THE CANCER LETTER

Vol. 9 No. 7
Feb. 18, 1983

Subscription $125 year North America
$150 year elsewhere

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CCOP REVIEW COMPLETED, ENOUGH GOOD APPLICATIONS IN FUNDING RANGE TO GET VIABLE PROGRAM STARTED

The three ad hoc committees organized to review the 191 Community Clinical Oncology Program applications completed their work last week, wrapping up what probably was the most massive review job on a single grant program in the history of NIH.

The result: There were enough good applications in the fundable range to get CCOP off the ground and make it a viable program.

The precise number of CCOPs that will be funded will not be known until NCI completes negotiations with the centers and cooperative groups involved as research bases on costs of that service. Also still to

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In Brief

COMPREHENSIVE CENTERS "JEWEL IN CROWN" OF CANCER PROGRAM, DEVITA SAYS; BOUTWELL NEW NCAB MEMBER

"COMPREHENSIVE CANCER centers are a jewel in the crown of the National Cancer Program," NCI Director Vincent DeVita said at the dedication of the $37 million Kenneth Norris Jr. Cancer Hospital & Research Institute of the Univ. of Southern California. The Norris is a nine story, 158,000 square foot structure which includes 60 beds for cancer patients on two floors, surgery suites, clinical laboratories, three floors of advanced research labs, an outpatient clinic, day hospital, facilities for diagnostic imaging and radiation oncology, and administrative headquarters of the USC Comprehensive Cancer Center. The facility was built with a $12 million construction grant from NCI and $25 million in private funds, including $5 million from the Norris family. Kenneth Norris is chairman of the hospital board and a USC trustee. . . . **KENNETH OLDEN**, associate director for research at Howard Univ. Cancer Center, has been promoted to deputy director. He replaces **CARRIE HUNTER**, who resigned both as deputy director and associate director for clinical activities. **ELLIOTT PERLIN** was named acting associate director for clinical activities. **JACK WHITE** is director of the center. . . . **ROSWELL BOUTWELL**, professor of oncology at McArdle Laboratory, Univ. of Wisconsin, is the new member of the National Cancer Advisory Board. He will fill out the term of Gerald Wogan, who resigned last year; that term will expire in 1984. . . . **DENIS PRAGER**, an assistant director of the White House Office of Science & Technology Policy who has been OSTP's representative on the National Cancer Advisory Board, will be leaving his job soon. No replacement has been announced. . . . **NCI HAS STARTED** recruiting a new chief of the Research Contracts Branch, a GS 15 position. That job became vacant when James Graalman was reassigned, an action he has formally appealed. Candidates for the position, a supervisory contract specialist, will be considered from anywhere in the country. Robert Namovicz, NCI deputy executive officer, has been acting chief of the branch.

CCOP REVIEW: THE MONEY WILL RUN OUT BEFORE THE GOOD APPLICATIONS DO

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be negotiated are indirect costs. The amount required for research base and indirect costs will come out of the $10 million NCI has earmarked for the entire program, with the remainder available as direct costs to participating CCOPs.

Best guess now is that at least 40 to 50 CCOPs will be funded, more if research base costs can be held to a minimum. Another factor will be how many of the applications in the fundable range were from the larger groups with the bigger budgets.

There may have been as many as 100 applications of sufficient quality to merit support, but the $10 million probably will have been spent before that number is reached. "We probably will run out of money before we run out of good applications," one NCI staff member said.

Program staff in the Div. of Resources, Centers & Community Activities and staff of the Div. of Extramural Activities who managed the review were impressed by the zeal and conscientiousness of the ad hoc committee members. The three committees were chaired by experienced hands—David Ahmann, Virgil Loeb and Charles Spurr—but many of the members were community physicians and hospital administrators who had never participated before in an NIH review.

The committees gathered in Bethesda the evening of Feb. 9 for their final meeting, worked late Feb. 10, wrapped up the review Friday, Feb. 11 and were packed and ready to leave when the Washington area's worst snowstorm in history left them marooned in their hotel. Few were able to leave for at least another 24 hours.

Dorothy MacFarlane, executive secretary to the Cancer Clinical Investigation Review Committee, supervised the three ad hoc committees with the help of three former executive secretaries called out of retirement. MacFarlane and other DEA staff handled the monumental task of processing the 191 applications and all the paperwork involved, did it smoothly and kept the review on schedule. They now must write the summary statements which will go to the National Cancer Advisory Board in May.

Robert Frelick, DRCCA project officer for CCOP, combed through the applications before the review and came up with this breakdown, which he presented at the recent meeting of the Assn. of American Cancer Institutes:

There were 1,652 components—hospitals and physician offices—in the 191 applications, 541 of them hospitals. Forty-nine applications had one component, 94 had two, 36 had from five to 10, and 10 had more than 10. Three were statewide consortia.

There were more than 3,000 physicians participating, including 2,400 medical oncologists. Some applications listed radiotherapists and surgeons as principal investigators.

The average medical school graduation date for participating physicians was 1965, "which reinforces our assumption that now we have enough well trained young oncologists to carry out this program," Frelick said.

Participating hospitals have a total of 197,000 beds and see 330,000 new cancer patients a year, a significan portion of the 800,000 plus in the U.S. diagnosed each year with cancer.

Seventeen cooperative groups were listed as research bases, some by only one applicant and one by 61 applicants. Thirty centers were listed as research bases, with from one to 10 applicants each. The projected number of protocol cases that would be available for studies totaled 22,000.

"I have the impression that if the program stopped tomorrow, we would already have improved communications between the communities and the centers," Frelick said.

"What about the research bases themselves? What if they received 5,000 plus new patients a year from the program? Do they have the staff capable of handling that many and monitoring them? We asked for estimated costs in the applications. The response was from zero dollars to over $1,200 per case.

"Some CCOPs had very sophisticated data management plans; others seemed not to know what we were talking about."

On the issue of quality control, Frelick said that DRCCA staff will make annual site visits to each CCOP and research base. "We anticipate that institutional review boards will be in order. Initially, no CCOP will be funded without an operational IRB. We will ask research bases for an annual report and their own evaluation of the status of members."

TREND SEEN IN CENTERS TO INTEGRATE CANCER CONTROL SCIENCE WITH SERVICE

Cancer control researchers from 25 cancer centers participated in the "Progress in Cancer Control" conference held recently in Bethesda, the third such meeting coordinated by the Assn. of American Cancer Institutes, the Assn. of Community Cancer Centers, and Roswell Park Memorial Institute.

Focus of this meeting was on cancer control research activities in centers. Curtis Mettlin, conference organizer, said the proceedings "reflected the trend in cancer centers to integrate science with service in their cancer control activities."

Presentations at the meeting included:

- A report from Anders Englund, executive director of the International Union Against Cancer (UICC), on a demonstration of the interaction of cancer institutes and national data bases in Sweden in monitoring cancer risks in the workplace.

"The role of the cancer centers in the prevention of occupational cancer diseases lies both in primary and secondary preventive steps," Englund said. "The active use of health records established during the normal medical procedures can serve as an effective tool in risk identification. In a similar fashion, the results of preventive actions taken can be monitored. Although early cancer detection programs for most applications still have failed to show their value, certain occupationally exposed subpopulations with a high risk might benefit and a cancer center would in such cases be well suited to supply the most advanced diagnostic facilities."

• Findings at Roswell Park that teaching of breast self examination in that institution's prevention-detection center improved breast lump detection skills over randomized control groups instructed by other modalities.

Annlouise Assaf reported that the study population consisted of 388 adult women participating in a randomized clinical trial of BSE training methods. Each woman returned to the clinic for a followup interview three months after her initial visit. BSE frequency was defined as the number of times per month that the woman reported practicing BSE in the three months following her initial clinic visit. BSE technique was determined by having the interviewer observe and record the steps used by the women examining silicone breast models with simulated breast lumps of varying sizes. The number, location, and size of the breast lumps found by each woman was categorized as detection accuracy. Results indicate that ability to find lumps of varying sizes in a breast model is more closely associated with BSE technique than with frequency of BSE practice.

• A retrospective study reported by Condict Moore of Louisville indicating a significant survival advantage for squamous cell oral cancer patients whose treatment plan evolved from multiple modality consultations vs. comparable patients whose treatment planning involved only a single modality.

"We often hear that the first treatment specialist has the best chance of curing the cancer patient," Moore said. "We feel this should be amended in today's multimodality therapy climate to read: planning from multiple modality treatment consultations before the first treatment offers the best chance of curing the patient. A study of a homogenous group of squamous cancers of the oral cavity forms the basis for this opinion. One hundred and thirty-six mouth cancer patients were analyzed retrospectively. They fell into two groups: a) those whose treatment plan evolved from multiple modality consultations; b) those whose treatment plan arose from a single modality. Analyzed for disease free survival by stage, a 20 percent advantage appeared for the group that has pretreatment multiple modality consultation. This result seems to support in general the second opinion approach, while specifically supporting the concept that in head and neck cancer multiple pretreatment opinions, from different specialties, particularly surgery and radiotherapy, confer a real advantage."

• A report on the role of the preventive medicine clinic at M.D. Anderson in carrying out clinical and epidemiologic studies of AIDS and Kaposi's sarcoma victims.

"During the last two years an increase in Kaposi's sarcoma (KS) and opportunistic infections (OI) has been reported," Guy Newell said. "These have since been found to be the sequellae of a defect in cellular immunity now called AIDs. Although initial reports were among young homosexual males, other groups with different lifestyles are being affected. We have studied over 120 subjects who volunteered for our preventive medicine clinic. Workup includes complete medical history and physical by one of us (Newell or P.W.A. Mansell), complete immunologic evaluation (by Evan Hersh), plus virologic studies and a detailed personal and lifestyle questionnaire. Among this group, 20 percent have no disease or subclinical disease, and fully 80 percent have measurable immune cellular deficiency manifest by clinical prodrome (45 percent), prodrome plus OI (25 percent), and KS plus or minus OI (10 percent). We have treated 15 cases of KS in 10 months. Suspected causes include viruses (CM, EBV, other herpes, retro, etc.); chemicals (nitrites, marijuana, cocaine, etc.); common infections (IM, hepatitis B, amoeba, etc.); multiple sexually transmitted diseases, and perhaps elements of sexual practices. The transmissability of the syndrome from person to person is not known, although suspected. The public health and scientific implications of understanding the causes are enormous."

• An analysis of the American College of Surgeons' recent survey of breast cancer. Charles Smart reported that those data showed a reduction in the number of patients treated by radical surgery, an increase in the reported use of the modified radical operation, and the apparent increase in five year survival of breast cancer patients between 1972 and the 1976 survey data.

Smart also noted that with the ACOS hospital cancer approvals program, involving nearly 1,000 hospitals which treat 60 percent of all newly diagnosed cancer patients in the U.S., the organization is in a unique position to do research on cancer control.

DCCP BOARD APPROVES CONCEPTS OF NEW GRANTS TOTALING $1.4 MILLION A YEAR

The Board of Scientific Counselors of NCI's Div. of Cancer Cause & Prevention last week gave concept approval to new grant supported research with an estimated $1.4 million in first year awards and to new and recompeting contracts worth an estimated $808,000 in first year awards.

One of the new grant programs is designed to stimulate virological studies of acquired immunodeficiency disease syndrome, at a cost of $1 million a year.

The Biological Carcinogenesis Branch of DCCP proposed to issue a request for applications to solicit R01 grant applications in virology/AIDS research. The Board's motion to approve, offered by Gilbert Omenn, directs that the awards be in the form of cooperative agreements, to permit greater DCCP staff participation; asks that the National Institute of Allergy & Infectious Diseases be brought into the project; and asks that safety officials from NIH and the Centers for Disease Control be consulted on biocontainment.

The staff narrative justifying the RFA:

Acquired immunodeficiency syndrom (AIDS) is a new disease which was first reported in 1981. There are now over 950 documented cases. Although first reported in promiscious homosexual males, the AIDS disease now includes both homosexual and bisexual males, heterosecual intravenous drug users, hemophilia patients, Haitians, some infants, and apparently normal heterosexuals of both sexes. In addition to disorders of immunological function, approximately half of the AIDS victims suffer from pneumocystis carinii pneumonia and about one-third of them have Kaposi's sarcoma (KS) or lymphomas. The mortality rate is near 40 percent overall, but closer to 85 percent for cases diagnosed early on in 1981. The long term prognosis for frank cases is very poor.

The recent involvement of hemophiliacs, apparently normal children, and some common epidemiological features now suggest a blood borne, venereal, or close contact transmissible biological agent as the causative factor. Two viruses, human cytomegalovirus (HCMV) and Epstein-Barr virus (EBV), have already been linked with AIDS, KS, and lymphomas. Human cytomegalovirus has been associated with KS by at least one molecularly oriented study of KS tissue, and Epstein-Barr virus determined nuclear antigen has been demonstrated in tissues of several AIDS patients with a Burkitt's-like lymphoma. Several viruses have already been associated with certain human cancers. There is the etiological association of EBV to nasopharyngeal carcinoma; the wart viruses with malignancies of the skin, cervix and anus; HCMV with KS; human T-cell leukemia-lymphoma virus (HTLV) with several malignancies; and the recent advances in the study of cellular and viral oncogenes relative to cancer induction. All these advances indicate that there is a rational basis for initiating systematic efforts to search for the transmissible agent responsible for the AIDS syndrome.

The purpose of this RFA is to stimulate studies aimed at a direct virological approach to the problem. It is designed to encourage studies on the search for, the isolation, and the characterization of the viral agent(s) which may be the primary causative factor in AIDS and KS. The studies proposed should encompass not only the classical virological methods of tissue culture, animal inoculation and serology, but also the contemporary technologies of viral immunology, cytogenetics, and molecular biology. Since HCMV and EBV, both transforming viruses, have been implicated in immune suppression and in association with KS and lymphomas, definitive studies of HCMV and EBV and their relationship to AIDS and KS may be considered as pertinent to the objectives of the RFA. However, projects involving either or both RNA-core or DNA-core viruses are encouraged. Examples of the types of studies that might be appropriate include: 1) direct in vivo and in vitro efforts at isolation, identification and characterization of the causative particular virus; 2) analysis of human tissue with appropriate tests indicative of the presence, state of integration, and chromosomal location of viral or pro-viral DNA; 3) recognition and identification of marker antigens of pathognomonic significance; 4) cytogenetic analysis for chromosomal changes that relate to disease induction; and 5) in vitro search for direct morphological transformation of appropriate target cells. Because of the changing nature of AIDS and the importance of prevention of the syndrome, applications for research on the development of an appropriate vaccine would also be welcomed should a viral agent be identified in the interval between initiation of this RFA and the time for receipt of applications.

Board member Marcel Baluda pointed out that there are now no "clear cut guidelines for biocontainment. I'm concerned about possibly funding some amateurish applications. I think we should insist on controls, be specific, and not leave it up to the individual investigators."

"Details on planning for containment should be in the RFA," Nicholas Petrakis said. Myron Essex suggested that CDC's expertise in biocontainment could be tapped.

DCCP Director Richard Adamson commented that NCI has been expecting traditional R01 to study the relationship of viruses to AIDS, "but they have not come in." Program Director Jack Gruber said that at present, there is only one such R01 in all of NIH. He said he hoped to be able to fund as many as six or eight grants from the RFA, but that depends on the nature and quality of applications. NCI will set aside $1 million to fund the grants in the first year, if enough high quality applications are submitted.

The Board agreed to expand an RFA it had approved last September with an earmark of $500,000 in first year funding to $900,000. That money would support research in hepatitis B virus and primary hepatocellular carcinoma and biological investigations of virus host interactions and mechanisms and causation of human cancer.

The need for the additional estimated $400,000 developed when, in writing the RFA, staff felt the program could be expanded to include a model system, cell culture, and possible chemical involvement in the etiology of the disease.

Baluda said that with the development of a vaccine against HBV, "the solution may be in sight," and suggested that is why there are only two current R01s in this area.

Essex said he disagreed that the vaccine will eliminate HBV "in the foreseeable future. It is a latent virus, and the cost of the vaccine is high."

Board Chairman Peter Magee suggested another aspect of the problem, that afflatoxin may be implicated in the etiology of the disease.

The Board approved the expansion unanimously.

Staff narrative:

Currently, epidemiological investigations link hepatitis B virus infections with primary hepatocellular carcinoma in man. This linkage was discussed at an NCI conference on hepatitis B virus and primary hepatocellular carcinoma held on May 3-4, 1982. The consensus of the attendees at that meeting was

that hepatitis B virus was the best model in humans of a specific agent related to a specific cancer. In addition it was felt that there was a lack of understanding of the biological mechanisms for the diseases processes attributed to hepatitis B virus and that all of these mechanisms are worthy of further investigation.

The intent of this RFA would be to encourage research to determine: (a) whether or not hepatitis B virus is a complete carcinogen in humans; (b) the molecular mechanisms underlying the interaction of the virus with hepatocytes in human and animal model systems; (c) the characteristics of model systems already developed in terms of their suitability for studying the development of hepatocellular carcinoma and establishing their relevance, if any, to human disease; (d) the gene products of the hepatitis B virus in terms of their function and whether any of the gene products are transforming proteins.

The following representative research is projected: (1) studies to determine whether or not the hepatitis B virus is a complete carcinogen in cultured human liver cells or in animal model systems; (2) investigations on the mechanism(s) of oncogenesis by HBV including the role of integrated DNA in transformation, examination of virus coded proteins for transforming potential and development of in vitro model systems for transformation; (3) studies on the progression of acute hepatitis through chronic hepatitis to primary hepatocellular carcinoma, including studies on why tumors develop in only a limited number of individuals infected with the hpeatitis B virus (possible host determinants of the process) and on the mechanism(s) by which chronic infections are maintained in the immunologically competent host; (4) studies on the cytopathology of the disease to shed light on the mechanism of liver damage, e.g., to determine whether virus replication, naural killer cells, cytotoxic T cells or other mechanisms might be involved.

These studies should provide the biological equivalent of the very strong epidemiologic evidence which now links hepatitis B virus to primary hepatocellular carcinoma in man and should also provide objective criteria for the evaluation of present and future vaccines which may be useful in the prevention of this disease.

The Board approved the following competitive contract concepts:

Cancer risk in women irradiated for benign gynecological disorders. Three years, estimated total cost $300,000 per year for multiple awards. The narrative:

Studies of populations exposed to ionizing radiation are conducted by the NCI epidemiology program to strengthen the quantitative basis for risk estimation, to improve understanding of the role of host and environmental factors that influence the dependence of cancer risk upon dose, and to provide insights into carcinogenic mechanisms. Between 1930-1960 it was not uncommon for women with endometrial hyperplasia and other benign gynecological disoders (BGD) to have their ovaries irradiated to control dysfunctional uterine bleeding. An investigation of such women treated with intracaviary radium, external beam x-ray, or both will provide risk estimates for cancer of pelvic and abdominal organs, sites that have not been well characterized for radiation risks, at dose levels much lower than those received by cervical cancer patients under study by our program. Further, any risk of radiogenic leukemia in BGD will be compared with the rather low risk associated with much higher exposures in cervical cancer patients. The unexpected reduction in breast cancer risk previously associated with radia tion for BGD in women past the age of menopause will be also evaluated as well as any modification of risk by host factors.

This study will investigate the dependence of cancer risk on variation in dose, radiation quality, and age at exposure. This study should provide dosimetric data for evaluating excess cancers of pelvic and abdominal organs and thus provide accurate risk estimates for sites where little information exists. Unique dosimetry resources developed under our program are available. This study should also help to clarify the paradoxical finding of increased leukemia risk associated with low dose but not high dose exposures to the pelvic bone marrow, and thus may provide further insight into the mechanism of radiation leukemogenesis.

Objective: To determine cancer incidence and mortality and estimate the risks of radiation-induced cancer in women treated for BGD.

Methods: A study size of at least 6,000 exposed women should be sufficient to provide adequate statistical power to detect and evaluate dose-response relationships for radiogenic leukemia and solid tumors. Therapy usually involved 600-800 rads to the ovaries, and bone marrow doses have been estimated to range between 70-190 rads. Estimates to other organs range between 25-400 rads. Our existing dosimetry program for cervical cancer can be adapted to estimate organ doses for this study. It is estimated that approximately 30 excess leukemias will be observed and 220 excess cancers of heavily irradiated sites such as the uterus and colon. Women irradiated between 1930-1960 would be included for study.

Currently, NCI is collaborating with the Karolinska Hospital, Sweden, in a study of 1000 exposed and 1500 non-exposed women treated for BGD. An additional 5000 exposed women have been identified in New York, Massachusetts, and Connecticut. We anticipate issuing a competitive RFP, and will consider multiple awards. Medical, therapeutic, and followup information would be abstracted from medical records. Death certificates would be obtained for those who died, and questionnaires sent to those lcoated alive. Mortality analyses will be made, and we are also planning comparisons with Connecticut population rates of cancer incidence, and with women treated without radiation for BGD if a large enough cohort of unexposed women can be assembled. Organ specific radiation doses will be determined for individual BGD patients.

Case control study of colorectal polyps among pattern makers. Estimated total cost, $100,000 per year, two years.

Pattern makers construct prototypes for mass produced items such as automobiles, agricultural equipment, and other products. They may work with wood, metal, and plastic and may, therefore, come in contact with wood dusts, metal dusts, plastic fumes, epoxy resins, solvents, cutting oils, and paints. Concern over adverse health effects from these exposures arose in 1978 when a pattern maker notified his union about

CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY; RFPs, RFAs NOT YET AVAILABLE

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 only 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. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

an apparent excess of cancer deaths among his fellow workers. Subsequent epidemiologic investigations of pattern makers noted a twofold excess of colorectal cancer. In response to these findings, the Pattern Makers League (PML), Workers Institute for Safety and Health (WI), and employers of pattern makers initiated a cancer screening and educational program.

By December 1983 approximately 80 percent of the 10,000 members of the PML are expected to have completed the initial screening examinations, which include physical examinations (primarily designed to identify colon cancers and colon polyps), medical histories, and self-administered questionnaires covering diet, occupation, and tobacco and alcohol use. The physical examination includes a rectal exam and sigmoidoscopy, stool guaiac test, complete blood count, urinalysis, lung function tests, and chest x-rays. Results from these tests are made available to the PML member and his/her personal physician.

Data from this comprehensive screening program provide an opportunity to investigate the role of occupational, dietary, and other factors in the origin of colorectal cancer and polyps. A study of colorectal polyps would be valuable for several reasons. First, it is widely believed that polyps, particularly adenomatous polyps, are precancerous lesions. Histopathologic characteristics provide the strongest evidence, although adenomatous polyps and colorectal cancer are also statistically associated with regard to geographic distribution, socioeconomic level, and time trends. Second, if polyps are precancerous lesions, then the time between first exposure to dietary, occupational, or other factors and appearance of polups will be less than the latent period for development of cancer. This may enhance our ability to identify and quantify poorly understood risk factors for colorectal cancer. Finally, most persons with polyps are asymptomatic and are less likely to have modified their dietary habits because of the lesion or therapy than are persons with cancer. Therefore, serum levels of micronutrients and subject recall are less likely to have been affected. This may counter one of the major methologic problems of case control studies. We anticipate that the number of cases of colon cancer will be quite small. However, to the extent possible we will compare characteristics of persons with colon cancer and colon polyps to determine whether or not the two diseases share similar etiologies.

A case control study is planned. Cases will consist of all pattern makers diagnosed with colorectal cancer or polyps through the WI screening program. Since women and minorities account for less than five percent of the PML membership, most cases are expected to be white men. In preliminary screening results from Detroit, the prevalence of polyps was 18 percent. If the prevalence of polyps in other areas to be screened were similar, approximately 1,400 polyp cases would be identified. The prevalence from Detroit is higher than commonly encountered and we will investigate whether or not this may be due to a rigorous examination that identified small lesions. Six cases of colon cancer were uncovered among the 1,200 pattern makers screened in Detroit, a number that was unusually high.

Controls will be PML members without colorectal disease, matched one to one to the cases of race, sex, and clinic of examination. Assuming an alpha level of .05 with 10 percent of the nondiseased population exposed to a causal factor, a study of 1,400 polyp cases and an equal number of controls would be able to detect a minimum odds ratio of 1.5 with 90 percent power, while a study of 700 polyp cases would be able to detect a minimum odds ratio of 1.7 with a power of 90 percent.

A two stage approach is planned. In the first stage, data collected by WI during screening will be analyzed to determine the prevalence of polyps (by age, anatomic location, size, histopathologic features) among pattern makers. Questionnaire data on occupational, dietary, and other factors will be compared among cases and controls to evaluate the role of these factors in the origin of polyps. A pathology review and industrial hygiene evaluation of workplace exposures will occur in this stage also. Slides or blocks of tissue from a sample of polyps will be obtained for a pathology review. If the diagnoses by the reviewing pathologists agree with those of the submitting pathologists, no additional review will take place; otherwise a full review of all cases may be required. All risk factor analyses will be related to specific histopathologic characteristics of these polyps. To obtain additional information on workplace exposures and to validate exposure information obtained from pattern makers, we plan to conduct "walk through" surveys of a sample of pattern making shops.

In the second stage, we will supplement the screening data by obtaining, on a sample of the cases and controls, more comprehensive information on occupational exposures and dietary patterns, and by taking blood samples to determine serum levels for lipids, vitamin A, vitamin C, vitamin E, carotene, selenium, zinc, and copper. It has been hypothesized that these micronutrients are associated with colon cancer in humans, but further clarification is needed. There is essentially no evidence, however, regarding the role of these factors in the origin of colorectal polyps.

The contract covered by this concept is for collection and analysis of blood drawn from a sample of the cases and controls. The specific cases and controls sampled for these determinations will be based on the results of the questionnaire and pathology analyses in stage 1. The WI has recently initiated a second round of screening in some geographic regions of the country. For efficiency and cost containment, we will attempt to recontact cases and controls during this second screen.

Support for this project will come from several sources. In general, screening and all aspects of the original data collection is supported by the WI, while supplemental data collection on the cases and controls will be supported by NCI. The WI receives support from several sources including NCI. The NCI support will be through professional service procurements, existing support service contracts, and new contracts. The major "new" funding from NCI will be for serum micronutrient analyses.

Board member Hilary Koprowski suggested that an effort be added to the program to find some antigens that might be predictive of cancer of the gastrointestinal tract. Joseph Fraumeni, director of the Field Studies & Statistics Program, agreed. Koprowski also suggested that "with use of innovative histochemistry, you might find out which polyps may turn into cancer and which not." Aaron Blair, project officer, agreed.

Omenn noted that access to occupational populations frequently is difficult. This proposal, in which DCCP by "piggybacking onto the WI study,. . . will be getting a high rate of participation. The suggestion by Hilary is extremely important."

The concept was approved, with the provision that some Board members be appointed to advise DCCP on the second phase of the study.

Inventory of union records systems. One year, $120,000. Narrative:

In order to carry out its responsibilities, the Industrywide Studies Branch (IWSB) of NIOSH must be able to identify and characterize worker populations exposed to agents being considered for epidemiological investigation. Union record systems (e.g., pension funds and benefit plans) can provide

valuable information when searching for appropriate study populations. However, there has never been an inventory of these record systems which documents and categorizes existing data. As an example of existing data sources, the International Foundation of Employee Benefit Plans (IFEBP) has a membership in excess of 4,000 benefit programs, the majority of which are sponsored by the AFL-CIO. The intent of this proposed project is to support a contract in developing an inventory of union data and specifically to:

1. Identify by name, address, and contact individual, the various member programs selected for the inventory.
2. Contact these programs and document pertinent information that would be useful in epidemiologic research, such as a description of the benefit program, size of the program, extent of information included in records, the time period covered by the program, and occupations or exposures that may be represented by the program.
3. This inventory of data will be delivered to NIOSH and NCI in a readily accessible form, e.g., computer tape or Wang diskette and the data will be made available to other researchers in the community at large.

Survey of compounds which have been tested for carcinogenic activity. This contract, presently held by Technical Resources Inc., will cost an estimated $285,000 in FY 1983. It will be recompeted for the 1984-86 fiscal years, with an estimated cost of $288,000 in 1984. Narrative:

This project and concept was presented to the Board of Scientific Counselors on Sept. 30, 1982. The survey, which has been published by PHS6NCI since 1951, covers a search of relevant journals (600-700 worldwide), reports, monographs, and books in several languages. Appropriate data are extracted, indexed and assembled in abstract form. The current concept covers extension of preparation and publication of this report for the years FY 84, FY 85 and FY 86. The prior years are in preparation and process of publication.

The Board gave approval of this concept for one year (FY 1984) with the proviso that a user survey be conducted to determine the effectiveness and needs for this report and whether current users would want these volumes if they had to purchase them. The Board requested that the results of this survey be brought back to the Board meeting in February at which time extension of the concept and funding for FY 85 and FY 86 would be contemplated.

Results of the survey were predictable: Most of those contacted said they needed the survey and relied on it; very few said they would pay for it. Adamson said that NCI could not on its own require payment for a government publication, that only the Supt. of Documents (Government Printing Office) could do that. The Board agreed to drop the idea.

The Board gave concept approval to the following noncompetitive contracts:

- Procurement of human blood platelets, two years, estimated cost $60,000 a year, with Community Blood & Plasma Service, Birmingham, Ala. This company already has a contract with NIH to supply blood products to the clinical center. DCCP needs human blood platelets for research in Laboratory of Chemoprevention.
- Application of Epstein-Barr virus markers to diagnosis and prognosis of NPC and occult tumors of the nasopharynx in the U.S., estimated cost $175,000 a year for two years. This is a two year extension of a contract with the Mayo Clinic.
- Radiation dosimetry for epidemiological studies, estimated cost $75,000 a year, five years. This will be a collaborative research interagency project with the Food & Drug Administration. NCI's contribution represents only a small part of the total cost.
- Followup study of women evaluated for infertility, estimated cost $100,000 a year for two years. This is an extension of a contract with the Mayo Clinic.
- Retrospective cohort mortality study. This is the project totally funded by the Air Force for a mortality study of civilian employees at Hill Air Force Base. The project originally was approved in 1981 and started in FY 1982 and is now being expanded. The existing contract with Westat for support services is being expanded from $606,000 to $901,000. The project also includes small contracts with the General Services Administration and the Mormon Church.

The Board postponed a decision on an RFA for experimental studies on natural inhibitors of carcinogenesis, with an estimated cost of $1 million a year for four years, when some members felt that the proposal as presented was aimed at active research areas which should not need further stimulation.

"I find this unattractive," Omenn said. "I don't believe you can cite inactivity. There are many such studies. I'm flabbergasted by this proposal."

The staff narrative written to justify the proposal listed a number of items that have been studied in animals as natural inhibitors of carcinogenesis which exist in food—various vegetables, fruits and seeds, and, recently, powdered green coffee beans, black tea leaves, and cocoa.

"The purified compounds (inhibitors) known to exist in food represent a chemically diverse set: organic isothiocyanates and thiocyanates, phenols, coumarins, terpenoid compounds, flavonoids, and indoles," the narrative said. "Vitamins C and E, and the vitamin A precursor, β-carotene, and selenium, known inhibitors of carcinogenesis, are of course constituents of foods. Macromolecular protease inhibitors such as exist in legumes which inhibit or retard the carcinogenic process, are also just beginning to be purified and studied. Finally, various sources and types of dietary fiber such as wheat bran and citrus pulp are known natural inhibitors in experimental carcinogenesis.

"Anticarcinogenic constituents in foods, and the foods themselves, have unknown potential for the inhibition of cancer in man. It should be emphasized that the studies performed to date indicate that these inhibitors are widespread in nature, of great chemical diversity, and are biologically effective in reducing cancer incidence and/or tumor burden in several species of experimental animals, many organ sites, against several categories of chemical carcinogens, and at several stages of the carcinogenic process. (Im-

portant recent work demonstrates that several natural inhibitors suppress carcinogenesis in the promotion phase, as well as their better known activities as blocking agents before and during initiation.) Furthermore, ascorbic acid and tocopherol act to inhibit both the in vitro and the in vivo formation of carcinogens. That these compounds have the possibility of being intrinsically nontoxic is also most significant. Some knowledge exists concerning mechanisms of action of these compounds with respect to effects on the activation of carcinogen metabolism and the induction of detoxifying pathways, and there is some knowledge of dose and schedule considerations as these relate to antineoplastic effects.

"All of this knowledge, however, is at a most rudimentary level, and most importantly, the full range of inhibiting substances present in foods, and their interactions, is virtually unexplored territory. Such knowledge is of critical importance not only from the standpoint of experimental chemoprevention of carcinogenesis, but also relative to the epidemiology of cancer prevention in dietary/nutritional studies. It is crucially important to expand studies on natural inhibitors of carcinogenesis in a broad spectrum of areas including the identification, isolation, purification, and characterization of preventive compounds, their mechanisms of action, assays for their identification, their preparation or synthesis in quantity, their pharmacological/toxicological properties, the conditions under which inhibition is demonstrable, the carcinogens, cocarcinogens, and/or promoters against which inhibition or suppression is demonstrable and the spectrum of tumors against which activity is seen. The objective of the proposed RFA is to stimulate further research in these areas with special reference to natural inhibitors of carcinogenesis."

Board member Pelayo Correa commented that it has been the consensus of workshops that the correlation of fruits and vegetables to the inhibition of cancer has been better than that of vitamins themselves. Edward Bresnick suggested that selenium and vitamin A precursers not be included in the RFA, since they already are being extensively studied.

Adamson said that the $1 million could fund as many as eight grants if they are close to the NIH average of about $120,000 a year for R01s. Board member C.C. Cheng said, "I wonder if four years is enough? Perhaps we could have smaller grants, for a longer time."

Board member Allan Conney said that the focus should be on foods with evidence from epidemiologic studies of a protective effect, such as the green and yellow vegetables.

The Board agreed to Adamson's suggestion to table the proposal until the May meeting, with a workshop to be convened in the interim to consider research needs in natural inhibitors.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs to the individual named, the Blair building room number shown, National Cancer Institute, 8300 Colesville Rd., Silver Spring, Md. 20910. RFP announcements from other agencies reported here will include the complete mailing address at the end of each.

RFP NIH-ES-83-8

Title: *Test for chemically induced transposition in drosophila*

Deadline: *Approximately April 15*

The National Toxicology Program, National Institute of Environmental Health Sciences (NIEHS), is soliciting qualified sources having the capability to develop a rapid screen methodology to detect chemically induced gene transpositions in drosophila melanogaster. Offerors should possess demonstrated proficiency and experience in drosophila genetics and molecular cloning techniques.

RFP NIH-ES-83-7

Title: *Drosophila mutagenesis testing*

Deadline: *Approximately April 8*

The National Toxicology Program is soliciting qualified sources having the capability to perform drosophila sex-linked recessive lethal and heritable translocation assays for detection of mutagenic and potentially carcinogenic chemicals. The successful contractors shall each be required to test approximately 80 chemicals over a four year period for mutagenicity using the sex-linked recessive lethal test and, if necessary, the reciprocal translocation test in drosophila melanogaster. Offerors should possess demonstrated proficiency and experience in the use of drosophila for detection of chemically induced mutations.

Above two RFPs:
National Institute of Environmental Health Sciences, Procurement Office
Attn: Hollis J. Hawkins
P.O. Box 12874
Research Triangle Park, N.C. 27709

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.