THE CANCER LETTER

Vol. 13 No. 28

July 10, 1987

Subscription: $160 year North America, $175 year elsewhere

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

PRI, Fending Off More Giants, Reportedly Wins New Operations/Support Contract At Frederick

Program Resources Inc., the little company that beat out giant Litton Industries five years ago for the huge operations and support contract at Frederick Cancer Research

(Continued to page 2)

In Brief

Sartorelli AACI President, McIntyre President Elect; Moertel To Receive ACCC Clinical Award

ALAN SARTORELLI, director of Yale Comprehensive Cancer Center, assumed presidency of the Assn. of American Cancer Institutes at the organization's annual meeting in Tucson. He replaces **John Potter**, director of the Lombardi Cancer Research Center. **Ross McIntyre**, director of the Norris Cotton Cancer Center, was elected vice president and president elect. New board members are **John Kovach**, director of Mayo Comprehensive Cancer Center; **Kenneth Olden**, director of Howard Univ. Cancer Research Center; and Sydney Salmon, director of the Arizona Cancer Center. . . . **CHARLES MOERTEL**, chairman of the North Central Cancer Treatment Group and first director of the Mayo Cancer Center, will receive the Assn. of Community Cancer Centers' first Clinical Research Award for outstanding achievement in clinical research. The award will be presented Oct. 2 at ACCC's fall leadersship conference in Chicago. . . . **"PERSPECTIVES IN** Cancer Treatment" is the title of a satellite symposium which will be Nov. 1 in Madrid, to be held during the Fourth European Conference on Clinical Oncology. Sponsored by Bristol-Myers, the symposium will be chaired by Gianni Bonadonna. Faculty will include Lawrence Einhorn, Richard Gralla, Tate Thigpen, John Ruckdeschel, Richard Cooper, Pat Loehrer, Aman Buzdar, John Clark, Niall Heney, Ki Hong and Jack MacDonald. . . . **ROSE KUSHNER**, author, activist on behalf of breast cancer patients and former member of the National Cancer Advisory Board, will receive the American Cancer Society Medal of Honor at the ACS annual banquet in November. . . . **MAGNETIC RESONANCE** imaging will be the subject of an NIH consensus development conference Oct. 26-28. Questions the conference will address include: Are there contraindications to or risks of MRI? What are the technological advantages and limitations of MRI? What are the clinical indications for MRI, and how does it compare with other diagnostic modalities? What are the directions for future research in MRI?

PRI Apparently Wins Seven More Years As Major FCRF Contractor

(Continued from page 1)

Facility, apparently has done it again. This time, the Annapolis based firm won the re-competition of the $60 million plus a year contract over proposals by a consortium of two international giants and another company more than 30 times PRI's size.

NCI is still engaged in negotiations with PRI on the new, seven year contract. Neither the company nor NCI will discuss any aspect of the situation or confirm that PRI in fact is the winner. **The Cancer Letter** has learned, however, that the other contenders have been informed that they are out of the running.

NCI had hoped to wrap up the negotiations by mid-July and make the announcement of the winners by the end of the month. That time-table might be held up somewhat, with the announcement now due in mid-August.

Four other contracts are involved in the recompetition: the basic research program, held by Bionetics Research Inc., the successor to Litton Bionetics Inc.; animal holding, held by Harlan Sprague Dawley; computer services, held by Information Management Services; and library services, held by Data Management Services Inc. The latter two are small business set asides.

Bionetics Research Inc. was in the enviable position of having the basic research field to itself, with no other organization willing to compete for that contract. The others reportedly were hotly contested.

PRI is totally owned by Richard White and William Donlon, each owning 50 percent of the company's stock. White is president, Donlon secretary; both are directors. Raymond Gilden is principal investigator for the FCRF contract and director of PRI's operations there. Thomas Compton is second in command and director of contracts and operations.

When PRI won the operations/support contract in 1982, it had about 200 employees. That number almost immediately jumped to 1,000, with 800 at Frederick alone.

The contract totaled $45.2 million in the 1986 fiscal year, and leaped to an estimated $66.3 million this year as NCI located much of its AIDS research there, along with LAK-cell-interleukin 2 work and other drug development efforts. The Biological Response Modifiers Program is located there, as is NCI's new supercomputer. The operations/support contract contributes to all of those efforts.

It has been estimated that the contract will involve more than $80 million by FY 1988.

All except the basic research contract are cost plus award fee contracts, with profits paid as awards from a pool set aside for that purpose for each of the four. PRI's award fee was close to $2 million last year.

The size of the contract--the largest in the history of NIH--attracted some heavy-weights this time. Bechtel Corp. and Battelle Memorial Institute joined forces in one proposal. Bechtel has annual revenues ranging from $8-15 billion a year, a professional staff of 30,000 and nonprofessional of 80,000. Battelle has 7,800 professional employees.

EGG, a publicly held company with 24,000 employees and annual sales of more tha $1 billion, submitted the other proposal which went to the final round with Bechtel/Battelle and PRI. One of EGG's subsidiaries is Mason Research Institute, which has performed a long list of tasks for NCI, NIH and the National Toxicology Program.

Proposals which did not make it into the finals were submitted by ICF Clement, which collaborated with the 14,000 employee, $750 million a year services firm, Dynalectron Corp.; and Bio-Molecular Technology Inc., a company formed by Berge Hampar, who had been NCI's general manager at FCRF.

PRI, under an agreement made last year which settled an intracompany dispute with Gilden and Compton, will split its award fee equally with about 50 of its key employees at FCRF. The fee is determined and awarded every six months. The pool set aside for it most likely will increase as the size of the contract increases. The percentage of the available amount probably will increase, if the history of PRI's first contract is a guide. The company started by getting only 53 percent of available money in its first six month period. In the six months which ended, March 31, 1986, PRI received 73 percent.

One of the factors in the failure of PRI's competitors may have been that they would have brought in their own people for the positions held by Gilden and Compton, and perhaps other key jobs. Gilden has been at FCRF for the entire 15 years since NCI took it over from the Army. NCI staff knows what Gilden and Compton can do; they couldn't be certain about new people in top positions.

DCE Board Okays Concepts For New Grants, Contract Recompetitions

Two new grant programs which would provide up to $3 million a year, a new contract for as much as $550,000 a year and recompetition of three contracts totaling $2.65 million a year--all in the Epidemiology & Biostatistics Program--have received concept approval from the Board of Scientific Counselors of NCI's Div. of Cancer Etiology.

The new contract supported project and one of the new grant RFAs (request for applications) will support AIDS related studies. The other grant project (actually, an RFA for cooperative agreements) will support development, validation and application of biochemical markers of human exposure and susceptibility for use in epidemiologic studies.

Contracts being recompeted include the $1.6 million a year support contract for radiation studies.

Descriptions of the concept proposals, which will be developed into RFAs (for grants) and RFPs (for contracts) follow, along with discussion by Board members and DCE staff:

Epidemiologic studies of HIV associated malignancies. A total of $2 million a year (increased by the Board from $1.5 million proposed by staff) will be set aside to fund about five grants, each for five years.

Since the association of AIDS with Kaposi's sarcoma (KS) and non-Hodgkin's B cell lymphoma (NHL) became apparent, NCI has been active in attempting to stimulate research in this area. Although many reports linking KS and NHL to AIDS have appeared in the literature, the precise relationship between malignancies and human immunodeficiency virus is unclear. Study sections have had difficulty in reviewing proposed epidemiologic studies in this area, due to the highly exploratory nature of the laboratory components.

As more individuals become infected with human immunodeficiency virus (HIV), and infections persist for longer periods of time, case reports suggest that cancers other than KS and NHL, early occurence of malignancies, and unusually aggressive tumors may also be associated with HIV infection. There is significant public health concern about the incidence and distribution of malignancies in infected population groups. Reduction of the rapid mortality now associated with AIDS by new treatment methods may lead to an increase in the recognition of HIV associated cancers.

The etiology of HIV associated malignancies may be based on retroviral oncogenicity or the consequences of immune alterations that potentiate the development of neoplasia. Further study of HIV associated malignancies will enhance understanding of the initiation and promotion mechanisms of virus related malignancy, the specific immune alterations predisposing to cancer, and the factors influencing tumor presentation and progression. For example, the incidence of KS differs among the populations at risk for AIDS; it remains to be determined whether concomitant infections, variations in viral strains, or differences in immune alterations are responsible.

A working group of experts in this area last year recommended the following (with reviewer comments included):

<>NCI should encourage further studies using pathologic, biologic, virologic and immunogenetic probes with the aim of elucidating the etiologic agents of KS and NHL that occur in HIV infected individuals.

<>Established cohorts currently being followed for AIDS incidence should be studied for the development of cancers, including malignancies other than KS or NHL. Others at risk for HIV infection, such as intravenous drug abusers and children of HIV infected mothers, should be studied more closely, because of differenes between risk groups in the incidence of malignancies.

<>Research focusing on host factors is recommended with particular attention to immunologic responses to viral antigens.

<>Attention should be paid to the effect of AIDS treatments on the incidence and natural history of HIV associated malignancies.

<>Studies of the malignancies occurring in individuals coinfected with more than one retrovirus, or with HIV and unrelated viruses, should be undertaken.

The objective of this RFA is to stimulate epidemiologic investigations to establish:

A. With greater precision the incidence, natural history and etiology of malignancies in HIV infected individuals, including malignancies other than KS or NHL.

B. Whether any epidemiologic risk factor patterns or laboratory analyses suggest an underlying mechanism of carcinogenesis in contrast to other clinical outcomes of HIV infection, including:

1. The effect of HIV genetic variation and coinfection with related retroviruses or unrelated viruses on the development of specific malignancies.

2. The relationship between the severity and expression of immune alteration in HIV infected individuals and specific forms of cancer, for example, the presence of antireverse transcriptase antibodies, neutralizing antibodies, and cytotoxic T-lymphocytes and their relationship to tumor development.

3. The effect of host factors such as histocompatibility antigen polymorphisms on susceptibility to HIV related malignancies.

C. The relationship of AIDS treatments and related immune perturbations to tumor development and progression.

Epidemiologic research relevant to this RFA includes, but is not limited to:

A. Epidemiologic studies, such as nested case control studies in existing in existing cohorts at risk for HIV infection, comparing individuals who develop malignancies with individuals who have other outcomes of infection for differences in host factors (e.g., genetic, chromosomal, and immunologic) and in causal agents or cofactors.

B. Epidemiologic studies comparing HIV associated tumors with their nonepidemic counterparts of the same pathologic types, including those occurring in other immunosuppressed states or appropriate comparison groups, to evaluate the role of host factors, causal agents, and cofactors.

Proposals responding to this RFA must pay special attention to questions of:

*Selection of appropriate laboratory measures useful in epidemiologic studies of HIV associated malignancies.

*Establishment of appropriate data base linkages

for case ascertainment within defined populations.

*Timely case ascertainment, for data and specimen collection, of malignancies tht are generally rapidly progressive, and completeness of case ascertainment when diagnosis may be purposely concealed.

*Techniques for tumor tissue collection and preservation.

*Standardized diagnostic techniques applicable to tumors that may remain undiagnosed until death, such as presymptomatic NHL of the central nervous system, or KS and NHL of lymph nodes.

*Representativeness of subjects selected for study, and selection of appropriate comparison groups.

*Confidentiality for study subjects, and issues surrounding determination and disclosure of HIV antibody status.

The multidisciplinary collaboration of epidemiologists, clinicians, virologists and other laboratory scientists will be essential for delineating etiologic mechanisms. Investigators responding to this RFA must be willing to participate in annual meetings to discuss problems and developments. Relevant data to be collected could include epidemiological risk factors, pathological confirmation of diagnosis, presence and titer of antibodies to HIV, presence of specific viral antigens, identification of free viruses or latent viral infections, tests of immune function, or cytogenetic analyses.

Iris Obrams, program director, presented the concept. Board member George Vande Woude questioned whether the staff's request of $1.5 million, which Obrams said would support three to four grants, was enough. "This is a unique time for these studies," he said. "All the stops should be pulled out, and get as many funded as possible."

"I would be willing to try to find another $500,000," DCE Director Richard Adamson said. "We probably will have enough AIDS money to do that. We would stay within the paylines, of course."

Development, validation and application of biochemical markers of human exposure and susceptibility for use in epidemiologic studies. This is a reissuance of an RFA first issued in 1985. Staff had asked for $800,000 a year, but the Board increased that to $1 million at Adamson's suggestion.

The problem of identifying effects of specific risk factors and evaluating their relative importance is an enormous one. Multiple exposure to a variety of agents

- -

The dollar estimates with each concept brought before the various boards of scientific counselors or other advisory groups are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended as guides for board members to help in determining the value of the projects in relation to the resources available to the entire program or division. In the case of RFAs, the amounts cited are the maximum that will be set aside to fund those particular grants, the final amount depending on NCI's budget and program priorities. Responses should be based on workscope and description of goals and methods included in the RFPs (contracts) or RFAs (grants and cooperative agreements). Availability of the RFPs and RFAs will be announced when NCI is ready to release them.

- -

over extended periods is the rule rather than the exception, and a wide range of susceptibility mechanisms may also be involved in carcinogenesis.

The usual epidemiologic techniques have been limited in their ability to reach firm conclusions by difficulties in defining past carcinogen exposure levels and susceptibility states, in evaluating low levels of risk, in assessing host/environmental interactions, and in estimating the biologically effective dose of carcinogens to the target tissue.

Many approaches to classifying past exposure have been utilized in recent epidemiologic studies with varying degrees of success. Such approaches include, for example, the assignment of individuals to exposed and unexposed categories on the basis of (1) past employment in a particular industry, (2) a record of job types held in the past, (3) use of ambient air monitoring data and soil or water quality measurements, or (4) questionnaire data on lifestyle factors such as diet and smoking history. The extent to which these surrogate measures of exposure reflect reality is questionabale, particularly when exposure is to complex mixtures of agents. The potential classification errors may be serious effects on study outcome. The inability of these methods to assess delivered dose to target tissues is also a serious limitation.

It would clearly be advantageous to have available biochemical measures (preferably minimally invasive) that would provide unambiguous markers of past exposure and perhaps permit a quantitative assessment of the extent of exposure. Certain substances, for example, are either passively accumulated or actively incorporated into body tissues. Others may react chemically with target molecules in the body or evoke immunologic or enzymatic responses which persist for extended periods. Such procedures, if available, would also allow one to study variation in human response to a shared exposure. This would be of great value in defining groups at varying risks, an essential prerequisite for preventive action.

The activities to be supported under this intiative will be investigator initiated. The specific approaches and methodologies best suited to accomplish the objective will be proposed by the extramural scientific community and evaluated for their scientific merit through the usual peer review process. The initiative will support research studies having as their principal objective the generation of information which is critically important for the conduct of future epidemiologic efforts utilizing laboratory probes. It is anticipated that persons responding to the RFA will be primarily (although not exclusively) basic scientists with extensive experience in the development and use of biochemical markers in laboratory settings, but with limited experience in the application of such methodology in epidemiologic settings. In the early phase methods development, the requirement for epidemiologic input is of lesser importance. However, as such methods reach the stage of validation and pilot application, epidemiologic considerations become critically important. At this point, if not before, epidemiologic collaboration should be evident in the application. A small group of government scientists will assist the award recipients by (1) consulting on proposed methodologies to maximize their epidemiologic utility, (2) providing a resource of information on the extent and distribution of exposures, and (3) providing information on cohorts of exposed individuals which could provide material for methods development and validation.

Objective of the proposed initiative is to encourage investigations designed to identify, characterize, validate and apply measurement methods for biochemical markers of exposure/susceptibility which would be useful in the conduct of epidemiologic studies. Applications may focus on any, some, or all of these phases in the development of useful laboratory methods. In the event that validation or application activities are proposed, it is important that competent epidemiologic collaboration be incorporated for those aspects of the study. Such factors as ease of conduct and expense as well as collection, storage, and transport problems should be considered along with the accuracy and precision of the method. For markers

demonstrated to have utility, assessment of the extent of intra and interindividual variability is important. Consideration should be given to biological variables, such as age, genetic predisposition, nutritional status, preexisting disease and lifestyle which may alter host response to a variety of carcinogens. Investigations in animal systems dealing with quantitative aspects, such as studies of sensitivity and specificity of assays for DNA and protein adducts, may be proposed as a component of investigations under this announcement. The range of materials, for which markers are of interest, is extremely diverse. Included would be any substance which has been proposed to alter the risk of malignancy and is so distributed that significant human exposure is likely to have occurred.

The seven grants funded under the 1985 RFA were awarded to Kurt Randerath, Baylor College of Medicine, for detection and measurement of human DNA adducts; Roger Giese, Northwestern, for chemical digestion-GC/MS analysis of DNA adducts; Ruggero Montesano, International Agency for Research on Cancer, for detection of alkylated DNA bases in human tissues; Rogene Henderson, Lovelace Biomedical Environmental Research Institute, for marker of exposure to pollutant gases; Sidney Mirvish, Univ. of Nebraska, establishing the basis of the nitrosoproline test; Frederica Perera, Columbia, biological markers of ethylene oxide and styrene exposure; and Helmut Bartsch, IARC, DNA damage as a marker of exposure to betel/quid tobacco.

A.R. Patel, program director, said that 30 applications were submitted in the first round, 22 approved and seven funded. Adamson added, "We paid everyone within the payline. Several more were within 10 points and could have been funded with an additional $1 million. I wouldn't object if we made this one up to $1 million. We would still stay within the payline (and not commit the entire amount if not enough grants scored under the payline to require that much)."

"I'm concerned about this," Board member William Benedict said. "On the positive side, the work going on now is high level, and the people doing it are the best. But I am concerned that we are going to spend $1 million while knowing nothing about what is going on with the seven awards. This is not a complete presentation."

John Cooper, chief of the Extramural Programs Branch, commented that those grants had been funded late in the year and that the first program reports had arrived only the previous week.

"One of the reasons for reissuing this is that so many came in last time," Adamson said. "These type of grants have a problem in the RO1 pool. Study sections do not have the appropriate expertise in molecular biology and/or markers." With an RFA, a special study section can be made up to more adequately review the applications.

"I'm excited about this," Board member Dietrich Hoffmann said. "Previous studies have opened up the methodology. Now we can be concerned with uptake and metabolism of carcinogens. Now we can measure what happens to metabolic uptake of carcinogens."

Board member Lee Wattenberg said that although he supported the concept, "markers of a more general nature are missing. . . Some biological exposure to events cause cancer. . . We can pick up high risk groups when we do not know what the specific exposure is."

"We don't have to worry abaout quality," Board Chairman Barry Pierce said. ~Study sections do that. The additional money broadens the base. It won't be spent if the quality isn't there."

"Those that came in just above the payline can go back, shape them up a little, and can come back with a good chance of being funded," Adamson said.

"I would like to see some response or activity from the first grants, even if it is only a first year report," Vande Woude said. "There is no data base to show what this will provide us with."

"Since this is a cooperative agreement, I would like to see some indication of NCI's collaboration with the investigators," Board member Lawrence Fischer said. "I don't see the names of those working with the seven."

"They don't collaborate with intramural investigators," Adamson said. "Extramural program staff works with them. Cooper added that the investigators meet with NCI staff and "are very receptive to working with federal people."

The concept was approved by a 9-4 vote, with Benedict, Vande Woude, Janet Butel and Thomas London opposed.

Retrovirus epidemiology and natural history in hemophiliacs and their sexual partners. New five year contract, estimated cost of $550,000 a year.

Presently, the groups at greatest risk for AIDS and HIV infection are homosexual men, intravenous drug abusers and hemophiliacs. Previous studies by the Environmental Epidemiology Branch have provided important new leads concerning the risks and cofactors for AIDS and the heterosexual spread of the virus. This concept proposes to take advantage of new opportunities to extend and expand studies among hemophiliacs.

In 1982, collaboration started with the hemophilia center of Pennsylvania State Univ. Medical School (Hershey). Subsequent to early work evaluating acid-labile interferon as a predictive marker for AIDS risk, furthr collaboration was developed with six hemophilia centers. To date, the NCI multicenter hemophilia study has enrolled and tested 851 hemophiliacs, of whom 59% are HIV seropositive. Rates of seropositivity vary by severity and type of bleeding disorder: Type A, severe 76%; A moderate, 45%; A mild, 29%; B severe, 42%; B moderate, 15%; B mild, 20%; Von Willebrand's disease severe, 21%; others, 0%. In these patients, study has continued of interferon and immunologic abnormalities. Preliminary results indicate that the decline of T-helper cells accelerates late in the course of HIV infection. Studies have also been initiated on the influence of HLA type on disease progression and started to enroll female sexual partners for transmission studies.

In the process of these studies, a number of significant advantages for studying hemophiliacs have become apparent. First, it is possible to determine the date of seroconversion from serial samples of frozen sera which were banked as part of other, earlier studies on many patients. Such information permits time dependent analyses of the natural history of HIV infection. Knowing the date of HIV infection permits reliable assessment of the cumulative incidence of health outcomes and of the effects of cofactors on disease progression.

Second, unlike some other AIDS risk groups, hemophiliacs have excellent followup because they are enrolled in health care programs with state or federal funding and are usually free of competing sources of infection from sexual acts or intravenous drug use.

Third, since mid-1985, Factor VIII has been free of HIV (because the plasma sources for Factor Viii are free of virus and perhaps also because of heat treatment of Factor Viii concentrate). Thus, new sources of HIV exposure or re-exposure have been eliminated.

Several new leads have emerged from initial studies in Hershey. For example, traditional models of infectious disease suggest that virus production is highest

just prior to the appearance of antibodies. Results from the Hershey cohort do not appear to support this model, but rather suggest that heightened transmission occurs when there is a decline in the immune status of the infected donor. This result correlates with the presence of antibodies and the possibility that virus production may increase with progression of immunodeficiency. Newly published antigen data indicates that virus derived antigen (p24) is more frequently present late in the course of illness than early.

A second result of the preliminary work in Hershey suggests that there is a marked shift in the rate of decline of T-helper cells in the 12 months prior to the development of AIDS. The reason for this shift and the potential for intervention needs to be studied more precisely with large numbers of study subjects.

A third observation is the recognition that thrombocytopenia may be a marker for accelerated progression to AIDS. Since this marker is most prominent 24 months before the development of AIDS, it raises the possibility that some circumstance of reticuloendothelial function, possibly associated with chronic liver disease, contributes to heightened risk.

A fourth result of the work suggests that certain HLA antigens may be associated with an accelerated course for AIDS. However, large numbers of hemophiliacs are needed to confirm this finding.

By the time that a new support services contract was awarded in 1986, the new hypotheses resulted in needs to enlarge the study in size and length beyond the level that would be available through the existing contract. Because many seropositive subjects in this risk group are now entering their fifth year since seroconversion, the rates of both illness and transmission are expected to increase, making continuing followup especially informative.

Studies of the natural history of infection among those hemophiliacs who are HIV seropositive will include (1) determining the cumulative risk of AIDS and other adverse health outcomes; (2) assessments of the influence of both fixed cofactors (age at infection, HLA type) and variable cofactors (blood products, other exposures, illnesses which might activate the immune system); and (3) studies of markers of illness (interferon, T-helper and suppressor cells). The availability of dates of seroconversion will be an enormous advantage in such studies. Through following seronegative subjects, it will be possible to monitor the continuing safety of Factor VIII from HIV infection and assess the importance of Factor VIII in transmitting other potentially oncogenic viruses, such as HTLV-1 and 2. Among the spouses, risk can be assessed of transmission to seronegative female sex partners and study behavior and other factors, such as the duration of infection in the hemophiliac, that might influence risk of transmission. Where appropriate, spouse pairs among the hemophilia cohort may become involved in intervention studies with therapy or vaccines, and they will continue to be educated to the risk of HIV transmission within the spousal relationship.

NCI personnel will play the major role in the design and conduct of the studies and analysis of the data in close collaboration with the hemophilia centers. The support services contract will be established to provide administrative and data management support and will arrange for data collection and specimen procurement with the collaborating hemophilia centers. The majority of the funding in this contract will be dispersed to the collaborating centers through the support services contractor. The contractor will implement uniform, standardized procedures based on existing manuals and forms, train new collaborating personnel in their use, review the work of the hemophilia centers for compliance with these standards and monitor the incoming data for problems or errors, which it will resolve directly with the centers.

The contractor will edit data, including laboratory results, and will enter all data into a data base on a continuing basis. It will also provide periodic reports to assess patient accrual, compliance of followup, and completeness of laboratory data. Analysis files will be constructed semi-annually to permit statistical reporting, including tabulations and specialized statistical work as directed by the NCI statistician. Back up copies of all data bases and analyses will be stored and made available to NCI personnel upon request. The collaborating hemophilia centers will enroll all hemophiliacs and their sexual partners, past and present, in ongoing studies. Each consenting participant will be interviewed, examined, counseled and bled for specimens every six months. All collaborators will provide relevant historical information (e.g., HIV status, immune parameters) as well as samples from all specimens banked as part of previous studies and submit these samples to be part of the NCI repository of specimens available from these patients.

In order to assure quality control and standardized procedures in this multicenter study, all research laboratory assays for HIV antibodies and antigens will be done by NIH at the Federick Cancer Research Facility laboratory which supports retrovirus research work for the epidemiology program. Interferon testing will be done in the original laboratory at the Uniformed Services Univ. of the Health Sciences. Most of the immunologic studies will also be conducted at NIH, but in some collaborating centers, studies of T-cell phenotype will be conducted on site in order to avoid duplication or for logistical reasons (e.g., need for rapid turn around time for clinical work, small volume of specimen in pediatric patients). When on site testing is accepted, the procedures and reagents will be approved by the project officer, and quality control will be assessed through direct comparison of samples by the NIH laboratories and the laboratories of the collaborating centers.

James Goedert is the project officer, with Robert Biggar and Mitchell Gail as coproject officers.

The Board approved the concept without dissension.

Support services for radiation and related studies. Recompetition of contracts now held by Westat Inc. and Research Triangle Institute. Estimated annual total cost of the five year contracts is $1.6 million.

Renewal of this concept to conduct field research with the assistance of support service contractors would permit the continuation of ongoing studies and the initiation of new investigations. The contract would be the major resource for the continued follow-up, monitoring and evaluation of cohorts of radiation exposed populations currently established and under study by the Radiation Epidemiology Branch. Continued monitoring of these cohorts includes obtaining address correction updates or death certificates, mailing periodic health questionnaires, conducting periodic phone interviews, coordinating additional tracing activities, linking rosters with the National Death Index, and conducting computer analyses as warranted.

New studies being considered which would require support services involve radon exposure and lung cancer risk, neutron therapy and leukemia risk, cancer following fluoroscopies during heart catheterization in childhood, collaboration on the subsequent followup of 5,000 children irradiated for head and neck conditions in Chicago, evaluation of Nuclear Regulatory Commission and dosimetry company records for creation of a registry of radiation workers, studies of nuclear power workers, cancer risk in women given radiotherapy for endometrial cancer, prenatal x-ray exposure and the risk of adult tumors, studies of the

risk of solid tumors possibly associated with chemotherapy, and second cancers in children treated with chemotherapy.

In essence, this contract establishes a mechanism for the provision of all of the support services required to conduct a wide variety of field studies. While the scientific direction and overall supervision for all projects is the responsibility of the professional staff of the Branch, support services provided by the contract include the development of liaison with organizations and individuals at a local or international level whose cooperation is needed for the conduct of a study; the design and development of forms required to conduct field investigations (interview forms, record abstracting forms, interviewer manuals, etc.); the hiring, training and supervision of technical personnel (interviewers, record abstractors, and persons to collect biological specimens); the actual collection of the required data; and the data reduction activities involved in field investigations (e.g., coding, keying, editing, and a variety of data processing activities). The contractor also must provide field supervision and develop quality control mechanisms to ensure the quality of the activities as well as the maintenance of control of all aspects of every study by the appropriate Branch investigators.

Finally, this contract also provides support for tracing activities to other investigators in the Epidemiology & Biostatistics Program by operating a management control system.

Support activities have been applied in one of three general ways. In some studies, the contractor is responsible for virtually all of the field activities required to complete a study. This generally occurs when the study is conducted in areas, or with collaborating institutions, that have none of these necessary capabilities. A second manner in which the contractor assists is by providing only selected types of support activities that cannot be accomplished by the locally based collaborators. Examples of this include forms development, interviewer training, or random digit dialing for control selection in areas where such activities are not conducted. The contractor may act as a coordinating center for multicenter collaborative studies. In these circumstances, in addition to providing these support services, the contractor assists in monitoring and implementing the standardized application of the study design across the areas.

In addition to core personnel who are committed to the support service contract, the contractor is expected to expand or contract the size of his staff to meet the different and changing requirements of the Branch program. Currently, there are eight study managers, five computer support staff, nine medical and other coders, three coding supervisors, and four phone tracers in support of the overall program of studies. There have been as many as 10 interviewers and 25 abstractors in the field as needed.

The concept was approved without dissent.

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

NCI CONTRACT AWARDS

Title: Support services/research for solid tumor chromosome analysis of persons at high risk if cancer
Contractor: Roswell Park Memorial Institute, $208,903; and Memorial Hospital, $276,611

Title: Epidemiology of T-cell leukemia/lymphoma virus in Panama
Contractor: Gorgas Memorial Institute of Tropical & Preventive Medicine, $597,236

Ford Named Acting CORB Chief; Hunter New Coordinator For CCOP

Leslie Ford, member of the staff of the Centers & Community Oncology Program in NCI's Div. of Cancer Prevention & Control, has been appointed acting chief of the Community Oncology & Rehabilitation Branch. Jerome Yates, DCPC associate director for centers and community oncology, has been serving as acting chief of CORB.

Yates plans to leave NCI Oct. 1 when he will become associate director for clinical affairs at Roswell Park Memorial Institute. Ford's appointment was made to provide some continuity after his departure, Yates said.

Yates also announced that Carrie Hunter, who has been working with the Community Clinical Oncology Program, one of CORB's responsibilities, almost since its inception, is the new coordinator for CCOP. Robert Frelick, who has headed CCOP, left NCI July 1 and returned to Wilmington, DE, where he is working in chronic disease control for the state Dept. of Health.

Wilma Dunlap, another key member of the CCOP staff, remains with the program. Anne Bavier also has working with the program and continues to do so.

Meanwhile, DCPC Director Peter Greenwald said that he intends to appoint a search committee to find a replacement for Yates.

Human Tissue Available Through NCI Supported Cooperative Network

The Cooperative Human Tissue Network, which is supported by NCI's Div. of Cancer Biology & Diagnosis, is available to all cancer researchers who provide evidence of human use approval, information about current grant funding, and a short summary of their research intent.

The network was created to improve access to adequately prepared and well documented human tumor and related normal tissue for cancer research.

"Much important research depends upon the availability of human tissue," said Roger Aamodt, program director for pathology/cytology in DCBD's Diagnosis Program. "During the past several years a number of pilot projects have provided investigators with high quality and histopathologically well characterized malignant, benign and normal tissue for research. One such program has supplied tissues for research resulting in

more than 100 publications reporting sophisticated research on topics ranging from cell culture of tumors to the identification of transformations of oncogenes."

Tissue will be provided on a rotating basis using the following priority order: (1) Peer reviewed funded investigators (including those in federal and national laboratories); (2) new investigators and those developing new research projects at academic centers; (3) other investigators.

A $15 per tissue preparation charge and the cost of shipping will be assessed. The network can provide a variety of human tissues and will assist in the development of collection protocols. The network also will provide a letter in support of grant applications documenting the availability of specific tissues.

To request tissue or to get further information about the network, investigators should contact the division headquarters which serves their respective states. They are:

Eastern Div., headed by Margaret Couture at National Disease Research Interchange, 2401 Walnut St., Philadelphia 19103, phone 215/557-7361. States served by this division are Alaska, Connecticut, Delaware, Hawaii, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, North Carolina, Rhode Island, Pennsylvania, South Carolina, Vermont, Virginia and West Virginia, Washington DC and Puerto Rico.

Northwestern Div., headed by Karen Donavan at Ohio State Univ. Comprehensive Cancer Center, Suite 302, 410 W. 12th Ave., Columbus 43210, phone 614/292-0890. States in this divison are Colorado, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Michigan, Missouri, Minnesota, Montana, Nebraska, Nevada, North Dakota, Ohio, Oregon, South Dakota, Utah, Washington, Wisconsin and Wyoming.

Southwestern Div., headed by Katherine Sexton, Tissue Procurement, LHR 524, Univ. of Alabama (Birmingham), University Station, Birmingham 35294, phone 205/934-6071. States in this division are Alabama, Arizona, Arkansas, California, Florida, Georgia, Louisiana, Mississippi, New Mexico, Oklahoma, Tennessee and Texas.

Nationwide, pediatric tumor tissue may be obtained from Michael Steinbuch, Childrens Cancer Study Group, Pediatric Tissue Procurement, Children's Hospital, Rm JO58, Columbus, OH 43205, phone 614/461-2205.

For autopsy specimens nationwide, contact the Southwestern Div.

BSCs To Get 10 More Concepts From Organ Systems Program In Fall

Ten more research initiatives are being developed by working groups in the Organ Systems Program for presentation to NCI's Boards of Scientific Counselors at their fall meetings.

Commenting on recent approvals of OSP research concepts by the BSC's (**The Cancer Letter**, July 3), OSP Coordinating Center Director James Karr said, "The continuing success of this aspect of the program clearly reflects the high quality of the working groups and outside consultants serving on subcommittees, and our close interaction with representatives of the four NCI (program) divisions. I think that this is what Dr. (Vincent) DeVita (NCI director) and the National Cancer Advisory Board envisioned when they got this 'experiment' started."

Concepts scheduled to go to the BSCs in the fall include:

Bladder--Radiation therapy-chemotherapy interactions.

Breast--Role of biologic markers in the detection of subclinical metastasis; mechanism of early pregnancy protection of mammary carcinogenesis.

Central nervous system--Molecular probes in neuropathology of CNS tumors.

Large bowel--Conservative treatment of adenocarcinoma of the distal rectum and anus; colon stem cells and lineages of colon cell differentiation.

Prostate--Carcinogenesis and neoplastic transformation of the prostate; regulation of prostatic involution as related to prostate cancer.

Upper aerodigestive--Steroid hormone actions in the mechanism of cellular proliferation in upper aerodigestive cancers; assessment of function effects of radiotherapy to the head and neck.

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

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