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CONCEPTS DRAFTED BY ORGAN SYSTEMS WORKING GROUPS FARE WELL IN FIRST PRESENTATIONS TO NCI'S BOARDS

The first round of concept proposals generated by the redesigned Organ Systems Program were acted upon by NCI and its divisional Boards of Scientific Counselors at their fall meetings, and they fared

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In Brief

CONGRESS SENDS REAUTHORIZATION BILL TO WHITE HOUSE; APPROPRIATIONS BILL GOES TO CONFERENCE

FINAL CONGRESSIONAL action on the Biomedical Research Authorization Act was taken last week when the House approved the conference report (the compromise between the House and Senate versions); the Senate had approved it the previous week. The bill was scheduled to go to the White House Oct. 29. Meanwhile, John Ultmann, chairman of the Coalition for Cancer Research, and leaders of cancer professional societies and cancer centers, were urging their colleagues to send messages of support for the bill to the President. He has 10 days from the time he receives the bill to act on it, or it becomes law without his signature. Senators Orrin Hatch (R.-Utah), coauthor of the measure, and Barry Goldwater (R.-Ariz.), among other congressional leaders, have asked the President to ignore the Office of Management & Budget and sign the bill. . . . **THE SENATE** last week approved the FY 1986 Labor-HHS appropriations bill. A conference with the House, which had already passed the measure, could be held as early as this week. Two major differences affecting NCI are in the Senate bill and Appropriations Committee report: restoring NIH positions cut by OMB in the last couple of years, and the directive that $4.5 million of the $6.6 million earmarked for construction grants be awarded to the Mary Babb Randolph Cancer Center at West Virginia Univ. That last item was the work of Sen. Robert Byrd (D.-W.Va.), who failed in a similar effort last year after Congress had added $4.5 million to the construction budget with the stipulation it go to WVU. The National Cancer Advisory Board disapproved WVU's application, and the money was spent on other construction grants. NCI had hoped that Byrd would again add money to the budget, if he still insisted on funding the Randolph grant, and had counted on the entire $6.6 million for other grants. Review has been completed on 14 construction/renovation applications, only $2 million of which will be funded if the Senate stipulation holds. . . . **FRANCO MUGGIA**, professor of medicine and chief of oncology at New York Univ., will join the Univ. of Southern California July 1 in the same capacity. He also will be director of clinical investigations at USC's Norris Cancer Center. Before he went to NYU, Muggia was head of the Cancer Therapy Evaluation Program in NCI's Div. of Cancer Treatment.

DCE BOARD OKs CONCEPT FOR $1 MILLION A YEAR RFA ON PREMALIGNANT COLON CA

(Continued from page 1)

reasonably well. All four proposals presented by the OSP working groups were cleared by NCI's Executive Committee, and at least three of the four were approved by the BSCs.

The Div. of Cancer Biology & Diagnosis Board of Scientific Counselors was scheduled to consider a concept for a program announcement for studies on prostate cancer metastasis at its meeting this week.

Concepts which have been approved include an RFA for studies of markers of premalignancy of colon cancer and their inheritance, to cost an estimated $1 million a year to support five grants, approved by the Div. of Cancer Etiology BSC; a program announcement for studies of mechanisms of drug resistance in colon cancer, expanded by the Div. of Cancer Treatment BSC to include all solid tumors, using tumor cell lines available from NCI; and a program announcement approved in September by the Div. of Cancer Prevention & Control BSC for a study of micronutrients and breast cancer.

Program announcements do not require setting aside of specific sums to fund the resulting grants, as is done with requests for applications. Grants generated by both PAs and RFAs all compete for funding from NCI's RO1-PO1 pool.

The OSP working groups, working through the Organ Systems Program Coordinating Center at Roswell Park Memorial Institute, are in the process of drafting a new round of concept proposals based on their surveys of research needs in their respective fields. Andrew Chiarodo, chief of the Organ Systems Section in DCPC, said some may be ready for presentation to the BSCs at their winter and spring meetings in 1986.

Leonard Augenlicht, a member of the Large Bowel Cancer Working Group from Montefiore Hospital in New York, told the DCE Board that the proposal for studies of markers of premalignancy of colon cancer and their inheritance was the top priority of the group.

A summary of the concept statement presented by Augenlicht and Vincent Cairoli, DCPC program director for colon cancer, follows:

Treatment for advanced colon cancer has very limited success, while encouraging results have been achieved in the treatment of early stage lesions. Therefore, the identification of individuals at risk and early detection are important. Identification of high risk groups in addition to the readily recognized genetic syndromes would permit close monitoring for a much larger segment of the at risk population. Application of preventive measures, early removal of preneoplastic lesions and early surgical intervention would reduce the incidence and improve the prognosis of these groups.

Colon cancer represents one of the rare opportunities to actually observe and characterize the premalignant state. Human colon cancer is a remarkably good system in which to assay in a rigorous way whether new reagents, such as monoclonal antibodies or cloned gene sequences, can be of significant value in the diagnosis, prognosis and classification of solid human tumors. Basic research on the identification and analysis of antigenic determinants and cloned sequences (including oncogenes) is progressing at a rapid pace, but the clinical data which is reported is often fragmentary and has not made use of carefully evaluated patient material from well defined population groups in a systematic fashion.

The critical question of whether these reagents can be used clinically remains unanswered. The advantage of establishing collaborative efforts is that sophisticated methodology which has developed over the last five years can address clinically important problems in a rigorous way and thus avoid a continuing proliferation of anecdotal results concerning the use of such methodology in human disease. Bringing clinicians who are skilled in the handling and analysis of colorectal material and experienced in the management of the disease together with basic scientists who are developing a variety of new reagents and markers should generate a wealth of new information which is clinically applicable in the population.

The overall goal of this initiative is to develop collaborative studies between basic science marker experts and clinical research groups with well defined patient populations at high risk for colorectal cancer. Specific objectives are to (a) define population groups which differ in their inherited risk for the development of colon cancer, particularly familial aggregates of adenomatous polyps and colon cancer, which will provide a resource for extending observations from the well defined, high risk genetic groups into the majority of colon cancers; (b) identify and apply biochemical, immunological, genetic, cytogenetic and molecular markers to individuals in these well defined groups to identify individuals predisposed to adenomatous polyps and colon cancer; to classify stages in the progression from normal colonic mucosa to invasive and/or metastatic carcinoma; and to distinguish between apparently similar stages in the different population groups. A long range goal would be to define a major gene for adenomatous polyps or another marker that could lead to the successful chromosomal mapping of a colon cancer gene which in turn could provide an understanding of gene environment interactions.

Collaborative studies are required between laboratories assaying markers and clinical groups characterizing families and collecting samples from them. The general approach is to clarify the genetic epidemiology of adenomatous polyps and colorectal cancer and to then use stage specific material from patients in such well defined population groups for evaluation of sensitive and specific markers of colorectal cancer (e.g. cloned gene sequences, monoclonal antibodies, and other biochemical reagents). Subjects must be members of well studied registries from which pedigree analysis would be available or could be accomplished, as appropriate. The several forms of dominant inherited colon cancer of high penetrance can serve as models for the study of common colon cancer. It is not known whether these syndromes are allelic or not, and since on the gene level they may represent different loci or mutations, samples of polyps from each of these entities should be studied. In addition, there are common clusters of colon cancer which do not show site specificity, which show the normal age distribution of colon cancer, and which do not inherit as a highly penetrant dominant disorder. Families in this category need to be well characterized since they may represent a significant proportion of colon cancer cases, and provide a resource of material from defined population groups for linkage to colon cancer markers. Epidemiology should be extended to the search for inheritance of the common, or discrete, adenomatous polyp. If such polyps have a low probability of progression to malignancy, they could produce much of the colon cancer in the general population. Hence, elucidation of patterns of inheritance may contribute to identification of those at risk.

Colonic biopsy samples should provide tissue at various stages in the development of the fully malignant state from genetically well defined population groups which differ in their risk for development of colon cancer, and in which the genetic and biochemical events producing the disease may be the same or different. Biochemical, immunological, genetic, cytogenetic and molecular markers of risk and progression of colorectal cancer should be identified and tested as indicators of the underlying genetic defect of inherited cancers and/or as indicators of the stage of progression of normal colonic epithelial cells through adenomas to malignant carcinomas. In particular, it will be important to distinguish the adenoma which will eventually progress to carcinoma from the adenoma which will not, if such a distinction exists. Particular attention should be given to the location and pathology of each biopsy analyzed. The hyperplastic polyp should also be included in these investigations.

A requirement of this project is that the studies of common polyps must be interactive with the molecular, genetic, immunological and biochemical marker studies of cancer pathogenesis. In addition, a mechanism will be instituted for the formal exchange of information and promising reagents (cloned sequences, MoAbs, etc.) among the funded groups to facilitate confirmation of results as rapidly as possible in a rigorous way. This approach should contribute to the clarification of polyp etiology, while polyp materials would improve the likelihood of identifying marker segregation for individuals predisposed to colorectal cancer.

Board member William London challenged the contention that there is little or no research going on in this area. "I know of at least one RO1."

"There are a number of people who are interested," Augenlicht said. "But the studies that are going on are limited. The problem is that the study sections either don't appreciate the application of these studies or don't appreciate the cost of doing this. Study sections won't vote sufficient priority scores or funds to do it. The ideas are out there but they can't get the funds to do it adequately or rigorously."

DCE Director Richard Adamson noted that grant applications generated by this RFA would be reviewed by a special study section.

The vote to approve was unanimous.

The program announcement concept presented to the DCT Board had these major objectives, with the overall goal to develop a new system for selecting agents with potential clinical activity against colorectal cancer:

1. Develop in vitro models of cellular resistance to anticancer drugs for human colon carcinomas. The models should include cell lines which have been demonstrated to be resistant to the specified drug in an in vivo system (athymic mouse, subrenal capsule, etc.), cell lines which are naturally refractory (i.e., resistant lines obtained from patients who had never been treated with cytotoxic agents) and lines which were initially sensitive to drug in the in vivo test system, but subsequently selected for resistance by repeated exposure to the drug in question.

2. Identify mechanisms of resistance in the model systems and the underlying molecular basis of drug resistance.

3. Develop approaches to circumvent specific mechanisms of resistance in colon carcinoma through the design of analogs of existing drugs or specialized application of novel drug combinations based upon a knowledge of mechanisms of resistance,

i.e., utlize the panel of lines developed in 1 and 2 above as a panel to screen for effective drugs against specific subpopulations of drug resistant human colon carcinoma cells.

Board members questioned why the announcement should be limited to colon carcinoma, since cell lines are available in lung, breast and other solid tumors. DCT Director Bruce Chabner agreed that the program announcement could be expanded to include other solid tumors.

The concept proposal noted that the use of cell lines with specific mechanisms of resistance could be utilized to identify potential activity against colon cancer subpopulations in a variety of ways, from screening for activity against a large number of mechanisms to the rational design of modified parental drugs for a specific purpose (e.g., analogs of mitomycin C with high reduction potential to overcome a lack of cellular activating enzymes). Potential agents could therefore be identified from new chemotypes being tested for activity in NCI decision networks, analogs of mitomycin C and nitrosoureas, old drugs which have not been effective against colon cancer but might be effective against specific subpopulations in novel drug combinations. "The manner in which these would be identified would involve the same in vitro and animal screening techniques that have historically been utilized to discover anticancer drugs, but with a different panel of target cell lines for both in vitro and in vivo tests," the concept statement said. "Groups with cell biology or molecular biology expertise could contribute significantly to the development of resistant colon cancer cell lines and the elucidation of resistant mechanisms. However, multidisciplinary collaborative teams would enhance the prospects for success."

PB-85II-018779

DCE BOARD APPROVES ADDITIONAL RFA, RECOMPETITION OF FIVE CONTRACTS

The Div. of Cancer Etiology Board of Scientific Counselors approved additional concepts worth an estimated $1.3 million in first year awards, including an RFA that would support five to six grants for the study of transformation mechanisms of human polyomaviruses.

Approved concepts included one new contract supported project and recompetition of five existing contracts, and six noncompetitive contracts.

The Board deferred action on a collaborative program with the Environmental Protection Agency for studies of biochemical indicators of chemical pollutant stress in the aquatic environment. NCI funds, estimated at about $200,000 a year for the three year awards, would support cooperative agreements.

"I have problems with the scope of this," Board member Edward Bresnick said. Board member William London added, "I wonder how relevant this concept is to the mission of DCE. It's interesting biology, but I wonder if it is in our province. It seems to be several steps removed from carcinogenesis."

"There are several reasons why it relates to DCE's mission and carcinogenesis," Bresnick responded. "Fish are targets of pollution in water, and fish are very sensitive to carcinogens. They are good models."

"But why look for the effect on the enzyme system (a principal objective of the concept) when we already know a substance is carcinogenic?" board member Renato Dulbecco asked.

"It can be an early warning system, in the real world," W.P. Schoor, the EPA project officer, answered.

"It is not clear what needs to be done," Board member Donald Davies said. His motion for deferral was approved unanimously.

Other concepts approved by the Board include:

The transformation mechanisms of human polyomaviruses. Proposed first year funding, $600,000 to support five to six grants, which will be awarded for five years.

The first human polyomaviruses, BK and JC viruses, were isolated from immunosuppressed patients in the early 1970s. Evidence has recently accumulated for a possible third human polyomavirus, B-lymphotropic papovavirus (LPV). These viruses are in the same group of small DNA viruses as simian virus 40 (SV40) and mouse polyomavirus. There was initial interest in these human polyomaviruses as possible etiological agents of cancer in man because they produce persistent infections in man, can transform animal cells in culture, induce tumors in rodents and, in the case of JC virus, induce tumors in lower primates. Research on these viruses waned in the late 1970s, primarily due to technical difficulties such as growing adequate viral stocks. Recently, there has been increased interest in these agents because some of the technical difficulties have been overcome and because their potential as model systems to study human cell transformation has been recognized. Moreover, recent data suggests that SV40 and mouse polyomaviruses, which have been used as model systems for studying transformation by the small DNA tumor virus group, have major differences among themselves in their mechanisms of transformation. Thus, those animal viruses may not be as good models for the viral transformation of human cells as was originally thought.

The current status of research on human polyomaviruses and cancer was reviewed at a workshop last March sponsored by the Biological Carcinogenesis Branch. The consensus was that these human viruses provide unique opportunities to study directly the mechanisms involved in the viral

transformation of human cells. Investigations with these viruses can take advantage of both cultured human cell lines as well as material derived from human tumors containing DNA from polyomaviruses. Such human tumors have recently been identified from the pancreas (insulinomas), bone (osteosarcomas) and brain (ependymomas). These data also suggest a possible etiological association between these viruses and some human tumors.

Since much of the work on human tumors is still in a preliminary stage, the workshop participants felt that direct evidence of an etiological association between human tumors and these viruses, or other unidentified human polyomaviruses, should be pursued with both tumor and normal tissues using better screening techniques than those previously employed and followed by characterization of the detected viral sequences. In contrast, studies using cultured cells have already demonstrated that alterations of the enhancer/origin sequences of these viruses can markedly increase the viral transformation efficiency. More in vitro studies are needed on these sequences. Similar in vitro studies are also needed on the function of the viral tumor antigen proteins, which are known to be required for transformation in animal systems. In addition, since it is difficult to transform most human cells in culture with these viruses, the development of modified human cell lines (partially transformed by oncogenes, other viruses, or chemicals) which can be transformed efficiently by polyomaviruses, would be very useful for studies of transformation. The workshop participants also noted that there was a lack of basic knowledge about the biology of human polyomaviruses, such as the target cells for primary and persistent infection and the mechanism of persistance. Thus, it was the consensus of the workshop that research in all the above areas is both timely and needed to fully utilize the opportunities offered by this group of viruses.

The major emphasis of research to be funded under this RFA will be basic studies on the mechanisms of transformation of human polyomaviruses and their possible role in the etiology of human cancer. Examples of such studies (which are not all encompassing) are: (1) characterization of the enhancer/origin sequences and the proteins and genes with which they interact, and determination of the significance of the hypervariability of these sequences and other regions found in natural variants of these viruses for transformation; (2) characterization of the viral tumor antigen proteins, particularly with regard to defining functionally and antigenically distinct domains within the proteins; (3) development and utilization of modified human cell lines which can be efficienctly transformed by these polyomaviruses or can support high titer lytic growth; (4) studies of the incidence and structure of polyomavirus DNA in normal human tissues and human tumors histologically similar to tumors induced by these viruses in animals; (5) functional analysis of polyomavirus DNA from human tumors with regard to the presence of gene products, transformation activity in transfection assays and the maintenance of viral sequences upon serio passage; (6) isolation and characterization of human B-lymphotropic virus and other new human polyomaviruses; and (7) studies of the mechanism of persistent polyomaviral infections in man and the identification of the target cells involved in this interaction.

Alan Schreier is the program director.

Board member Renato Dulbecco, who chaired the workshop, stressed that antibodies to human polyomaviruses are widespread in human populations and said the workshop concluded DNA probes are necessary. He emphasized that not much is known about the basic biology of the viruses. "Since these viruses are widespread in human populations, they undoubtedly do have tumor inducing ability," Dulbecco said.

Board member Janet Butel suggested that JC and BK be studied separately. Dulbecco agreed that one lab should not work on both viruses. Butel said she thought most labs would focus on BK, but Dulbecco. said JC is the one that should be emphasized.

Butel questioned emphasis No. 6 (above), wondering how much attention should be placed on other viruses when so little is known about these two. Schreier said there was a feeling that there were "perhaps a lot of cousins we know very little about." He mentioned the example of papillomavirus, how there are now more than 40 identified now, when there were only two a few years ago.

DCE Director Richard Adamson said the RFA could be written to give No. 6 lower priority than the other items.

Industrial hygiene and biochemical monitoring of exposures encountered by anatomists and embalmers. This will be a new contract supported effort, with one award with an estimated first year cost of $72,000, for two years. It will be funded through NCI's agreement with the National Institute for Occupational Safety & Health.

Excess mortality from leukemia and brain cancer has been noted in recently completed epidemiologic studies of professional groups engaged in handling of biologic materials from widely separated locations (embalmers from New York, California, and Ontario; pathologists from the U.S. and Great Britain; and anatomists from the U.S.). Although pathology reports were not reviewed, the death certificates indicated a preponderance of gliomas and myeloid leukemias. Individuals in these professionals may be exposed to a number of different agents including formaldehyde, a demonstrated carcinogen in laboratory animals. Although there has been concern about its human carcinogenicity, mortality studies of industrial workers exposed to formaldehyde have not reported associations with brain cancer or leukemia.

The lack of positive findings in studies of industrial groups raises questions as to whether or not formaldehyde is the etiologic agent for the cancer excesses among anatomists and embalmers. Professional groups also use a number of other chemicals to preserve, fix, and stain biologic tissues. These compounds include xylene, toluene,

methyl benzoate, propylene oxide, glutaraldehyde, phenol and various stains. Two studies are being planned to followup these findings and to assess the suggested risks for cancer among embalmers and anatomists. First, a nested case control study of brain cancer and leukemia among cohorts of embalmers and anatomists assembled at NCI is being developed to obtain historical information about the work environment and associated cancer risks. This study is being conducted under the support service contract for occupational studies. The present concept covers the second study, which is a toxicologic investigation to gain detailed information on exposure to formaldehyde and other chemicals which will be integrated with information obtained by interview in the case control study.

The objectives of the project covered by this concept are to (1) identify chemicals used now and in the past by embalmers and anatomists to preserve, fix, stain and handle biologic tissues; (2) document through environmental monitoring levels of exposure of embalmers and anatomists to formaldehyde, glutaraldehyde, phenol and other selected chemicals; (3) obtain blood and urine samples on a limited number of anatomists and embalmers to assess delivered dose and early evidence of biologic damage from selected chemicals noted in objective 2 for which feasible and suitable analytic methods are currently available. Biologic monitoring results will be correlated with ambient air levels.

This project will be completed in three phases as outlined above, with results from each phase evaluated before proceeding to the next step. Phase 1 will consist of an evaluation and determination of chemicals used by anatomists and embalmers, now and in the past. Industrial hygienists will review current and historical laboratory practices of these professions, conduct discussions with individuals in the field, and perform walkthrough inspections of laboratories. Data from phase 1 will be evaluated to determine the need for, and the scope of, the succeeding phases in terms of the level of effort and specific chemicals to be monitored. Phase 2 will consist of industrial hygiene monitoring of chemicals selected in phase 1. Chemicals, occupational groups, and types of institutions selected for monitoring will depend upon the availability of suitable monitoring techniques, similarity of current exposure levels to those of the past, and likely levels of exposure. Personal and area air samples will be collected and analyzed using NIOSH recommended procedures. Phase 3 will consist of biologic monitoring which will be initiated if results from phases 1 and 2 indicate that meaningful human exposures occur and if monitoring techniques exist for the relevant exposures. Facilities with higher exposures to greater numbers of chemicals will be preferred for phase 3. Biologic monitoring will clearly be indicated if evidence exists that dermal and ingestion exposures occur in addition to exposure by inhalation. Persons at the same institutions as the exposed subjects, but not working in the laboratory or otherwise exposed to the chemicals, will serve as controls. Additional industrial hygiene monitoring will be conducted in conjunction with the biologic monitoring.

This will be a collaborative project between NCI and NIOSH. NCI will be responsible for the overall coordination of the study and will have specific responsibility for phase 1 and 3. NIOSH will design and oversee the industrial hygiene monitoring in phase 2 with consultation from NCI.

Aaron Blair and Patricia Stewart and the NCI project officers and Leo Blade is the NIOSH project officer.

Continuation of followup on participants in the Breast Cancer Detection Demonstration Project. This will be a new contract, for a competitive award to a single institution or organization. Estimated first year cost is $250,000, with a total cost over five years estimated at $3 million. DCE will provide half those funds, the Div. of Cancer Prevention & Control the other half. The DCPC Board of Scientific Counselors had previously approved the concept.

The proposed study would be a continuation of a followup study initiated five years ago on a sample of 64,000 of the 280,000 women who had previously participated in the five year Breast Cancer Detection Demonstration Project cosponsored by NCI and the American Cancer Society. The cohort currently consists of 61,387 women. This is comprised of 3,027 women who had received a diagnosis of breast cancer while in the screening program; another 24,377 who had a biopsy or an aspiration during the program that was determined to be benign; 9,127 women who had a surgical evaluation recommended by the program but did not undergo biopsy; and 24,156 who had neither surgery nor a recommendation for further evaluation. This last group was a sample of all such women and were matched to the surgical series on age, race, center and duration of participation in the screening program.

Several opportunities exist within this cohort study for evaluating issues that have been difficult to resolve by case control studies alone. For example, extremely high rates of menopausal hormone usage in this cohort will enable a thorough assessment of the possible relation to breast cancer including the potential effects of progestogen supplementation. Other unsettled issues from case control studies include the relationships reported with smoking and alcohol use, possibly reflecting the retrospective nature of the exposure assessment. In addition, extensive information collected during the course of screening will enable an evaluation of mammographic patterns and histopathogenic subtypes of benign breast disease in relation to subsequent morbidity, mortality and survival patterns. The cohort approach will also help elucidate interactions between the effects of standard breast cancer risk factors, anthropometric measures, nonhormonal medications, genetic predisposition, and other suspected influences of an environmental or host nature. This cohort will also make it possible to evaluate risk factors for other cancers in women, for example, the possible role of reproductive factors in colon cancers and exogenous

hormones in reproductive tract, colon and lung cancers.

The resources that make continued followup of the cohort particularly attractive include: (1) the cohort is quite large and is currently in the high risk cancer age range (e.g., apprximately 2,600 cases of malignancy would be expected over the five years of followup, including 750 cases of breast cancer); (2) this is a cooperative population with a demonstrated willingness to participate in followup studies, and a varient of information useful for tracing has already been collected; and (3) a substantial amount of interview, radiographic, and histologic information exists for this cohort which can be used to evaluate prospectively a large number of issues with respect to cancer etiology and control.

All women in the cohort have at least one set of mammograms and most have four to five years of mammograms. For the approximately 24,000 women who underwent breast surgery during the five years of screening, a standardized pathologic review of this material has been performed and computerized. For three quarters of these cases, representative slides from these surgeries have been collected and retained. In addition, hospital discharge records and pathology reports have been obtained for all breast surgeries occurring in the first five years of followup. This should allow an expansion of pathology based review studies to be done when appropriate. Information on a variety of risk factors exists on the entire cohort, including detailed reproductive histories, the use of oral contraceptives and menopausal hormones, family history of malignancies and personal medical history. In addition, on a sample of approximately 12,000 women, very detailed information from a home interview exists, including standard breast cancer risk factors, tobacco use, estimates of height and weight at various periods during a woman's life, use of various prescription drugs, and alcohol consumption.

A large number of hypotheses could be tested in a prospective manner utilizing these data bases. In addition, a large number of other hypotheses could be pursued via case control evaluations within this cohort, once the cases have been identified.

To minimize costs associated with further followup, it has been decided that exposure and outcome information will be obtained via questionaires that are mailed biannually from a centralized locale. Telephone interviews would be pursued among nonresponders, but only after several attempts have been made to obtain information by mail. The emphasis of the questionnaire will be on outcomes, including all cancers and breast abnormalities, but limited exposure information will also be obtained. For any cancers or breast operations reported, surgeons and hospitals will be contacted to obtain copies of the hospital discharge summaries and pathology reports. For any subjects found to be deceased, copies of death certificates will be requested.

In addition to these interview and validation activities, this contract will serve to develop a useful repository of information on these participants. This will include retrieving and developing a ready access system of screening forms currently stored in Philadelphia at the Data Management & Analysis Center (whose contract will shortly terminate); mammograms that are stored at each of the 29 screening centers; and pathology slides that are currently available at Vanderbilt Univ. for a sample of the women who underwent surgical evaluation during the course of screening.

Robert Hoover and Louise Brinton are the project officers.

"Will there be anything on histology, to bring this into modern terminology?" Board member Nicholas Petrakis asked. "The whole field has changed since this started."

Hoover said that "there is a lot of enthusiasm now for rereading the material, the slides, under the new classifications." Responding to Board member Mimi Yu's comment that the contract would cost a lot of money, Hoover said, "About $1 million less than many estimates for a large cohort like this."

The concept was approved unanimously.

Additional concepts approved by the DCE Board will be reported in the next issue of **The Cancer Letter.**

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, Md. 20892. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CN-65005-03
Title: Reduction of avoidable mortality from cancer in Black populations
Deadline: Jan. 22

NCI's Div. of Cancer Prevention & Control is soliciting proposals for a study which will be directed at circumventing barriers to primary prevention and secondary prevention that Blacks face for specific cancer sites. Specifically, the study should (1) identify key factors that contribute to avoidable mortality; (2) implement interventions to address these factors; (3) evaluate the effectiveness of the interventions; and (4) identify prototype approaches to the reduction of avoidable mortality for widespread dissemination.

It is anticipated that a five year incrementally funded cost reimbursement type contract will be awarded. Four preproposal conferences are planned,

for Nov. 13 in Atlanta; Nov. 14, in Chicago; Nov. 15 in New York; and Nov. 22 in Los Angeles.
Contracting Officer: Shirley Kyle
Blair Bldg Rm 2A01
301-427-8745

RFP NCI-CN-65006-03
Title: Primary prevention (smoking) of cancer in Black populations
Deadline: Jan. 22

The Div. of Cancer Prevention & Control is soliciting proposals to determine the long term effect of interventions designed to prevent the onset and/or reduce the prevalence of cigarette smoking in Blacks. Specifically, the effort would develop and evaluate innovative intervention strategies to prevent or reduce cigarette smoking in Blacks; and develop and evaluate assessment procedures for determining the long term effectiveness of smoking interventions among U.S. Black populations.

It is anticipated that a five year incrementally funded cost reimbursement type contract will be awarded to the successful offeror. Four preproposal conferences are planned, for Nov. 13 in Atlanta; Nov. 14 in Chicago; Nov. 15 in New York; and Nov. 22 in Los Angeles.
Contracting Officer: Shirley Kyle
RCB Blair Bldg Rm 2A01
301-427-8745

RFP NCI-CM-57746-30
Title: Plant collection programs
Deadline: Dec. 16

The Div. of Cancer Treatment's Developmental Therapeutics Program wishes to establish contracts for the collection of plants for evaluation as sources of potential antineoplastic agents, with the ultimate goal being the discovery of novel structural types which can be developed for the selective treatment of cancer in man.

Three main areas are being targeted for collection--Madagascar and adjacent islands and tropical and subtropical areas of Africa; Central and South America with emphasis on the tropical rain forest areas; and Southeast Asia. It is anticipated that one award will be made for each of those areas. Each will be evaluated and awarded as a separate entity. Offerors may submit separate technical and cost proposals for one or more of the areas.

For each area the successful offeror will be expected to provide qualified personnel, materials and equipment for the collection, identification, storage and shipping of 1,500 plant samples per year to an NCI designated extraction facility for a period of five years. Collections will comprise approximately 0.3-1.0 kg (dry weight) of each plant, and each plant will be identified as far as possible at the time of collection.

Properly prepared voucher specimens of each plant will be collected for the purposes of unambiguous identification, and for permanent deposition at a minimum of two herparia designated by NCI. The contractor will be expected to provide detailed documentation, including complete identification, of each plant collected. The collection teams should include a qualified plant taxonomist and personnel experienced in plant collection and identification, and having familiarity with the customs of the local populations. The principal investigator should be trained in botany or a related field, preferably at a PhD level, and should have at least five years of experience in plant collection and identification. It is anticipated that re-collections of up to 40-80 plants per year, in quantities of 10-50 kg, will be required, starting in the second year. The number of initial small scale collections will be reduced in proportion to the number and size of the large scale re-collections undertaken.

Collections will include species from as wide a variety of families and genera as possible. A list of species and genera extensively screened by NCI will be provided in order to aid in the determination of priorities in the collection program. In the case of trees and large shrubs, samples of plant parts may be collected and stored separately for individual evaluation, with each part being considered equivalent to a plant sample for purposes of estimation of level of work.

The contractor will be responsible for obtaining all necessary permits including visas, collecting, shipping and export permits from foreign governments and agencies, as well as import permits and quarantine clearance for delivery of samples and voucher specimens to facilities in the U.S. Where necessary, the government will provide letters of support.

It is anticipated that cost reimbursement, incrementally funded type contracts will be awarded for periods of 60 months, starting about Sept. 1, 1986.
Contract Specialist: Elsa Carlton
RCB Blair Bldg Rm 224
301-427-8737

NCI CONTRACT AWARDS

TITLE: Operations office for inter-institutional nuclear magnetic resonance (NMR) studies
CONTRACTOR: AMC Cancer Research Center, Denver, $1,173,031.
TITLE: Information resource activities to identify, characterize and evaluate reports and scientific literature in the area of chemoprevention
CONTRACTOR: Sigman Computer Services, Palo Alto, $49,946.

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