THE CANCER LETTER

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FIRST CHOP AWARDS MADE, 17 OTHERS IN NEGOTIATION FOR NCI PROGRAM TO UPGRADE COMMUNITY CANCER CARE

NCI has made the first six awards in the Community Hospital Oncology Program and is in various stages of negotiation with the remaining 17 that will be awarded according to current plans of the Div. of Resources, Centers & Community Activities.

All awards are for 18 months of planning. Contractors successful in the planning phase will receive awards for two additional years of implementation.

(Continued to page 2)

In Brief

HHS IMPLEMENTS DEBARMENT REGULATIONS; JOFTES, CAIN HEAD NEW NCI CONTRACT, GRANTS BRANCHES

DEBARMENT REGULATIONS which will permit HHS to exclude investigators from grants for a variety of causes will go into effect Nov. 10. The regulations were published in the *Federal Register* Oct. 9. Causes for debarment include conviction for a criminal offense related to obtaining the grant; conviction for other offenses "indicating a lack of business integrity or honesty;" conviction under antitrust laws arising out of submission of applications or proposals; serious violation of laws or regulations relating to grants; record of unsatisfactory performance under prior awards; prior outstanding debarment; and "any other cause significantly affecting fiscal responsibility as a recipient of federal funds." The regulations set forth procedures the government must follow to debar an individual or institution, and provide for appeals. NIH Director Donald Fredrickson, appearing before the National Cancer Advisory Board to explain the policy, said, "I'm not sure that scientists and people in government or Congress suffer from any more sin than they ever have. But in the post Watergate era, more attention has been given by the press to episodes." . . . **REVIEW & REFERRAL** Branch in NCI's Div. of Extramural Activities has been reorganized into two branches. The Contracts Review Branch is headed by David Joftes, who was chief of the R&R Branch. Dennis Cain is chief of the Grants Review Branch. . . . **ISAAC TAYLOR**, who has been in private practice in North Carolina and visiting professor at the Univ. of North Carolina, has been named associate director for administration at the Hubert H. Humphrey Cancer Research Center at Boston Univ. by Paul Black, director of the center. . . . **"CANCER RESEARCH**: Impact of the Cooperative Groups," is off the press and available in hardback from Masson Publishing USA Inc. for $44.50. Edited by Barth Hoogstraten, the book is a review of accomplishments of the Groups over their 25 years of existence, originally compiled for the review of clinical trials by the Div. of Cancer Treatment last year.

DRCCA BOARD TO WATCH CLOSELY CHOP EFFORT AS FIRST AWARDS ANNOUNCED

(Continued from page 1)

The six awards announced were:

Our Lady of Lourdes Hospital, Binghamton, N.Y., $123,600; Georgia Baptist Medical Center, Atlanta, $131,500; Deaconess Hospital, Evansville, Ind., $154,500; Penrose Hospital, Colorado Springs, $119,700; Marshfield Medical Foundation, Marshfield, Wisc., $117,480; and Southwest Washington Hospitals, Vancouver, Wash., $123,150.

The Vancouver CHOP will be the only one in the rural hospital category. There were only three proposals from rural hospitals; NCI determined the other two were not acceptable.

The Cancer Letter has learned that NCI is in the process of negotiating CHOP contracts with hospitals in the following communities:

- Multiple hospital category—Minneapolis, Cincinnati, Toledo, Roanoke, Brooklyn, and Wichita.
- Single hospital category—Los Angeles, and one other in Southern California; two others in Georgia; and one each in Ohio, Hackensack, and Dallas.

The Cancer Letter was not able to identify the other three communities in which negotiations may be in progress.

When NCI enters into negotiations with a prospective contractor, it means that that proposal has been identified through the review process as one which was selected to receive an award. However, it does not guarantee that an award will be made; that depends on the successful completion of negotiations.

Objectives of the CHOP awards were described recently to the DRCCA Board of Scientific Counselors, whose members indicated they would watch the program closely. The program "will field test in multiple community cancer care settings a model for the development of a multidisciplinary clinical oncology program," the report said. "The purpose of these community hospital oncology programs is to provide scientific evidence that implementation of the COP model (developed in the earlier Community Oncology Program) will improve the scope and quality of cancer care for patients over that received prior to development of the program."

The cooperating hospitals and health care professionals will:

- Plan and implement a program to encourage community cancer care practices in accordance with these criteria for care.
- Use a data management system (e.g. through upgraded tumor registries) to assess the extent to which community cancer care practices correspond to the recommended criteria.
- Use the information obtained to correct, modify, and improve the clinical oncology program and to document effective changes in community cancer care.

The report said the following assurances "should be considered essential elements of a clinical oncology program designed to bring optimal, multidisciplinary cancer care to the community:

"1. Appropriate and complete pretreatment evaluation and staging of newly diagnosed cancer patients.

"2. Multidisciplinary recommendations are incorporated into patient management decisions.

"3. Appropriate specialized treatment protocols are available in the community and referral to specialized centers will be facilitated for patients needing such care.

"4. Cancer nursing procedures are of the highest standards and are under the advice and guidance of trained oncology nurses.

"5. Necessary cancer rehabilitative and appropriate supportive care resources in the community are available and utilized.

"6. The terminally ill receive the benefits of modern pain and symptom management in an atmosphere that emphasizes the quality of survival and death with dignity.

"7. Up to date cancer management information is continually made available to physicians, nurses, and other health care personnel.

"8. A cancer data management system is in place that permits monitoring of program effectiveness, documentation of program accomplishments, assessment of community cancer care practices, and patient outcome status.

"9. The community cancer care program will continue after federal funding ceases."

Board member Charles Moertel expressed concern about how the program would be evaluated. "How will you separate (progress achieved through CHOP) from the phenomenon that there already exists rapidly increasing quality of care due to the increasing number of oncologists practicing in communities?" Moertel asked.

Donald Buell, DRCCA program director for medical oncology-community activities, replied that COP and CHOP were designed to provide a strong administrative base, to expand oncology nursing and allied health capabilities and other activities to the point where "the weight of evidence will determine if the program made a difference."

"To what extent do programs such as this exist without NCI funding?" Board member Peter Greenwald asked.

Buell was not able to answer that question, but said, "We're hoping to get a model, so we can say, this works, you can build your own, and it won't cost as much as it is for CHOP contractors because they will not have the reporting requirement."

DCCP BOARD APPROVES RECOMPETITIONS, ASKS OTHER INSTITUTES TO PAY SOME

The Board of Scientific Counselors of NCI's Div. of

Cancer Cause & Prevention gave concept approval for the recompetition of several of the division's large resource contracts and for the noncompetitive renewal of another resource contract and two research contracts.

New projects and one recompetition approved by the Board were reported in last week's issue of ***The Cancer Letter.***

Contracts which will be recompeted through issuance of RFPs:

Development of laboratory animal virus diagnostic reagents and operation of a service laboratory. First year award not to exceed $570,000. The DCCP staff narrative explaining the proposal:

The objectives of the competitive continuation of this ongoing contract are to provide serodiagnostic services for the detection of rodent viruses in laboratory rodent colonies; to provide the means to eliminate such viruses from laboratory animal populations; and to supply laboratory animal produced viral reagents and tumors in support of ongoing cancer research programs at NIH.

It is anticipated that the contract will perform approximately 40,000 serological tests on sera from mice, rats, hamsters and guinea pigs. Approximately 200 animal tissues, transplantable tumor and ascites lines, cell cultures and viral reagents will be tested for murine virus contamination via the mouse antibody production (MAP) procedure. Special tests for the detection of LDH virus in tumor or oncogenic viral preparations and XC plaque assays for the presence of murine leukemia in cell cultures and animal tissues will be performed. In addition, this contract will provide support service such as viral reagents, antisera, immunosorbent assays (ELISA), tissue samples, isolators, mouse breeding and autopsies to several NIH programs involving: (1) the effects of host genetics on the expression of murine leukemia; (2) the pathogenicity of murine type C virus isolates; (3) recombinant DNA risk assessment experiments and (4) assistance on the diagnosis and control of murine epizootics of suggested viral etiology.

Microbiological Associates Inc. is the present contractor and has received more than $500,000 in each of the last three years for work performed. DCCP had proposed that the contract be recompeted for three years.

Noting that up to 90 percent of the resources provided under the contract are used by NIH labs and that only 6 percent go to NCI labs, Board members expressed concern about the entire cost coming out of DCCP's budget. Brian Henderson suggested that other institutes be asked to share in the cost. Louis Siminovitch said that wider use of the resources by scientists outside NIH probably was due to lack of knowledge of their availability.

Henderson's motion that the contract be recompeted for one year rather than three, with negotiations to be undertaken with other NIH institutes to help pay for it, was approved.

Production, purification and concentration of potentially oncogenic DNA viruses. First year award not to exceed $315,000 on a three year contract. The narrative:

Of the viruses implicated in human cancer, perhaps the best case for a viral-tumor association can be made for EBV. It is important to provide sufficient amounts of the infectious and transforming virus and of viral DNA so that studies can proceed to further elucidate the possible role of this agent in human disease.

The competitive continuation of this contract will continue to prepare, process, purify and distribute high quality Epstein-Barr virus (EBV) of both B95-8 and P3HR-I strains. It is anticipated that the contract will supply, on a yearly basis, approximately 1.0×10^{10} transforming units of B95 virus, approximately 1.0×10^{10} early antigen inducing units of P3HR-1 virus and approximately 1200 μg of 55S EBV DNA for biochemical/molecular biology studies of the role of EBV in human cancer.

Life Sciences Inc. is the present contractor and received $260,000 in 1978 and $300,000 each of the following years under the contract. Although the renewal will be open for competition, Board member George Klein said, "There is no other source. They produce excellent material."

Production of avian myeloblastosis virus and AMV reverse transcriptase. First year award not to exceed $560,000 on a four year contract. The narrative:

An important aspect of studies of biological carcinogenesis involves studies utilizing cDNA copies of oncornaviral genomes or parts of such genomes for use as probes to identify viral sequences in normal or malignant tissues and to identify degrees of relatedness of various viruses. Such studies could aid in determining and assigning functions to various parts of the viral genome and in determining the possible function of postulated "src" or "onc" genes. For these studies, a large and consistently active supply of "reverse transcriptase" is vital. Additionally, reverse transcriptase is of great importance to certain recombinant DNA studies. Furthermore, the provision of large (multi-gram) quantities of avian myeloblastosis virus for studies on the mechanisms of induction of avian tumors is necessary.

Objectives of the competitive continuation of this ongoing project are the large scale in vivo production of BAI strain A avian myeloblastosis virus (AMV) and the preparation and distribution of AMV reverse transcriptase enzyme. It is anticipated that this contract will produce and distribute, on a yearly basis, approximately 150 grams of AMV, and 8 million units of reverse transcriptase to investigators in the United States and abroad.

Life Sciences Inc. is the present contractor and has received over $500,000 in each of the last three years. Fifteen percent of the material goes to NCI labs and the rest to outside investigators.

Noting that these materials are not commercially available, Siminovitch suggested that was because the NCI contract usurped the market. Jack Gruber, member of DCCP's Biological Carcinogenesis Branch, said they were available commercially at one time but that they were inferior.

"This is a classic dilemma," said Richard Adamson, DCCP acting director. "Certainly if it were available, we would get out of the business (of providing it)."

"This is the best bargain," Board member Charlotte Friend commented. "We would pay more for it commercially. This quality is superior."

Computer support for resources information data management. First year award not to exceed $250,000 on a three year contract. The narrative:

Objectives of the competitive continuation of this ongoing resource activity are to assist in processing, storage, and retrieval of data associated with the research resource compo-

nent of the Biological Carcinogenesis Branch. Computerization of resources data makes it possible for the branch to exercise close control over the inventory of viruses, sera, human tissues, and other materials provided by the branch and used in cancer research. In addition, computerization makes it possible to obtain rapidly information necessary to determine availability, location, quantity, etc. of all resources within the purview of the branch, thereby permitting rapid response to needs of the program while avoiding resource excesses or shortages.

Efforts will be directed toward: a) the design and development of new and revised systems for the management of the collection, storage, and distribution of research materials; b) data entry to support the operation of existing systems; c) the development and production of reports systems; and d) documentation of revisions to current and newly developed systems and programs.

The contractor uses NIH computer facilities, and that will continue under the new contract.

Reports on concept reviews by the boards of scientific counselors of NCI divisions provide readers of *The Cancer Letter* with advance notice of the institute's spending plans which will show up in RFPs and RFAs in subsequent months. Those interested in participating in programs approved by the BSCs should be aware of two points:

- The dollar figures cited as first year awards for each contract program are NCI staff estimates only and should not unduly influence development of proposals. These will be competitive awards and cost is a factor in selection of successful proposals.
- In no event should proposals be written until requests for proposals (in the case of contracts) or requests for applications (for grants and cooperative agreements) are available. Announcement of their availability will appear in *The Cancer Letter.*

The Board gave concept approval to three noncompetitive renewals:

○ Life Sciences Institute, about $400,000 a year for four years, for production and maintenance of selected reagent grade specific pathogen free animals.

○ Massachusetts General Hospital, not to exceed $280,000 for the first year on a two year renewal, for activation of oncogenic viruses and induction of cancer by immunologic and nonimmunologic methods.

○ Veterans Administration, an interagency agreement not to exceed a little more than $500,000 a year for three years, for an inhalation bioassay of cigarette smoke in male beagle dogs.

Similar studies have shown significant histologic changes in the respiratory tracts of beagles exposed to smoke from high tar, high nicotine cigarettes. The new study will evaluate the physiological and pathological effects of chronic inhalation of smoke from high, medium and low tar/nicotine cigarettes.

Cigarettes are manufactured specifically for the study, and the low T/N variety is equivalent to those on the market with 5 mg of tar or less. These cigarettes, however, do not contain the flavor additives which are present in most commercial low T/N brands, and NCI acknowledges that the test results will not present an accurate assessment of the hazards of those brands. The test will shed information on the relative effects of high, medium and low tar and nicotine exposure.

The Board approved the renewal if provisions are made to include the Ames test, CEA measurement and other appropriate markers.

DCT BOARD APPROVES CONCEPT OF NEW, RECOMPETED CONTRACTS: $11 MILLION

The Board of Scientific Counselors of NCI's Div. of Cancer Treatment has given concept approval to new contract supported projects with a first year estimated total of $3 million, and to recompetition of existing contracts with an estimated first year total of $8 million.

The new projects include a study on correlation between human tumor stem cell assay and phase 2 trials, calorimetry in cancer patients, evaluation of local hyperthermia treatment techniques, intraoperative radiotherapy, planning analysis for heavy particle radiotherapy treatment, and manufacture of capsules for delta-9-THC which DCT will distribute for treatment of nausea in cancer patients.

Descriptions of the new projects along with comments by Board members follow:

Correlation between human tumor stem cell assay and phase 2 trials. Estimated first year award of a three year contract, $300,000. The narrative:

The objective of this project is to establish the correlation between the effectiveness of chemotherapeutic agents tested in a laboratory assay of human tumors (namely, the human tumor stem cell cloning assay) and the efficacy of the same agent(s) tested in a clinical phase 2 trial. Specifically it is necessary to establish the ability of the assay not only to predict resistence, but also sensitivity in a series of patients with the same disease treated with the same drug. In addition, the proposed study should evaluate whether the tumors which do not grow in the assay have a clinical response rate equivalent to those which do grow.

The following trial design is suggested, but others will be considered:

1. The clinical study in a single agent/single disease phase 2 trial in patients with biopsiable tumor.
2. Prospective comparison of clinical and laboratory results (i.e. patient tumor to be biopsied and therapy with study drug begun immediately after biopsy so that clinical and laboratory results are collected and evaluated independently.
3. A single disease should be selected for study which a) is relatively sensitive to the proposed chemotherapeutic agent, b) has a high proportion of patients with biopsiable tumors, c) has a reasonable probability of growth in the laboratory assay. Preference will be given to offerors who propose to conduct this study in patients with the least prior chemotherapy.
4. The agent which is selected should be known to produce a clinical response frequency which is high enough so that the positive correlation (i.e. prediction of drug sensitivity) can be made with reasonable confidence.
5. The number of patients entered should be sufficient to

estimate the frequency of false positive and false negative correlations.

Calorimetry in cancer patients. Estimated first year award of a two year contract, $330,000. The narrative:

This project proposes the development of a clinical protocol for the longitudinal study of 24 hr. calorimetry in patients with cancer. Patients with a selected, surgically resectable tumor will be studied at the time of diagnosis, restudied when rendered tumor free, and then followed longitudinally until the time of relapse. Previous studies using the basal metabolism rate have been flawed by a poorly characterized, heterogenous patient population and methodologic assumptions. Furthermore, studies were brief, conducted at only one level of activity and nutrition, and at one point in the natural history of the disease. There was, however, a suggestion of increased metabolic activity. The methodology is now available for the prolonged continuous minute-to-minute monitoring of heat production and respiratory calorimetry with only moderate restriction on activity. The objectives of this project will be to confirm that patients with malignancy have an increased resting caloric expenditure; to ascertain whether patients with malignancy have an abnormal caloric response to exercise or to eating; and to ascertain the effect of protein-calorie supplementation on the caloric homeostasis of patients with advanced malignancy.

Board member Carmack Holmes noted that in the past the Board had determined that hyperalimentation studies should not have a high priority. John MacDonald replied that this proposed study was to "try to understand the basic mechanisms."

NCI Director Vincent DeVita said that the Board did approve one clinical trial which is under way. No benefit for hyperalimentation has been demonstrated yet and there are some complications, DeVita said.

"If there is a study that says this is not doing any good, why have a study that finds out why it is no good?" asked Board member Alexander Fefer.

"Patients do lose weight," MacDonald said. "With a study which reveals the mechanism of why they lose weight, perhaps we can devise treatment to help them gain weight."

"Something funny goes on leading to cachexia," DeVita said. "Also, others do not unanimously agree that hyperalimentation does not do any good. There is a lot of pressure on us to do more in nutrition, and we're trying to do more in the right way."

Evaluation of local hyperthermia treatment techniques. Estimated first year of a five year contract, $860,000. The narrative:

International interest in hyperthermia treatment of cancer has been rekindled over the past 10 years due to radiobiological evidence and clinical observations that it is a potent radiosensitizer. Furthermore, heat appears to potentiate the effects of some chemotherapeutic agents and can also be tumorcidal in its own right. Because of these preliminary results, numerous phase 1, 2, and 3 studies have been initiated. At this time there is lack of clarity as to clinical goals, proper equipment to use in different circumstances, accuracy in temperature and monitoring, and radiobiologic engineering; i.e., sequencing of heat and radiation, etc. It appears that the usefulness of the several heat generating modalities (radiofrequency, microwave and ultrasound) will vary depending upon the location of the tumor and normal tissue composition.

This project is designed to develop a coordinated program at five or six institutions with demonstrated expertise in clinical hyperthermia and which have at least one state of the art heat generating device (microwave, radiofrequency, and ultrasound). It is intended that NCI will provide a second state of the art device if necessary which differs from that at each of the participating institutions so that comparative studies of the advantages and disadvantages of each of the heat generating modalities can be evaluated for major anatomical regions (brain, head and neck, superficial lymph nodes, mediastinum, lung, upper abdomen, pelvis, and extremities). An important need exists to document these advantages and disadvantages with consistent endpoints and similarity of the temperature measuring devices. Only then will the clinical results be fully interpretable. After one and one-half to two years of evaluating the heating techniques in the various anatomic sites, clinical phase 2 studies will be conducted to standardized treatment procedures for selected tumors. The increased communication and coordination of effort among these institutions should provide a foundation for definitive phase 3 randomized trials by one or more of the clinical trials groups at the end of the third year.

David Pistenma, chief of the Radiotherapy Development Branch, said that NCI is spending $4 million a year on hyperthermia, about half in equipment development grants. The studies are not coordinated and involve "hundreds of patients at a number of institutions." The proposed study will be aimed at selecting "the best equipment available and develop guidelines for its use. The situation is getting out of control. We're at a very basic stage (in use of hyperthermia), and we would like to bring some order into it."

Board Chairman Samuel Hellman said, "In areas where there is a lot of interest, grants should be used unless there is good reason otherwise. I'm convinced this field is in disarray, and the contract mechanism is appropriate."

A motion to approve the project was approved after Board member Enrico Mihich offered an amendment to require program review at three years with the possibility contracts would be terminated at that time. Mihich's amendment was approved, with Sharon Murphy and Sydney Salmon voting against it.

Intraoperative radiotherapy. Estimated first year award on a five year contract, again with a program review at three years with the possibility of termination then, $180,000. The narrative:

Over the past 25 years little progress has been made in the treatment of gastrointestinal malignancies. Local-regional failure and the development of distant metastases are problems of comparable scale in cancers of the pancreas, stomach, and rectum. Attempts at improving local control rates with external beam radiotherapy alone or with interstitial implants have been unrewarding. The limiting factor is the radiosensitivity of the small intestine, liver, and kidneys which compromise the radiation dose that can be delivered safely. A recent initiative for the improvement of local control is the use of intraoperative radiation therapy with electrons or with orthovoltage x-ray equipment. During the surgical procedure the tumor bed is exposed and the normal tissues are removed from the tumor bed. A single large dose of radiation can then be delivered to the tumor bed either alone or in combination with a radiation sensitizing drug, the optimum means of using the latter agent. Supplemental external beam radiation therapy can be given before surgical procedure or after healing of the surgical

wound. Preliminary results with regard to local control and the lack of complications in studies conducted at NCI and Massachusetts General Hospital are encouraging.

Presently, three institutions are conducting phase 1/2 studies and at least three additional institutions are expected to begin intraoperative radiation therapy studies within the next year. This project is intended to provide coordination of the intraoperative radiotherapy programs at five or more institutions and to provide support for clinical research and patient care at these institutions. The coordination activities will include 1) establishing a central registry of information on patient treatment and treatment equipment and techniques and 2) establishing a committee to develop common guidelines for surgical and surgical pathology procedures, radiation dosimetry, treatment techniques, and data management. Further meetings of the principal investigators would facilitate improvements in techniques, both for increasing local control and reducing complications. At the conclusion of the phase 1/2 studies conducted by this small contract-supported group, it is hoped that standardized procedures will have been developed sufficiently to allow incorporation of the intraoperative program into randomized phase 3 clinical trials by one or more clinical trials groups.

Heavy particle radiotherapy treatment planning analysis. Estimated first year award on a three year contract, $275,000.

The high priority heavy particle radiotherapy program consists of pretherapeutic studies and both phase 2 and 3 studies with neutrons, pi mesons, protons, helium ions, carbon ions, and neon ions. The clinical program has been limited by physical constrains of equipment designed primarily for physics purposes, the small number of patients that can be treated on an annual basis, and lack of ability to deal with tissue inhomogeneities in treatment planning and treatment. NCI is providing for clinically dedicated neutron therapy systems (two will commence operation in 1981 and two in 1983) which will both increase the number of patients that can be treated and the sophistication of the treatment. Dedicated CT scanners have been provided to the Lawrence Berkeley Laboratory, Los Alamos Scientific Laboratory, and Massachusetts General Hospital for the particle therapy programs at those facilities. Software is just now being developed to utilize electron density information from CT scanners to incorproate density and homogeneity corrections into radiotherapy treatment planning which is absolutely essential for charged particle therapy and highly desirable for neutron therapy. Thus, it is now possible to evaluate the capabilities of each type of particle beam in treating tumors in each major anatomic site (brain, head and neck, superficial lymph nodes, pelvic and para-aortic lymph nodes, mediastinum, lung, upper abdomen, pelvis, and extremities.)

These studies will provide for an integrated effort by radiotherapists, physicists, and radiobiologists to define the advantages and disadvantages of the treatment of tumors in each of these anatomic sites with each type of particle beam by 1) performing sophisticated treatment planning using CT scan derived electron density information for inhomogeneity corrections; 2) confirming the dose and LET spectrum distributions for each particle beam for tumors in each of the anatomic sites in patients insofar as possible or in complex phantoms; and 3) relating the dose and LET spectrum distributions to OER, RBE, and other pertinent biological parameters by using existing radiobiological data or performing additional radiobiological experiments. This heavy particle radiotherapy treatment planning analysis will supplement information from ongoing clinical trials to guide the design of future clinical protocols and to assist in establishing future construction needs.

Manufacture of clinical formulations in soft gelatin capsules. Estimated first year award of a three year contract, $300,000. The narrative:

This contract will be utilized to manufacture dosage forms of delta-9-tetrahydrocannabinol (delta-9-THC). This need has been generated by a sudden mushrooming of interest in this drug. Previously it had been distributed in small amounts for research purposes by the National Institute on Drug Abuse. NIDA does not now have the capability or willingness to meet the expected enormous demand for use by cancer patients. Presently, NCI does not have the capability to manufacture this highly specialized soft gelatin dosage form either. The work scope of this contract will include formulation of various strengths of delta-9-THC, appropriate quality control testing of the bulk and finished product, packaging and labelling. All products manufactured under this contract must be prepared under FDA's Current Good Manufacturing Practices.

Shelf life evaluation of clinical drugs. Estimated first year award of a three year contract, $300,000. The narrative:

This contract will involve the use of outside contract facilities and capabilities to provide a resource for shelf life evaluation of clinical drugs for the Div. of Cancer Treatment. This contract is considered essential to meet the increasing program needs for shelf life information both for complying with FDA's Current Good Manufacturing Practices and for our own use in determining proper storage and handling of the products. One of the major areas of impact of the CGMPs is the greatly increased, extensive shelf life and stability testing requirements. Establishing a separate shelf life testing contractor would free the formulation contractors of this burden, provide to NCI timely, uniform testing and reporting of the shelf life of the clinical drugs, and help NCI meet the expanded FDA requirements. The work scope of this contract will include storage of assigned samples of clinical products under various specified conditions for at least four years, analytical and pharmaceutical evaluation of these products on a prescribed timetable, and preparation of reports of the results of such testing for determining expiration dates in support of NCI's INDs. The contractor will provide experienced personnel well versed in the chemical and pharmaceutical evaluation of clinical drugs (especially injectables) and knowledgeable in FDA's requirements as they apply to such testing. The key personnel must have a demonstrated ability in developing stability-indicating analytical methodology for clinical products.

Quick reaction task order for clinical trials. Estimated first year award on a five year contract, $500,000. The narrative:

The aim of this project is to provide new flexibility and scope to the cooperative clinical trials program. Currently clinical trials are funded after peer review for 3, 4, or 5 year periods. Budgetary constrains can limit the flexibility of performing clinical trials within the Cooperative Groups. For example, if a new concept for clinical trials is developing which will require funding in addition to the available grant funding, support must be obtained through a grant supplementation, new grants or the development of a grant supported intergroup study in which members from several different cooperative groups participate. All of these approaches to funding require 9-12 months before monies can be awarded to investigators.

It is proposed that operation offices of Cooperative Groups would compete for these contracts. When master contracts have been awarded, NCI staff will develop requests for the initiation of several types of clinical trials. The tasks must be determined to be of high priority by NCI and might include the types of tasks illustrated by the following examples: 1. Sophisticated chemotherapy trials which would require specialized laboratory support. For example, studies utilizing combinations of agents designed to produce synergism through biochemical modulations. These could include such combination chemotherapy studies as 5FU + PALA, 5FU + thymidine, and deoxycoformycin + Ara-A. 2. Intergroup studies. These would be studies which would require the pooling of patient resources from several groups to complete. Such studies may

require very large numbers of patients or patients with either rare diseases or uncommon stages of more common disease. For example a randomized chemo-immunotherapy study of stage 1 & 2 melanoma has been proposed which will require in excess of 100 patients with early stage melanoma and cooperation in treatment by surgeon, immunotherapist and chemotherapist. This study could only be performed under the intergroup mechanism.

The awarding of task order contracts to the operations offices of Cooperative Groups will add new flexibility and rapidity of response for clinical trials. The task order mechanism will alow the CTEP to award monies for innovative clinical trials or intergroup studies to investigators within 90-120 days rather than 9-12 months.

Planning, analytical and conference support services. Estimated first year award on a two year contract reserved for small business, $150,000. The narrative:

Over the past several years, the scope of the Cancer Therapy Evaluation Program has been strengthened and expanded. In concert with recommendations of the Board of Scientific Counselors, new emphasis has been placed on cancer therapies other than those emerging from the division's Drug Development Program. Nationally known physicians have joined the program and have begun to support and encourage new areas of cancer treatment research. The tasks performed under this contract will be in support of developing new treatment modalities and combinations, including the following kinds of projects: a) logistical support for conferences designed to elucidate the state of the art in various cancer therapies, to provide a framework for planning future directions in cancer therapy research, and to provide advice to the program about new areas of research, b) collection and analysis of data in the field of biomedical research as well as documentation of conferences that have been held, and c) administrative support such as transcription, editing, and publication of conference proceedings. A partial list of the topics for workshops and conference to be assisted under this contract in 1981 includes:

High LET radiobiology, high LET radiologic physics, two radiosensitizors working groups, two meetings of the Council of Radiation Oncology Chairpersons, hyperthermia, intraoperative radiotherapy, basic combined modality studies, clinical combined modality studies, whole body radiation for treatment of malignant lymphomas, use of radiosensitizors and radioprotectors with chemotherapeutic agents, new drug liaison meeting, Phase 1 Working Group meeting, Osteosarcoma Working Group meeting, soft tissue sarcoma meeting, and Renal Carcinoma Working Group meeting.

A second type of requirement under this contract will be for necessary quick reaction to requests for graphics, presentations, and documentation in direct support of CTEP. This contract will provide CTEP more flexibility in planning and executing its mission in support of clinical research.

DCT contract programs approved for recompetition will be reported in next week's issue of The Cancer Letter.

FEDERAL GRAND JURY CLEARS EPPLEY, SHUBIK OF MISCONDUCT ALLEGATIONS

The federal grand jury which has been investigating allegations of possible criminal misconduct at the Univ. of Nebraska's Eppley Cancer Institute for the past 18 months has found no evidence which would support those charges.

The grand jury report on the probe said "the investigation is herewith closed."

The investigation was initiated following a report by the General Accounting Office on its study of Eppley's carcinogenesis research contract with NCI. GAO found what its staff felt were a number of irregularities, most of which involved failure to meet reporting requirements by Eppley and failure to properly monitor the contract by NCI. GAO also objected to what it said was lack of clear separation between Eppley's federally supported activities and work the institute performed on contract for private industry. The NCI contract has been phased out.

Charges also were made by others, including some critics of Eppley and its director, Philippe Shubik. The grand jury report cleared Eppley and Shubik of those charges, too.

Shubik, who appeared before the grand jury voluntarily and cooperated with the investigation, said he was gratified by the report but expressed regret for the damage suffered by Eppley due to the allegations. Shubik has been on sabbatical for more than a year as a visiting professor at the Univ. of Heidelberg.

The grand jury report said:

"Based on a careful consideration of all of the testimony, documents, records, and summaries of interviews, the grand jury has reached the following conclusions:

"1. Personal services. The available evidence falls short of establishing the kind of concerted, intentional abuse that would justify a presentment of federal criminal charges with respect to said occurrences.

"2. Double-dipping. The available evidence as to this allegation does not suffice to demonstrate intentional fraud on the part of either Eppley employees or of the Eppley Cancer Institute's administration. Thus, this allegation is not supported by evidence sufficient to give rise to federal criminal charges.

"3. Kick-backs. The grand jury has developed no significant evidence establishing that payments of kickbacks were ever made to Eppley employees for services and supplies furnished to the Eppley Cancer Institute.

"4. Univ. of Nebraska Foundations. The grand jury is unable to determine that these claimed irregularities rise to the level of criminal fraud within the meaning of the federal criminal code.

"5. Non-federal research. The grand jury is unable to find, on the basis of the evidence available to it, any knowing, intentional, and concerted scheme or artifice to defraud the federal government on the part of any of the responsible administrative or research personnel at the Eppley Cancer Institute. For that reason, the grand jury has determined that federal criminal charges in the general nature of 'fraud against the government' would not be appropriate.

"6. Support services. The final allegations explored in detail by the grand jury raised the question of whether Eppley Cancer Institute support services (i.e., test animal supply and maintenance and histo-

logy services), funded entirely by the federal government pursuant to the contract between the National Cancer Institute and Eppley, were utilized for the performance of non-federal industrial contract and grant research.

"The evidence developed over the course of this investigation is inadequate with respect to this allegation to support the return of federal criminal charges against responsible individuals at the Eppley Cancer Institute. The grand jury cannot fairly conclude that there was any intentional, conscious, or willful scheme to defraud the federal government on the part of any person or persons at the Eppley Cancer Institute.

"7. Additional allegations. Over the 18-month period of its investigation, the grand jury also explored in depth an assortment of additional allegations of criminal misconduct at the Eppley Cancer Institute. None of those allegations are supported in the evidence adduced before the grand jury, and they will thus not provide a basis for presentment of federal criminal charges.

"By way of summary, then, it is the conclusion of the federal grand jury, based solely upon the evidence adduced before it in the course of its investigation, that no sufficient factual basis exists to support the presentment of an indictment charging any person or persons at either the Univ. of Nebraska generally or at the Eppley Cancer Institute specifically with violations of federal criminal statutes."

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. Some listings will show the phone number of the Contract Specialist who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Address requests to the Contracting Officer or Contract Specialist named, Research Contracts Branch, National Cancer Institute, Blair Building, 8300 Colesville Rd., Silver Spring, Md. 20910. Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CO-14340-36

Title: *Analytical services in support of the Div. of Extramural Activities of NCI*

Deadline: *Dec. 3*

NCI has a requirement for analytical and technical support services for the Div. of Extramural Activities. Under a recent reorganization, DEA has the following responsibilities:

—Fiscal administration of all grants awarded by NCI.

—Scientific review of all grant applications and research contract proposals assigned to NCI.

—Programmatic administration of the research training program, construction program and organ site program.

—Serving as executive secretary to the National Cancer Advisory Board.

To fulfill this basic support role, DEA must coordinate its activities with all other divisions of NCI to minimize duplication of efforts and increase efficiences of other divisions in the management of their research programs. Specifically, contractor support in the following task areas will be required: Analytical support, data collection, data analysis, financial/fiscal data analysis, conference coordination and documentation coordination.

This project is for a one year period. Offerors will be limited to those firms having operating facilities within a 50 mile radius of Bethesda, Md. as daily person-to-person contact is often necessary.

Contract Specialist: Barbara Tanenhaus
Biology & Diagnosis
301-427-8877

NCI CONTRACT AWARDS

Title: Development and validation of an in vitro mammalian cell mutagenesis system for carcinogenesis screening, continuation

Contractors: SRI International, Menlo Park, Calif., $451,556, and Litton Bionetics, $489,854.

Title: Carcinogenicity studies in rodents

Contractors: International Research & Development Corp., Mattawan, Mich., $1,888,701, and Microbiological Associates, $1,500,402.

Title: Long term followup of Breast Cancer Screening Project participants

Contractor: Samuel Merritt Hospital, Oakland, Calif., $559,934.

Title: NCI budget formulation and fiscal projection model

Contractor: JRB Associates, $202,043.

Title: Synthesis of radiolabeled retinoids for metabolic and pharmacologic studies

Contractor: SRI International, $757,012.

Title: Carcinogen bioassay of three chemicals: N-methylolacrylamide, vinylcyclohexene diepoxide and ethylenediamine

Contractor: Battelle Memorial Institute, Columbus Laboratories Division, $1,639,416.

The Cancer Letter _Editor Jerry D. Boyd

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