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DRCCA BOARD GROUP RECOMMENDS NO NEW NATIONWIDE SCREENING PROGRAMS UNTIL MORE RESEARCH IS DONE

A committee of the Board of Scientific Counselors of NCI's Div. of Resources, Centers & Community Activities has recommended against undertaking any new site specific nationwide screening programs following a review by the committee of breast, lung, cervical and colon cancer screening efforts.

"The reasons for this seemingly negative recommendation vary for different cancers and screening modalities," the committee said in its report. "The best established and most efficacious modality—the pap

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In Brief

HELLMAN SUCCEEDS PEREZ AS ASTR PRESIDENT, HANKS NAMED PRESIDENT ELECT; KLIGERMAN GOLD MEDALIST

SAMUEL HELLMAN, director of the Joint Center for Radiation Therapy at Harvard, assumed the presidency of the American Society of Therapeutic Radiologists at the Society's annual meeting last week in Orlando. He succeeded **CARLOS PEREZ**, director of the Div. of Radiation Oncology at Mallinckrodt Institute of Radiology. **GERALD HANKS**, Sacramento radiation therapist, was named president elect. . . . **MORTON KLIGERMAN**, ASTR past president and presently professor in the Dept. of Radiation Therapy at the Univ. of Pennsylvania, received the ASTR Gold Medal Award. One of the world's leading figures in the development of radiation treatment of cancer, Kligerman is particularly noted for his training of many of the present leaders in the field and for his work in testing pion beam radiation therapy at Los Alamos. . . . **MORE THAN** 1,900 attended the ASTR meeting, largest in its history. The organization also has an all time high membership at over 1,700. . . . **UNIV. OF SOUTH FLORIDA** in Tampa is building a $66 million cancer center, hopes eventually to win NCI recognition as a comprehensive cancer center. . . . **AWARDS PRESENTED** at M.D. Anderson's 26th annual Clinical Conference this week: **BERNARD FISHER** received the Heath Memorial Award "for outstanding contributions to the better care of patients with cancer." He delivered the Heath Lecture of "The Relation of Tumor Biology to Breast Cancer Management. **GIANNI BONADONNA** received the Jeffrey A. Gottlieb Memorial Award for his work with cancer chemotherapeutic drugs. His Gottlieb Lecture was entitled, "Operable Breast Cancer: The Challenge of Adjuvant Chemotherapy." **PAUL ROSEN** received the Joanne Vandenberge Hill Award for his work on the pathology of breast cancer and delivered the William O. Russell Lecture in Anatomical Pathology on the topic, Vascular Lesions of the Breast."

DRCCA COMMITTEE OFFERS SUGGESTIONS ON SCREENING RESEARCH, PROGRAMS

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smear—requires further quality control efforts at numerous nodal points in the health care delivery system—from the taking of the smear to the diagnosis of preinvasive neoplasia. When existing inadequacies have been documented through research/evaluation efforts, interventions can be proposed and ultimately large scale screening programs may again be supportable.

"With lung cancer, existing screening modalities are unable to detect the cancer sufficiently early in its natural history for existing therapies to lower mortality from the disease.

"Breast cancer may become more amenable to screening with modifications in current screening modalities (mammography) and the development of new screening technologies.

"For colon cancer, the most widely accepted screening modality (hemoccult testing) has been demonstrated only equivocally to be efficacious, and then only in very selected population groups. A screening modality applicable to target populations will have to exhibit greater acceptability.

"Having made these essentially negative recommendations with respect to large scale, population based screening programs, we also wish to note that special situations do exist where screening can be beneficial and funded programmatic effort would be indicated. One example would be in industrial settings where workers are exposed to carcinogenic materials which are known to increase the risk of site specific cancers. Other special situations, applicable to limited numbers and types of people, could be cited."

The committee, chaired by Board member Barbara Hulka, reviewed the Breast Cancer Detection Demonstration Project, a screening program funded by NCI through 27 contracts between 1973 and 1981. Long term followup was initiated in 1980. The committee recommended that the followup be continued through the originally designated five year period.

"At the four year interval the program should be thoroughly reviewed so that the current contractors have the opportunity to formulate additional research questions and develop the means for addressing them," the report said. "If such interests are expressed, there would be sufficient time for scientific evaluation and recruitment of funding for such proposals. The review at the fourth year will also facilitate an orderly phaseout period during the final year of the long term followup contract."

The report said the committee was "impressed with the magnitude and variety of detailed data that have been and are being collected on women in the long term followup program. Although many of these data items may be deemed desirable, it is most unlikely that it will ever be possible to utilize them fully through reports and publications." Therefore, the committee suggested that the contractors consider modifying their data collection strategies and reduce the amount of information obtained. Hulka acknowledged, however, that it may not be feasible to change data collection methods now.

To assess the state of lung cancer screening, the committee looked at three randomized controlled clinical trials funded in 1973 and 1974 to evaluate the efficacy of sputum cytology in conjunction with chest x-ray as a screening modality. The primary outcome of interest was lung cancer mortality. The three sites for the trials were the Mayo Clinic, Johns Hopkins Univ. and Memorial Sloan-Kettering Cancer Center. The Mayo design was different from the other two in that prevalent cases were screened out prior to randomization and the treatment group received chest x-ray and cytology three times per year whereas the control group received no planned intervention. At the other two sites randomization took place prior to identifying prevalent cases and the intervention was yearly x-ray plus four-monthly cytology, and the controls received yearly x-ray alone. The Mayo trial could evaluate intensive cytology plus x-ray versus no planned intervention. The no intervention group was, however, occasionally contaminated by chest x-rays obtained for reasons unrelated to the screening protocol, the contamination phenomenon being common to most randomized trials.

The results of the three studies were similar. Two (Mayo and Sloan-Kettering) showed approximately equal lung cancer mortality rates for treatment and control groups. The Johns Hopkins study did, however, have slightly higher mortality among the control subjects, a finding which was not statistically significant using standard statistical techniques, and which was limited to one age band, those 60-69. Since this finding was not replicated in the other studies, it was thought to be a chance event, the report said.

"Subject screening is almost complete at all centers and in two more years the five year postscreening followup will be complete on almost all subjects. Although there is little reason to expect any alteration in the existing results, the screening committee recommends that the three programs and their data management center receive continued funding for the remaining two years as originally planned. It would, however, be appropriate to consider a reduction of funding during these last two phaseout years."

The report noted that NCI contracts for funding pap test demonstration projects in 32 states were initiated in 1973. These contracts have recently been concluded. The programs incorporated educational elements for providers and the public, and promoted use of cytology services. "These were not designed as research efforts, nor were evaluation strategies pro-

posed. The screening committee did not find it relevant to evaluate this terminated program," the report said.

DRCCA has no currently funded contracts addressing colon cancer screening, the report pointed out. "The committee did have the opportunity to review preliminary data from the Univ. of Minnesota study funded by NCI's Div. of Cancer Biology & Diagnosis. This is a randomized trial of hemoccult testing with appropriate diagnostic evaluation for those exhibiting blood in their stools. At this point, there is no difference in colon cancer mortality between screened and unscreened persons. The study started in 1975 and will be continued into 1988."

The committee suggested that advice on future directions relative to screening could be organized by rational planning as displayed by a matrix that lays out the five phases of cancer control research and each cancer site (the phases are hypothesis development, research on study components or methods, case control studies, defined population studies, and demonstration and implementation).

"A systematic analysis of each site would identify both work already done or underway, and gaps in screening where research could be stimulated in order to promote the orderly progression of cancer control research."

Quality control needs to be considered in any new screening ventures, the report said. "There is considerable variation in the quality with which various screening activities are performed. Examples include techniques for taking and reading pap smears; the interpretation of cytology; radiation dose, mammographic technique, image quality and the interpretation of x-ray mammograms; and the conduct of culposcopy. The division should consider developing research projects to assess the quality with which activities such as these are performed, and to identify ways of improving the quality of screening. . . .

"Other questions that should eventually be studied concern the education, training and certification of people conducting screening, and the development of procedures to monitor the performance of screening activities.

"The division should develop a protocol or set of guidelines for identifying new technologies that have potential for cancer screening and for evaluating those technologies to determine their potential value and role. Specific projects might include the development of protocols for comparing new tests with existing technologies, and the development of criteria to determine when a new screening technology should be subjected to a randomized controlled trial.

"A unique set of circumstances led to breast and cervical cancer screening projects which were not designed to answer important research questions. Midstream adjustments to protocols and data management partially corrected this deficiency regarding the breast cancer project but not the cervical cancer project. The committee recommends that future screening projects be conducted as controlled clinical trials, given that the prior phases of cancer control research have been met. The design of these trials should be accomplished in cooperation with NCI and consulting statisticians, epidemiologists, clinicians, and social scientists. NIH and NASA have experience with designs incorporating multidisciplinary teams of investigators and multifaceted research projects with analysis plans incorporated from the outset.

"In the case of breast cancer screening a number of new technologies may soon be ready for consideration as screening modalities. These include new modification of transillumination, nuclear magnetic resonance, and possibly a new breed of ultrasound devices. For comparison and determination of the marginal value of individual modalities, future screening projects should include both new and proven modalities as independent procedures in multimodality screening."

The Board accepted the committee's report unanimously, after Board member Virgil Loeb commented "This is a good report. I'm concerned, however, that people will get the idea that early diagnosis is not important."

Board member David Eddy, who served on the committee, said, "With $70 million being spent on screening in the last 10 years, it's easy to get jaded when you look at the results. But early detection still is important."

DCT BOARD APPROVES RECOMPETITIONS WORTH $4.8 MILLION IN FIRST YEAR

The Board of Scientific Counselors of NCI's Div. of Cancer Treatment has given concept approval to the recompetition of contracts worth an estimated $4.8 million in first year awards, including the $2.5 million a year task orders for preparation of bulk chemicals and drugs held by six companies.

The Board also gave concept approval to a new competitive procurement, for data management support for the Radiation Research Program, estimated to cost $100,000 a year.

Contracts approved for recompetition:

Preparation of bulk chemicals and drugs. Estimated first year award, $2,530,000, five years. Present contractors are Aerojet Strategic Propulsion Co., Aldrich Chemical Co., Ash Stevens Inc., Pharm-Eco Laboratories Inc., Starks Associates Inc., and Warner Lambert Co. The staff narrative describing the program:

The chemical preparation laboratories are, in the strictest sense, service laboratories, and are designed and selected to prepare known chemicals and bulk drugs which are needed by the Program. The compounds selected for preparation are not readily available in the quality or quantities needed from the original supplier or on the open market.

The laboratories are used to obtain data for the preparation of the necessary quantities of clinically important chemicals and to develop the most economical means for their prepara-

tion. It should be pointed out that many methods of synthesis which are practical for small quantity are not technically feasible or economically practical when used for a large scale synthetic operation. The conversion of small scale to large scale production often requires developmental studies which are conveniently carried out by the preparation laboratories.

The preparation laboratories, taken collectively, provide the means of obtaining nearly any type of chemical compound, regardless of structure, and the ability of providing large quantities of very high purity drugs. A wide variety of chemical structures have and are being prepared and most preparations involve multi-step sequences. All materials prepared are fully characterized. The quantity of a given material to be resynthesized may vary from 10 grams to 200 kilograms. Factors governing the amounts depend upon use, ease of preparation, stability and cost.

These contracts will continue to provide the additional quantities of compounds required by the Program. Many of the compounds being developed in the various phases of the program are not available in the quality and/or quantity needed from other sources and the chemical preparation laboratories will be used to provide these compounds.

Study of the clinical pharmacokinetics of anticancer drugs. Estimated first year cost, $121,872, three years. Present contractor is Ohio State Univ.

The principal objective of this contract is to collect pharmacokinetic data on new and established antitumor agents in patients undergoing treatment of malignant disease and to analyze these data for individual variability which can be correlated with clinical response or some other pharmacologic parameter. Specifically, these studies will be primarily concerned with the measurement of drug and/or metabolite levels in the plasma with time after a standard dose of the drug. Apparent volume of distribution and plasma protein binding should be determined. These studies may also require measurement of urinary, biliary, and fecal excretion of drug and/or metabolites. Measurement of other fluids (e.g., cerebrospinal fluid) and tissues may be necessary. Approximately 30 patients per drug per six months will be required to provide adequate statistical documentation of individual variability in pharmacokinetic behavior. It is expected that two drugs will be evaluated annually and these are to be selected by the project officer in consultation with other investigators of DCT. Information on the analytical methodology for the measurement of the drug and/or metabolites in body fluids and tissues will generally be provided by NCI. Circumstances may arise which require modification, use of other analytical procedures, or development of new analytical procedures.

It is expected that the contractor will continue at the current rate of studying two drugs per year in approximately 30 patients per drug. Analytical methodology is being developed to study the following drugs during clinical trials: dihydroazacytidine, 2-fluoro-AraAMP, SR-2508, teroxirone, and the combination of AraAMP and DCF.

Detailed drug evaluation and development of treatment strategies for chemotherapeutic agents. Estimated first year cost, $600,000, four years. Present contractor is Southern Research Institute.

The contract with Southern Research Institute is scheduled for incremental funding at approximately $2 million for its final year, 2/16/83-2/15/84. To encourage competition, this multifaceted contract is being recompeted as four separate projects (in vivo screening, model development, detailed drug evaluation, and tumor quality control). Two of these, in vivo screening and model development, received concept approval for recompetition as resource contracts at the June 1982 Board of Scientific Counselors meeting. Approval to separate the remaining tasks, detailed drug evaluation and tumor quality control, and compete them as individual contracts is now being sought.

This contract and related previous contracts at the same institution have made many contributions to the elucidation of principles underlying the success or failure of cancer treatment and to the development of drug evaluation methodology. Studies on the development of the "cell kill hypothesis" and its application to current treatment strategies have won international recognition. Recent accomplishments include the development and characterization of a number of murine leukemic and solid tumor systems which are now available for detailed drug evaluation studies on new agents and the pursuit of new treatment strategies. Tumors are available (1) from different organ systems, including several colon and breast tumors, (2) with different growth rates and metastatic potential; and (3) with "natural" and "acquired" resistance to most standard chemotherapeutic agents. Using these models the contractor has demonstrated that a major cause of treatment failure is the metastatic spread and overgrowth of drug-resistant tumor cells probably as a result of somatic mutation. These observations require that new drugs and new treatment strategies be developed.

One of the main tasks of the proposed contract will involve the design and conduct of detailed drug evaluation studies on about 50 compounds per year identified as active in primary screening. The primary screen uses a battery of standard systems with routine schedules of drug administration and liberal endpoints to enhance the opportunity of identifying active materials. This contract will focus on the design of sequentially more challenging tests involving a variety of in vivo and in vitro tumor systems in an effort to select the most promising agents for clinical trial. The scheme to examine agents in sequentially more rigorous tests after identifying them in the P388 prescreen and panel of four tumors (B16 melanoma, L1210 leukemia, M5076 ovarian tumor, and the MX-1 human tumor xenograft) was approved at the June 1982 Board of Scientific Counselors meeting.

In detailed drug evaluation a number of parameters may be altered, such as tumor system, site of tumor implantation, timing of drug treatment (early or delayed drug treatment of tumor bearing animals), and route and treatment schedule of drug administration. Promising agents will be further evaluated singly or in combination in an effort to elucidate treatment strategies to address the following causes of treatment failure: (1) failure to control metastatic spread of disease and (2) failure to control the overgrowth of drug resistant tumor populations.

Recognizing that tumors are comprised of heterogeneous populations of cells with varying biological properties, such as growth rates, metastatic potential, and responses to chemotherapy, efforts will be made to develop treatment strategies to achieve total cure of neoplastic disease. After removing primary tumors (or in some cases before removal), animals will be treated with single agents or combinations of agents using simultaneous, sequential or alternating schedules of drug administration. New agents will be evaluated first in culture and then in vivo for their cross resistance to standard agents in an effort to find synergistic combinations of new agents which are not cross resistant with currently utilized drug combinations. Studies will be conducted in a variety of murine leukemia and solid tumor models, including drug resistant tumors with defined mechanisms of resistance.

Quality control and protocol development. Estimated first year cost, $300,000, four years. Present contractor is Southern Research Institute.

Historically, Southern Research Institute has conducted, as a part of its overall effort, quality control studies involving experimental tumors and various animal supplier sources. These studies have provided assurances that specific tumors

perform within acceptable parameters and are sufficiently stable for large scale usage or conform with historical standards. This type of study is critical for a fair assessment of the scientific integrity of the in vivo screening program. Kinetic data has also been provided which was utilized for drug treatment scheduling and for interpreting experimental results.

It is imperative that variations in laboratory data be analyzed to the extent that problems can be isolated and identified as to cause, e.g., animal source, tumor source or laboratory technique. In addition, protocols must be prepared for candidate tumor models, e.g. Fidler metastatic tumors, which establish growth parameters, optimal drug treatment schedules and routes, and provide the necessary transition from a pilot study to a cost effective large scale screening effort. Detailed protocols are also needed in order to verify the reported drug induced resistance of variant tumors to drug classes of major program interest and to adapt such tumors for large scale screening usage.

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

The dollar estimates listed 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). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

Selective acquisition of chemicals and drugs for cancer chemotherapy. Estimated first year cost, $527,365. Present contractor is Starks Associates.

This contract is in support of DS&CB's fundamental responsibility to acquire selected novel synthetic compounds for evaluation as potential anticancer agents–a key front-end activity of NCI's linear array for drug development.

The major focus of this contract is the active solicitation, acquisition and management of approximately 10,000 compounds per year of diverse structural types. These compounds are selected by DS&CB from a much larger pool of compounds (20,000) located through this contract in quantities adequate for the primary anticancer screen. Many new leads are identified, and this contract acquires a significant proportion of the larger samples needed for secondary screening (tumor panel). With the advent of the new NCI computer system, this contract will assume the responsibility of direct input of compound and data to the new system.

A highly professional staff is needed. The project team must include individuals capable of presenting NCI objectives in their liaison activities with domestic and foreign industries, universities and research institutes. The individuals must be highly qualified in organic and medicinal chemistry especially as related to anticancer research. Additional team members are required with special skills in information and document control including automated information systems.

Board member Paul Marks balked at approving the concept. "Starks goes around looking for 20,000 compounds on the cheap. We need to address the concept of whether this is the way to go about something that is so fundamental to your operation," Marks told John Driscoll, acting director of the Developmental Therapeutics Program.

Replying to Board member Efraim Racker's question on whether any compounds identified through the contract have been entered into clinical trials, Driscoll said "a number will be going into clinical trials next year. Essentially, all we're grooming now, 40 compounds (were found through the contract).

"There's no question, we're going to move away from random selection to rational design," DCT Director Bruce Chabner said. "The new Drug Discovery Groups are part of that. We don't know enough today to take money and rationally design drugs. Five percent (of the drugs selected by the contractor) are active. Five hundred thousand dollars will not buy much in design."

"I'm in favor of this contract," Board member Leon Goodman said. "It is an inexpensive way to look for new drugs. This leads to synthetic analogs, and eventually to rational design."

"I still think this can be misleading," Marks said. "It's not just the $500,000. This is the thing that drives the entire apparatus. If this is not effective, spending a lot more money is unnecessary. I don't agree, that we should not cut this because we have nothing else. We don't have the data. Year after year, we're told this contract should be continued because we don't know anything else."

The success rate for independent development of anticancer drugs by pharmaceutical companies is not good, Chabner said. "Most companies are lucky to get one or two in the lifetime of their management. The question is, do we give up on the system totally, do we have something to replace it?"

Marks agreed to Board Chairman Samuel Hellman's suggestion for a more extensive in depth discussion of the issue at the February meeting. The motion to approve the concept carried 7-3, with Marks, Racker and Susan Horwitz voting against it and three others abstaining.

Characterization and analysis of proteinaceous material. Estimated first year cost, $150,000, three years. Present contractor is the Univ. of Iowa.

The contract is a program resource which is responsible for development of suitable qualitative and quantitative methods to ascertain purity, identity and quality of various drugs and biological response modifiers from bath to batch in both bulk form and in pharmaceutical dosage forms. Reports of characterization and analysis are used as a basis for assessing the suitability of bulk BRM or finished dosage forms for evaluation and development in preclinical and clinical trials. The data obtained from analysis of various BRM are also used in support of NCI filing of IND on new drugs and BRM with antitumor potential to the Bureau of Biologics.

The resources of the Univ. of Iowa have been shared between the Developmental Therapeutics Program and the Biological Response Modifiers Program. Examples of substances that have been characterized and analyzed include largomycin, tumor necrosis factor and human interferons. These substances have been analyzed for identity, purity, composition, solubility and stability.

Future characterization and analysis will focus on BRMs with potential antitumor activity. The level of effort in the recompetition will remain about the same with somewhat increased resources required for materials and supplies as a result of a requirement for cell culture capability for in vitro cellular immunology assays. It is anticipated that most compounds requiring analysis will be proteinaceous and approximately six compounds will be studied annually.

The Board gave concept approval to increasing by $100,000 the cost of the Biological Response Modifiers Program contract with Memorial Sloan-Kettering Cancer Center for the production of monoclonal antibody to human cytokines. BRMP Director Robert Oldham said the program anticipates increasing the number of antibodies directed against cytokines. Marks, MSK president, left the room during the discussion and vote. The contract was originally negotiated for $411,000 over three years.

Screening of radiosensitizers and radioprotectors. Estimated first year cost, $279,000, three years. Present contractors are Arthur D. Little and Fox Chase Cancer Center.

Increased efficacy of radiation therapy is achieved through the use of compounds which sensitize tumor cells to or protect normal tissue cells from ionizing radiation. Until now, only one class of chemical compounds has been evaluated as sensitizers (nitroimidazoles) and as radioprotectors (aminoalkylthiols). It is important to screen other classes of chemical compounds to determine whether any of them show potential as radiosensitizers or protectors. The proposed contract will provide the capability of detecting new leads which could eventually lead to the development of more effective radiosensitizers and radioprotectors.

Approximately 200 compounds representing various classes and structures have been screened to date in both the sensitizer and the protector screens. Some of these compounds appear as effective as the standards to which they are compared but they represent different classes in which more effective analogues could be developed. It is too early to evaluate the effect of the current screening contracts, but the potential they represent make them worthy of continuation.

It is requested that both the radiosensitizer and radioprotective screening contracts be combined since both screens utilize similar biological methods of testing. A single contract would give the program increased flexibility and efficiency. Compounds which appear in vitro to be superior to the standard (misonidazole for radiosentizers, WR-2721 for radioprotectors) will be evaluated in vivo, using mice and/or rats. The effect of the compound in modifying the response to radiation will be measured in three different tumor systems (from the DCT panel of mouse tumor screens as stated in the treatment linear array for radiosensitizers and radioprotectors), each measured by a separate endpoint. The endpoints will include the regrowth delay of tumors, tumor cell survival and the modification of the radiation dose required for curing 50 percent of the tumors. All testing will be compared with the standard. The contract also provides for the option of assessing potential longterm tissue injury by performing histopathology on a limited number of tissues and compounds.

The only new competitive procurement approved by the Board was for data management support of the Radiation Research Program, estimated at $100,000 a year for three years. The narrative:

The Radiation Research Program has awarded contracts in four targeted areas of clinical trials research. The contractors of each research area constitute a working group who will gather data on patients during the course of their treatment for cancer to evaluate: hyperthermia equipment, intraoperative radiotherapy, photoradiation or to compare nuclear magnetic resonance scanning with other scanning techniques available. None of the 16 contractors representing the four areas of research has the capability of providing a centralized data storage and rapid retrieval system for all other contractrs. Centralized data storage and analysis is necessary to maximize the probability of getting sufficient good quality data for analysis.

This contract will provide the data management support and, where appropriate, statistical analysis for the contract-supported research projects of the Radiation Research Program.

Individual patient data will be submitted to the data management contractor on the appropriate data collection forms designed by each working group. The data will be keypunched, edited, and entered into the data base for the specific working groups. It will be available for retrieval or analysis by the individual contractors or in-house statistical staff. The data from all contractors of each working group will be used to develop the final deliverables required of each working group.

PROGRAM ANNOUNCEMENT

Title: *Tobacco and the blue collar worker*

The Div. of Resources, Centers & Community Activities of NCI has the principal federal responsibility for assuring the rapid and effective application of cancer research findings in the fields of prevention, detection, diagnosis, pretreatment evaluation, treatment, rehabilitation, and continuing care. DRCCA's goal is to develop the means for reducing cancer morbidity and mortality.

As part of its responsibilities in the area of cancer prevention, DRCCA is expanding its program initiatives under the NCI's Smoking, Cancer & Health Program which has been designed to facilitate the development of effective approaches to smoking prevention and cessation. The purpose of this announcement is to encourage research activities which will: (1) identify those factors that lead to recruitment, maintenance, cessation, and recidivism as related to tobacco use in the blue collar population; (2) identify concurrent and interacting conditions which may lead to shifts in tobacco usage patterns; and (3) develop prevention and cessation strategies which can be integrated into planned or ongoing workplace based health and/or antismoking programs.

This program announcement was developed in response to survey research data which indicate that 51 percent of the blue collar workers are smokers as contrasted with 37 percent of the total smokers in the U.S. population. In addition, research data suggest that blue collar workers have a potentially greater risk of exposure to known and suspected carcinogenic substances in the workplace. This occupational exposure may act in synergy with smoking behavior thus exacerbating the risk of cancer for this population.

These projects will focus on the development of research strategies to identify, within a well defined population group(s)—e.g., asbestos workers, who are tobacco users—the antecedents, correlates and con-

sequences that are related to recruitment, maintenance, recidivism, and cessation of tobacco use in blue collar workers. The study design should include identification of those concurrent and interacting conditions which may lead to shifts in tobacco usage patterns—e.g., from nonuser to user, occasional user to regular user, regular user to nonuser, cigarette smoker to smokeless tobacco user, etc.

The project should focus on the individual, social, and environmental factors that determine the influences affecting tobacco use in the blue collar worker, e.g., occupational related stress, social support and interaction effects, need for stimulation, maintenance of status, etc. Knowledge of the adverse health effects that result from the interaction between tobacco use and exposure to known and suspected carcinogens in the workplace will be a general requirement. The study design should include a reliable definition of the status of tobacco usage among blue collar workers and should consider multiple forms of tobacco use, e.g., regular tobacco cigarettes, cigars and pipes, non-tobacco smoking products, chewing, and dipping. In addition to self-report, the study design should include biochemical measurements to validate self-reporting, as well as to provide independent estimates of levels of tobacco use. The investigator should address application of research results to future prevention and cessation strategies.

Description of the research population, rationale for the method of sampling, definition of the variables and size of the sample, as well as proven access and cooperation from the intended research sample and appropriate labor and management representatives will be required.

A letter of intent and requests for additional information should be sent to: Catherine S. Bell, MS, Program Director for Smoking & Environmental Carcinogenesis, NCI, DRCCA, BMB, Blair Bldg. Rm 629, 8300 Colesville Rd., Silver Spring, Md. 20910, phone 301-427-8656.

Application kits may be obtained from an organization's application control office or from the Div. of Research Grants, National Institutes of Health, Bethesda, Md. 20205.

The application receipt dates for grants submitted under this program announcement are the usual DRG receipt dates for investigator initiated grants: New grants (Type 1) March 1, July 1, and Nov. 1; and renewal grants (Type II) Feb. 1, June 1, and Oct. 1. Research and demonstration grants are to be submitted on Form PHS 398. Completed applications are to be sent to: Div. of Research Grants, NIH, Room 240, Westwood Bldg. 5333 Westbard Ave., Bethesda, Md. 20205.

NCI CONTRACT AWARDS

Title: Hybridoma assays and related laboratory tests
Contractor: Meloy Laboratories, $656,986.

PROGRAM ANNOUNCEMENT

Title: *Smokeless tobacco and non-tobacco smoking product use: Identification of initiation mechanisms in children and adolescents*

The purpose of this program announcement is to encourage research activities which will: (1) identify factors that lead to the use of smokeless tobacco and/or non-tobacco smoking products (NTSP) by children and adolescents; (2) identify those conditions which may lead to shifts to and from regular tobacco cigarette smoking in children and adolescents; and (3) develop prevention and cessation strategies which can be integrated into school based health and/or antismoking programs.

Shifts in tobacco usage patterns and initiation of non-tobacco smoking behaviors have been reported by the research community. Data published by the USDA indicate that 11 million Americans use smokeless tobacco annually. This figure represents a 12 percent annual increase in smokeless tobacco use since 1974. In addition, the recent introduction of NTSP increases the potential for recruitment to smoker behavior by offering alternate smoking products.

Epidemiological evidence suggests that use of smokeless tobacco increases the risk of oral cancer. While little scientific evidence is available on NTSP, preliminary reports suggest that constituents in the gas phase of the smoke are suspected contributors to impairment of lung functioning, as well as acting as potential promoters of neoplastic disease.

These projects should focus on the development of research strategies to identify, within well defined population groups—e.g., junior high school students—the anticedents and correlates associated with initiation of smokeless tobacco and/or non-tobacco smoking product use and identification of these concurrent or interacting conditions which may lead to shifts from these products to regular tobacco cigarette smoking. The study design should focus on children and adolescents where the transition determines the influences affecting the decision to initiate smokeless tobacco or NTSP use and/or the decision to shift from these products to regular tobacco cigarette smoking. Evaluation of possible changes in knowledge, attitudes, beliefs, and behavior concerning the use of nontraditional smoking and tobacco products and/or the decision to shift from these products to regular tobacco cigarette smoking will be considered a major component of the research design.

Due to the generally similar behavior correlates between use of these products and cigarette smoking, demonstrated knowledge of the relevance and significance of current smoking prevention and cessation strategies aimed at children and adolescents is to be included in the research design. Knowledge of the psychological and social mechanisms potentially inherent in recruitment to these products is a general

requirement. In addition, the investigators must demonstrate an indepth knowledge of state of the art research in the areas of smokeless tobacco and NTSP as well as regular tobacco cigarette smoking as it relates to the research population. In addition to self-report, the study design should include biochemical measurements to increase the validity of self-reports, as well as to provide independent estimates of levels of tobacco use.

Description of the research population, rationale for the method of sampling, definition of the variables and size of the group, as well as proven access to and cooperation from intended research population, school authorities, parents, etc. will be required.

This program is, therefore, seeking applications for research and demonstration grants concerned with basic and applied studies in prevention of disease, concerned with behavior, attitudes and motives, cognition, information transmission, and other appropriate research areas.

Letters of intent should be sent to Catherine Bell, and completed applications to Div. of Research Grants, as in the preceding Program Announcement.

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 NCI-CM-37563

Title: *Literature monitoring service*
Deadline: *Dec. 10*

This procurement is totally set aside for small business. The size standard for small business is 500 employees or less.

The Drug Synthesis & Chemistry Branch, Developmental Therapeutics Program, Div. of Cancer Treatment, NCI, is seeking sources to provide a literature review service for identifying new compounds published in the chemical, biochemical, and biological literature which warrant acquisition for screening as potential anticancer agents. Specifically, the contractor should:

1. The key task will be to provide a list of published compounds from which the DS&CB can select at least 6,000 per year. The DS&CB will select only those published compounds it considers worthy of anticancer evaluation. However, it would be unacceptable for the contractor to provide a mere list of compounds many times the 6,000 per year. Thus, it will be necessary for the contractor to exercise considerable professional judgment to provide the minimum number of potential selections of sufficient quality so that at least 6,000 per year are selected by DS&CB.

2. Utilize a very broad base of past and current primary literature sources and published abstract services to continually monitor published works (including patents) in chemistry, biochemistry and biology, for the period of performance of the contract.

3. Work closely with the DS&CB on a continuing basis to develop guidelines enabling the contractor to recognize synthetic compounds likely to be selected by the DS&CB.

4. Identify relevant published research findings which may lead to new or refined criteria for the selection of synthetic compounds for anticancer screening.

The principal investigator should be an organic or medicinal chemist having experience in literature research techniques. The offeror should indicate the anticipated clerical support required.

Contract Specialist: Ann Linkins
RCB, Blair Bldg. Rm 228
301-427-8737

RFP NCI-CP-31016-78

Title: *Holding facility for small laboratory animals*
Deadline: *Approximately Dec. 17*

NCI has a requirement for a holding facility for small laboratory animals. The contractor's place of performance for this contract must be within a 35 mile radius of the Frederick Cancer Research Facility, Frederick, Md.

Animal holding will involve large numbers of rats (up to 1,500) and fewer numbers of mice (approximately 400). Space should be provided for 750 rats at any one time for feeding studies and 750 rats for injection with chemical carcinogens. It is expected that the approximate number of animals housed at any given time will be approximately 1,500.

It is estimated that 160 mice will be required for feeding studies and 300 mice will be required for skin painting and injection studies.

Contracting Officer: Elizabeth Osinski
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The Cancer Letter _Editor Jerry D. Boyd

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