do it and do it well, let's let peer review determine the number that should do it. If there are more good ones than we have

provided for, you can come back for more money."

Lewis Kuller insisted the program should be directed "to state or county health departments. Too often, an agency can be a local cancer society, or PRO, or state medical association. They box out the health departments. If this program is intended to strengthen state and county health departments, say so up front. Anybody and his brother can say he's a health agency."

DCPC Director Peter Greenwald said he would be happy to limit the program to state and county health departments. But Day said, "If you really want to go after cervical cytology, you wouldn't go to state health departments, you would go to Planned Parenthood. Many county health departments have delegated that to Planned Parenthood. For smoking prevention, you might want to focus on the schools, the state department of education or school districts. I would opt for flexibility, and let it rest with peer review."

"If the goal is to strengthen health departments, then you need to direct it to them," Kuller said. "If you go to school districts, then you haven't accomplished a damn thing."

"I missed the point that the goal is to strengthen state health departments," Barbara Hulka said. "I thought the goal was reduction of morbidity and mortality of cancer. I much prefer the plural approach."

"We need continuity," Kuller said. "The only agency with continuity is the state health department. If you go to others, as soon as NCI pulls out, that's the end of it."

Bettinghaus explained that the concept proposal was generated by the fact that state health departments are starting to get state and local money for cancer control, and that they need some assistance in planning and carrying out programs to use it. "I can imagine there are areas where state health departments don't have that responsibility and funds, so you may want to consider extending this help to other agencies."

Board Chairman Lester Breslow recommended that the RFA include language stating that the program was intended to be "in cooperation with state and local health departments. They would not have veto power, but this would accomplish what we are after."

The Board agreed to include that language and to remove the limit on numbers to be funded, leaving that to peer review, approving the concept unanimously.

Title: Selected cancer prevention clinical trials. Estimated annual total budget, $4 million for six five year awards funded through cooperative agreements.

Goals and major objectives are to stimulate development and submission of a number of investigator initiated risk reduction clinical trial proposals to assess interventions with preventive agents and/or diet in cancer prevention.

A number of compounds and/or dietary components have been associated with the inhibition of carcinogenesis in animals and other test systems or have been associated with reduced cancer incidence in epidemiological investigations.

Results from animal studies using whole animals and cultured cells suggest that a number of these compounds and/or dietary components affect the later stages of carcinogenesis. They are therefore particularly suitable for evaluation in controlled clinical trials where reduction in risk might be measurable within five years. Clinical trials are the only method to confidently address the question of effectiveness and safety of preventive agents and diets in humans.

This would be a followup to earlier RFAs released in 1982, 1983 and 1984 which had requested grants, and then later, cooperative agreement proposals in this area. Over 100 applications were received and 17 studies have been funded. Of the approximately 30 applications received in February 1984, those with fundable priority scores will be awarded in late spring or early summer 1984. This current RFA is directed primarily to intervention studies at selected sites or with selected preventive agents. Studies of populations at risk to bladder, breast, colon, and head and neck cancers are particularly appropriate at this time. A number of investigators who experienced difficulties with access to inhibitory agents, high risk groups, and/or clinical chemistry monitoring capabilities are now in a more favorable position to apply and consequently a number of high quality applications can be expected.

Several trials involving skin and lung cancer risk reductions with carotenoids and retinoid compounds have been implemented and additional studies at these sites with the agents indicated are not encouraged at this time.

Studies of populations at increased risk to colon, breast, bladder, and head and neck cancer are particularly appropriate at this time. A veriety of investigations appears appropriate.

Recent reports suggest that susceptability to colon cancer may be related to high dietary levels of protein (meat) and/or fat, elements of which may be converted during digestion to initiators and promoters by altering the composition of bile acids and cholesterol metabolites. Fiber and vegetables are thought to be anticarcinogenic diluting the fecal mass and possibly contributing to anticarcinogenic enzyme activity. Other factors including intestinal flora and bile acids, consumption of carbohydrates especially sugar, increased oxidase production, and low roughage in the diet may also contribute to cancer of the colon.

Dietary excess of fat may also be related to cancer of the breast. Modification of carcinogenesis and tissue proxidation by selenium and dietary fat have been reported in animal models. Intervention studies of breast or colon cancer incidence by dietary modification or supplementation are relevant to this request.

Studies of occupational cohorts who have been exposed to known initiators and/or promoters are encouraged. Situations where the dose response to the promoter can be estimated are particularly relevant. Other high risk cohorts might be candidates for intervention studies. For example, organ transplant patients are at high risk to cancer. Azathioprine and adrenal corticosteroid hormones

were widely used in the past for kidney transplant patients and cyclosporin A has been used recently. Non Hodgkin's lymphoma is the most common type of cancer in these patients and risk is 32 times. The lymphoma often arises rapidly within a year or two after the transplant and often develops in the brain, an unusual site for this type of cancer. Skin cancer, Kaposi's sarcoma, and lung cancer also occur at higher rates among this group.

Another category of possible prophylactic trials involve studies of populations at risk to second malignancies. Several examples are presented as follows: a number of studies have reported that Hodkin's disease patients treated with alkylating agents have an incidence of leukemia. The risk of leukemia after treatment of Hodgkin's disease has continued to increase, especially among patients who received both MOPP and radiation therapy.

Alkylating agents used to treat other cancers have also been linked to second cancers at other sites. Epidemiologic studies have reported a 100 times increase in AML among multiple myeloma patients after melphalan was introduced. A recent survey of women treated for ovarian cancer showed that melphalan and chlorambucil increased the leukemia risk in a dose response fashion.

The risk of acute leukemia has also been shown to rise after use of alkylating agents to treat lung cancer, polycythemia vera and non Hodgkin's lymphoma. Methyl CCNU, used to treat cancers of the stomach, colon, and rectum was recently shown to increase a patient's risk of developing leukemia by 16 fold. Most surveys of chemotherapy related second cancers have focused on leukemia because it develops within four to five years after exposure.

Several additional examples are presented. A study of interferon in reducing cervical dysplasia and hepatitis B vaccine in reducing liver cancer risk in certain exposed populations are problems of relevancy.

Other proposals of interest will be considered.

Applicants will develop their research protocols in accordance with their individual strengths and interests. The research protocols should in general follow the format of the NCI prevention program protocol outline. The NCI core data questionnaire should be utilized for data collection and analysis. NCI staff will be involved in the approval of the protocol, in the safety aspects of the study, in obtaining investigational new drug permits from the Food & Drug Administration, and in the quality assurance aspects of the clinical laboratory procedures.

Winfred Malone of the DCPC Chemoprevention Branch and Ritva Butrum of the Diet & Cancer Branch are project officers.

The remaining concepts approved by the Board will appear in next week's issue of **The Cancer Letter.**

RFPs AVAILABLE

Requests for proposal 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. 20205. 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-CN-45179-50
Title: Evaluation of chemoprevention agents by in vivo screening assays
Deadline: Approximately July 22

The required services will be defined by master agreement orders issued during the period of performance. Pursuant to master agreement orders the contractor shall conduct in vivo screening studies in laboratory animals (primarily rats and mice) using gavage and other routes of administration to administer designated chemopreventive agents in animal models using any carcinogenic mechanism (that is consistent with the evaluation criteria) such as the administration of carcinogens, promoters, hormones, irradiation, cells, or other carcinogenic agents.

This research will be provided under cost reimbursement and/or fixed price master agreement orders. Offerors will not be considered eligible for award unless they can conduct specific individual master agreement orders in accordance with FDA Food Laboratory Practice regulations in facilities that are fully accredited by the American Assn. for Accreditation for Laboratory Animal Care.

The contract period will be three years.

Contract Specialist: David Monk
RCB Blair Bldg Rm 2A07
301-427-8745

NCI CONTRACT AWARDS

TITLE: Synthesis of selected chemical carcinogens
CONTRACTORS: Midwest Research Institute, $607,570, and SRI International, $586,131.

TITLE: Incidence and patient survival date for the State of Connecticut SEER Program
CONTRACTOR: Connecticut Dept. of Health, $599,464.

TITLE: Current cancer research project/protocol analysis center (CCRESPEC)
CONTRACTOR: Andrulis Reseearch corp., Bethesda, Md., $3,059,664.

The Cancer Letter _Editor Jerry D. Boyd
Published forty-eight times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter.