THE CANCER LETTER

Vol. 1 No. 8

Feb. 21, 1975

Subscription $100 per year

1411 ALDENHAM LANE RESTON, VIRGINIA TELEPHONE 703-471-9695

OHIO PLANS TO BUILD FOUR NEW CANCER CENTERS WITH $140 MILLION BOND ISSUE IF VOTERS APPROVE

Ohio Gov. John Rhodes is advocating a program which, if the voters approve, will give the state an impressive start in development of a cancer center network and perhaps encourage other states to follow the example.

Rhodes has proposed a massive bond issue to finance a huge state construction program, including $140 million for start up costs to build cancer centers in Cincinnati, Columbus, Cleveland and Toledo.

The overall bond program was conceived as a means to stimulate the economy in Ohio and at the same time provide badly-needed public

(Continued to page 2)

In Brief

GAO STUDYING CANCER PROGRAM SO CONGRESS WILL HAVE OWN DATA; NCI JOB FREEZE STILL HURTS PROGRAM

CONGRESS IS conducting its own investigation of the National Cancer Program and NCI. Not willing to accept the Administration's contention that major items in the program can be cut back or deferred, Congress put its watchdog agency, the General Accounting Office, to work studying NCI operations. GAO investigators have been sitting in on committee meetings, talking with NCI executives and others to get the facts for appropriations committees. . . . **JERRY PETTIS**, the California Congressman who was killed in a plane crash last week, was the top-ranking Republican on the new Ways & Means Health Subcommittee. Ways & Means for many years operated without subcommittees. The health unit will have jurisdiction over national health insurance, Medicare and Medicaid legislation. **DAN ROSTENKOWSKI**, Chicago Democrat and a strong proponent of NHI, is chairman of the Health Subcommittee. . . . **JOB FREEZE** at NCI threatens to choke the cancer program, is still the "single greatest deterrent to progress" according to Director Frank Rauscher. In 1971, when the NCI budget was $226 million, the institute had 1,476 positions. In 1974, when it spent $589 million, it had 1,820 positions. The Office of Management & Budget has imposed a ceiling this year of 1,818 although NCI has 1,850 on board now and won't be able to do any more hiring until attrition reduces the number to OMB's limit. Rauscher says he needs at least 200 more positions. **TED COOPER**, acting asst. secretary for Health (and who may have the job permanently by the time this appears in print), told Rauscher he's thinking of moving some of the positions under his control at HEW headquarters back to the agencies. Former Asst. Secretary Charles Edwards attempted to consolidate control of health programs by transferring key people from the agencies to headquarters. . . . **PUBLICATIONS**: *Cancer Rates and Risks*, 2nd Edition compiled by the NCI Biometry Branch, available from USGPO, Washington D.C. 20402, DHEW Publication (NIH) 75-691, $1.80.

OHIO PLAN COULD ESTABLISH PATTERN FOR OTHER STATES; NCI FUNDS LIMITED

(Continued from page 1)

facilities. There is no better way to invest some of the money than in cancer centers, the governor reasoned.

Announcement of the Ohio plan couldn't have come at a better time, as far as the National Cancer Program is concerned. Budgetary and policy restrictions imposed by the Ford Administration have threatened to limit federal support of new cancer centers. The Administration is opposed to NCI support of more than 21 comprehensive centers (the total now is 17 and NCI wants eventually to encourage development of about 30). The Administration also does not want to fund new construction for any centers.

NCI revealed last week (*The Cancer Letter*, Feb. 14) that it probably would slow development of new centers and channel more money into existing ones.

But even if the policy restrictions are reversed by Congress or the courts, NCI could supply only a limited amount of the money required for center development and operation. At best, the NCI centers program was intended only to offer "seed money" plus a certain amount in matching funds and some help with planning and start up costs.

Except for Cancer Control demonstration projects, most of NCI's money is directed to support research. The financial burden for treatment facilities, even those which are used in research, falls mainly on local and state organizations, third party carriers, volunteers and patients.

Only New York, Texas and Missouri now have state cancer hospitals, although others have centers supported by state and local government.

The Ohio plan, as described by Rhodes, would have as its primary prupose the provision of cancer treatment facilities in the four localities. They probably would be affiliated with medical schools but would be free-standing centers, with patients and facilities available for research and teaching.

The governor did not discuss relationships of the proposed new centers with the budding center in Columbus at Ohio State or the center in Cleveland planned jointly by Case and the Cleveland Clinic. NCI has funded a core grant at Ohio State, where they are hoping to build a comprehensive center. NCI is also giving planning support to the Case-Cleveland project which has been approved but not funded for a core grant.

The bond election is scheduled for this spring.

GRANTEES MAY GET MORE FREEDOM IN ADJUSTING BUDGET REDUCTIONS

NCI has decided to permit grantees more freedom in determining how they can spend their money when reviewing bodies have reduced their budgets or disapproved of parts of their projects.

That policy won't apply to all grants and may vary from program to program. But Thomas King, director of the Div. of Research Resources & Centers which administers NCI grants (except for Control & Rehabilitation), told the Centers Review Committee, "This was the way I did research for 25 years, and I would like others to have the same opportunities I had."

King said that one of his biggest headaches is negotiating with applicants after a review committee has cut their budgets. In their critiques, reviewers frequently go beyond discussion of the scientific merit of the proposal and get too much involved with details, King said.

When portions of an otherwise qualified proposal are not merited in the opinion of the reviewers, "I would like to see reviewers reduce the budget by that amount. Give us an overall figure, but let NCI staff handle the details," King said.

"The staff should be free to negotiate with the applicant, determine what the reduction would do to the overall program. The applicant is the best person to know what it would do. We should let the applicant adjust his own budget areas, rather than permit someone in Washington determine all the little details."

Committee members were surprised by King's statement, although agreeing with the policy for the most part.

"That's diametrically opposed to what we've been asked to do in the past," said one. "I'm delighted, however." Another said he disagreed. "Many projects need direction in determining what to cut out."

Committee member Harry Eagle, Albert Einstein College of Medicine, asked King if the policy would permit the applicant to activate those portions of the program reviewers specifically disapproved. "If so, why have site visits?" Eagle said.

"The applicant should be given the dollar figure and the critique which says what shouldn't be done," King responded. "If he flaunts his disregard for the critique (and proceeds with the disapproved portions) it would show up when he comes in for renewal."

"But does he have the right to flaunt it?" Eagle asked.

"How can you tell him how best to use his money, other than offer him the critique?" King said.

Another committee member commented that an applicant who "has to slash a little here, a little there, would have a difficult time putting it together to make the goddam thing work. You are doing him a service if you say, 'This you can do, this you can't'."

Eagle returned to the question of disapproved projects. "I agree that, if a budget is reduced, the applicant should have authority to do what he thinks best. But in a multiple project program, does he have the right to activate the disapproved portion?"

"I was thinking of the traditional grants, not the more complex ones," King said. "I'm getting a sudden immersion into cold water."

"If the principal investigator wants to go ahead, we

can't control it," another committee member said. "But he has the reduced budget. Let the renewal application determine it (that is, if he was justified in ignoring the reviewers' critique).

"Once a grant is made, and if the PI doesn't change the objective, there is nothing we can do," another member said. "He can do anything he wants. The committee can make recommendations, and if he plans to come in for a renewal, he'll take those recommendations seriously."

DIAL ACCESS OFFERS CONSULTATION TO HEALTH PROFESSIONALS ON CANCER

The "Dial Access" system of cancer education and control through telephone consultation developed as a cooperative venture by the Southern Medical Assn. and M.D. Anderson has handled more than 18,000 calls in the year since it began serving physicians, dentists, nurses and other health professionals in 17 states.

The system is supported by a contract from NCI's Div. of Cancer Control & Rehabilitation. It provides the user toll-free telephone consultation service based on more than 300 tapes. The tapes are narrated by physicians who are experts in the study and management of various types of cancer. Most are from the M.D. Anderson staff ("That's because I can insist they participate," said Lee Clark, president of MDA's parent, the Univ. of Texas System Cancer Center. "We hope to broaden our base and get others into the program.").

The tapes are concise (six to eight minutes), may cite up to three references, and have author identification. The information is constantly being updated with review by authors and recording of additional tapes. Hours for the service are 9 a.m. to 9 p.m. Monday–Friday and 10 a.m.-2 p.m. Saturday (Eastern Standard Time).

The 17 states in the toll free area are Alabama, Arkansas, D.C., Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, Missouri, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia and West Virginia.

Health practitioners may use the system by dialing the appropriate number, stating his identity and requesting by specific number any topic listed in a catalog that will be mailed on request. To get the catalog, write to Roy Evans Jr., assistant executive director, Southern Medical Assn., 2601 Highland Ave., Birmingham, Ala. 35205.

The tapes are grouped in 24 categories in the catalog. Each subject is listed by title and author.

"The rationale for the use of the system is to provide concise information for health professionals who are caught in a swirl of new knowledge and reinterpretation of old data, with various possible therapeutic nuances, all of which may be applicable to a given cancer patient or in an education situation," a booklet describing the program states.

"For the future, an expansion of subjects and topics from authors in a variety of geographic regions is essential, the criterion for author participation being expertise in a discipline," the booklet summarizes. "Local idenfication with the system seemingly has not been a factor; a local identification can be preserved by participation through authorship of tapes and local notification of practitioners of the availability of a system. Cost estimates would favor one centrally named station regardless of its location.

"This system must be looked upon as an additional resource. It is not a research library, yet it is an extension of the library; it is not a postgraduate course, yet it may be used as such, with instant availability in a patient problem."

The project is headed by Robert Hickey and George Blumenschein, M.D. Anderson; Gordon McHardy, Browne-McHardy Clinic, New Orleans; and N.C. Hightower Jr., the Scott and White Clinic, Temple, Texas.

FEDERAL REGULATION PROHIBITS RELEASE OF CONTRACT BUDGET ESTIMATE WITH RFP

Some readers of *The Cancer Letter* who have responded to NCI RFP announcements have suggested that each RFP summary include an estimate of the project's budget. They complained that lack of this information makes it difficult to determine if the expense of preparing a proposal is worth the potential return.

NCI contract executives responded by pointing out that in most cases, federal procurement regulations prohibit release of cost estimates prior to the award of the contract.

One rationale for the regulation is that bidders might tend to develop proposals geared to the estimate. "We want their best proposal," an NCI executive said. "If it's more than our estimate, we can either transfer funds to cover it, if it is a very good proposal that we feel we need; or we can negotiate with the bidder and trim some portions out, if we have to stay within the estimate."

He pointed out that most RFPs include a level of effort estimate, in terms of man-years by key personnel the project will require. Prospective bidders should be able to determine from that the approximate size of the project, he said.

LITTON BIONETICS AWARDED $342,618 FOR OPERATING FREDERICK CENTER

Litton Bionetics received $342,618 as its fee for operating the Frederick Cancer Research Center for NCI during the last six months of 1974. The award was 80% of the maximum permitted by the contract for the period, $428,273.

NCI has started negotiations with L-B for renewal of the contract for the year starting next July. It will be the fourth year the firm will operate the center

following the original award in 1972, and it may be the last before NCI throws it open again to competition. NCI executives anticipate it will be recompeted eventually, and their thinking now is that this probably will be done next year.

Thecontract is the largest ever awarded by NIH. So far this year, it has amounted to $14.3 million and could reach $18 million by the end of June.

The fee was based on a "very good" efficiency rating of 92, which entitled the firm to a fee of 80% of the potential. The highest rating of "excellent" requires a numerical score of 96 or better.

Contract Awards

FLOW LAB $1.9 MIL. TOPS 24 VIRUS CONTRACTS WORTH $11.8 MILLION

A contract worth more than $1.9 million awarded to Flow Laboratories for studies on type-C viruses in relation to oncogenic potential headed 24 contracts totalling $11.8 million announced this week by NCI's viral oncology branch.

Pfizer received the next largest award, $1.7 million for large scale tissue culture virus production for cancer research.

Other awards included:

Contractor: Meloy Laboratories, $787,870.

Title: Investigate carcinogenic activity of selected viral preparations in primates
Contractor: Litton Bionetics, $889,043.

Title: Inelastic laser light scattering studies on nucleic acids, nucleoproteins and viruses.
Contractor: Michigan Cancer Foundation, $40,450.

Title: Comparative leukemia and sarcoma viral studies
Contractor: Univ. of California (Davis), $497,664.

Title: Murine Mammary tumor virus production facility
Contractor: Meloy Laboratories, $409,784.

Title: Support services for studies on the application of animal virus model systems to human neoplasia
Contractor: Litton Bionetics, $392,650.

Title: Develop laboratory animal virus diagnostic reagents and operation of a service laboratory
Contractor: Microbiological Associates, $462,000.

Title: Study genetic and immunologic factors in viral leukemogenesis
Contractor: Albert Einstein College of Medicine, $269,559.

Title: Application of advanced electrical and optical technology to problems in oncology
Contractor: General Electric Co., $52,820.

Title: Support services for immunological and biochemical studies of mammalian viral oncology
Contractor: Hazleton Laboratories, $113,334.

Title: Production and maintenance of germ-free animals.
Contractor: Life Sciences, Inc., $189,470.

Title: Immunoprevention of spontaneously occurring neoplasms
Contractor: Microbiological Associates, $695,500.

Title: Studies of new papovaviruses isolated from man
Contractor: Johns Hopkins Univ., $69,919.

Title: Research on oncogenic and potentially oncogenic viruses, virus production and vaccine development
Contractor: Merck, $666,670.

Title: Studies of the molecular mechanism of carcinogenesis by oncogenic viruses
Contractor: Univ. of Illinois (Chicago), $118,000.

Title: Virological studies of breast cancer
Contractor: Pfizer, $150,000.

Title: Support services to maintain studies of spontaneous and virus induced neoplastic transformation
Contractor: Meloy Laboratories, $947,439.

Title: Virus and reagent production and purification
Contractor: Flow Laboratories, $820,000.

Title: Study nonsense suppressor genes in mammalian (3T3) cells
Contractor: Baylor College of Medicine, $49,235.

Title: Studies on herpesvirus (EBV) and its role in human cancer
Contractor: Hebrew Univ. (Jerusalem), $103,567.

Title: Immunological studies on the relationship of embryonic antigen to virus induced tumor antigens
Contractor: Univ. of Tennessee, $25,560.

Title: Replication of oncogenic RNA viruses and its relation to human cancer
Contractor: Columbia Univ., $360,860.

CONTRACT AWARDS

Title: Planning for a state-wide cervical cancer screening program
Contractor: North Dakota State Dept. of Health, $49,268.

Title: State cervical cancer screening program
Contractor: New Jersey State Dept. of Health, $49,177.

Title: Continuation of antineoplastic agents study
Contractor: Oregon State Univ., $85,309.

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. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology & Diagnosis Divisions are located at: NCI, Landow Bldg., NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NO1-CP-55660-68

Title: *Development of techniques for quantitation of physiological reflux in the pancreatic duct*
Deadline: *April 7*

A study will be initiated of the likelihood or propensity of bile or other ingredient within the bile duct or duodenum tract of man refluxing or coming in contract with cells of the pancreatic duct and the head of the pancreas. The target cell or cells for pancreatic cancer induction have not been clearly defined; for the purposes of this study it may be assumed that acinar cells or ductal cells are the primary sites of origin of this disease.

This research project is viewed as having a definite Phase I – development of techniques to quantitate physiological reflux within the pancreatic duct–and a possible Phase II if Phase I produces satisfactory results – application of the developed techniques to an in vivo system for measurement of effects of postulated factors influencing normal physiological reflux.

It is not mandatory to submit proposals on both phases nor to have capabilities to conduct Phase II studies in order to propose Phase I investigations. Prospective offerors must have knowledge of, experience with and/or training in the pancreas and its biochemistry, and the facilities and equipment to perform the proposed research.

RFP NO1-CP-55659-68

Title: *Glucuronidase sulfatate and other deconjugating enzymes in the pancrease and its secretions*
Deadline: *April 7*

The enzymatic potential of the pancreas and its secretions or other appropriate tissues for deconjugation of various chemical entities will be examined in vivo or in vitro using tracor techniques.

Proposers should assess various possible methodologies for research, relevance and potential for meaningful results and subsequently provide the rationale upon which the conceptual approach is based. This RFP is not seeking a long term study on the carcinogenicity of bile or its components.

Prospective offerors must have knowledge of, experience with and/or training in the pancreas and its biochemistry, and the facilities and equipment to perform the proposed research.

RFP NO1-CP-55656-68

Title: *Potential for carcinogen metabolic activation in the pancreas of experimental animals*
Deadline: *April 7*

NCI wants to examine the potential of pancreatic cells from various animal species in vivo to transform chemical compounds to other forms which may or may not be carcinogenic; i.e., to activate metabolically chemicals which (1) are known to be activated by other organ enzymatic activities, or (2) are suspected of being substrates to pancreatic metabolic processes, or (3) may reasonably be considered a precursor to a pancreatic carcinogen.

Prospective offerors must have knowledge of, experience with and/or training in the pancreas and its biochemistry, and the facilities and equipment to perform the proposed research.

RFP NO1-CP-55654-68

Title: *Chemical and structural requirements for preferential uptake and excretion by the pancreas*
Deadline: *April 7*

NCI has been supporting a program on carcinogenesis of pancreatic adeno-carcinoma. The models under development are a result of administration of direct acting carcinogens at doses that cannot be considered physiological. If chemical carcinogens cause pancreatic cancer in the human, they must reach the pancreas either through its blood supply, or by reverse flow through the pancreatic duct from the common bile duct or duodenum.

At the present time, there is no reason to think that only one of these routes may be exclusively involved in all cases. The route of entry may depend upon the structure of the chemical carcinogen involved. Work performed to date on preferential uptake has been limited to two basic chemical structures which have been shown to concentrate in the pancreas. Other substances with similar or even different structures undoubtedly exist which have an affinity for the pancreas.

Identification of these is most important to the program. A variety of chemicals representing different structural arrangements will be administered to

one or more species of experimental animals. Deposition studies, using either radioactive labeled chemicals or assay of tissue for the key structural moiety, would be performed, being cognizant of possible metabolic conversion by the liver or other organs, including the pancreas itself. Excretion through the pancreatic juice would be similarly assessed.

Prospective offerors must have knowledge of, experience with and/or training in the pancreas and its biochemistry, and the facilities and equipment to perform the proposed research.

Contract Specialist for the four RFPs above: S.W. Ranta 301-496-6361

RFP NCI-CB-53918-31

Title: *Measurement of immunological reactivity to human cancer*

Deadline: *April 28*

NCI is seeking a laboratory to perform multiple in vitro procedures and assays on human tumor and blood specimens provided by NCI staff. It is intended that these assays will be used for immunological monitoring of patients with cancer, and for comparison of immunological reactivity between cancer patients and controls. The emphasis will be on the use of procedures already established. Some improvement and refinement of assays should be done, but not at the expense of the routine monitoring.

1. The specific tasks to be performed, on approximately 500 specimens per year are:

a. Prepare with sterile technique single cell suspensions from a variety of human tumors. These cell preparations will be used for immunological testing, extractions, and for clinical immunotherapy.

b. Prepare extracts from tumor cells, by hypotonic saline extractions, by 3M potassium chloride, and possibly by other techniques, for in vitro testing and for possible use in delayed hypersensivity skin tests in patients. These extracts will have to be prepared under sterile techniques and monitored for sterility and osmolality. It will be desirable for an individual with immunochemical experience to participate in this aspect of the project.

c. Freeze viable cells by programmed rate freezing in liquid nitrogen, for later use in assays or for patient inoculation.

d. Place selected tumor and control cells in tissue culture, and maintain established cell lines, to be supplied by NCI, in culture, a capability must exist for growing up large numbers of selected cell lines, and for monitoring tissue cultured cells for contamination by bacteria or by mycoplasms.

e. Perform rosette assays for T lymphocytes in peripheral blood.

f. Perform direct leukocyte migration inhibition assay with tumor extracts.

g. Perform lymphocyte stimulation experiments with mitogens, antigens, allogeneic lymphocytes, antologous tumor cells and tumor extracts.

h. Perform isotopic and visual cell-mediated cytotoxicity assays, with lymphocytes from tumor patients and controls and target cells from tumors or cell lines derived from tumors.

i. Perform other assays, as specified by project officer.

j. Perform necessary computations, analyses of data, and correlations with clinical information.

k. Provide adequate storage of tumor extracts and serum specimens at −70 degrees C.

2. Provide adequate and rapid transportation facilities for pick-up without delay of clinical specimens from NIH clinical center, hospitals in area, and from local airports.

3. Participate in regular working meetings and conferences with project officer and other NCI staff.

4. The organization must have immediately available the necessary facilities for the above procedures, and must also have the appropriate staff available by the initiation of the contract. The principal investigator must be an experienced immunologist. Expertise in assays of cell-mediated immunity and in tissue culture is also required. Prospective contractors expecting serious consideration must provide sufficient evidence of recent past experience in this field.

5. The facility must be within 30 minutes normal driving time from the NCI's Bethesda campus.

RFP NCI-CB-53911-31

Title: *Rhesus monkey histocompatibility studies*

Deadline: *April 28*

The rhesus monkey (M. mulatta) major histocompatibility complex is composed of two closely linked loci determining serologically defined antigens, a nearby locus determining reactivity in MLC, a possible Ir region determining humoral response to defined antigens, and at least one independently segregating locus determining weak reactivity in MLC. Further analysis of this system in the monkey is of great importance for progress in transplantation biology, since the system bears close analogy to that of man and since experimental manipulations such as immunization and controlled transplants may readily be performed in such a system.

NIH solicits proposals for the maintenance of a pedigreed family colony of monkeys owned by NIH; for performance of certain histocompatibility studies upon these and other monkeys; and for the long-term observation of certain survivors of previous transplant experiments. Specifically, in the first contract year, the contractor shall:

1. House and maintain approximately 150 rhesus monkeys (20-25 pedigreed families of 2-4 subs each; plus random unrelated monkeys) furnished by the government for contractor maintenance.

2. Perform microlymphocytotoxicity testing (duplicate testing with panels of 50-150 antisera provided by the project officer) on all family monkeys and 200 random wild caught rhesus monkeys per year. Access

wild caught monkeys to be provided by government.

3. Breed family monkeys to enlarge families by live births in the entire family colony per year.

4. Attempt to locate sources of intact, pedigreed monkey families and random monkeys, all nonbiohazardous, for the potential purchase and resupply of monkeys to this project.

5. Raise and characterize alloantisera directed against SD, LD, and lymphocyte subpopulation alloantigens, immunization to include skin grafting, lymphocyte collection and inoculation, collection, titration, and −60 degrees C storage of antisera, and characterization of antisera in panels of wild caught and family monkeys, and demonstration of monospecificity by absorption; 25 immunized monkeys per year.

6. Perform mixed lymphocyte culture on family monkeys and unrelated monkeys, including inhibition with antisera, to evaluate "lymphocyte-defined" antigens and antisera to such antigens according to protocols developed in cooperation with the project officer on the basis of known genetic information about families' RhL-A types. 150 combinations in triplicate per week will be required.

7. Provide data in form suitable for storage and analysis by NIH computer facilities. This requires use of a Wylbur terminal. Experience not required.

8. Provide samples of blood, serum, or lymphocytes, as specified by the project officer, from 3 monkeys daily. Provide daily transport of these samples from the contractor to the NIH, Bethesda, such that unprocessed blood reaches NIH by 9:30 A.M. and not more than 3 (three) hours after drawing, and such that lymphocyte samples arrive by 11:30 A.M.

9. Supply 10-25 ml of blood, on at least 3 occasions per year, from each of at least 20 monkeys not furnished by the government.

10. Store reagents supplied by the government, requiring approximately 15 cubic feet at −60 degrees C and 1 cubic foot in liquid N_2.

11. Provide, on up to 30 monkeys which are subjects of previous transplantation and which are provided by the government, long-term maintenance and observation, including weekly observation of general condition, monthly weight, complete blood count, and serum chemistry screen; and complete gross and microscopic pathological examination at death, to be performed by an experienced pathologist.

12. Perform 10 thoracic duct cannulations per year, collect lymphocytes for 24-48 hours and maintain cannulated monkeys alive. Collected lymphocytes to be used in absorbing alloantisera raised by the contractor in accord with paragraph 5 above.

13. Freeze and maintain in liquid N_2 20 aliquots of 10^7 lymphocytes collected from each of 40 monkeys using standard cell freezing methods.

Contractor's facility must be sufficiently near NIH, Bethesda, to permit the requirements of paragraph 8 of the workscope to be met; and to permit the required close, frequent consultation between the principal investigator and the project officer.

RFP NCI-CB-53910-31

Title: *National Cancer Institute immunodiagnostic reference center*

Deadline: *April 7*

A series of serum proteins (especially oncofetal proteins) have been demonstrated to be elevated in the serum of certain patients with cancer, and sensitive radioimmunoassays have been developed to quantitate these proteins in the serum. NCI wishes to establish a single facility for evaluation of the diagnostic usefulness of these assays and of new assays as they are developed. Such tests will also be evaluated for usefulness as markers in following the effectiveness of cancer therapy.

Task IA—Radioimmunoassay for alphafetoprotein (AFP) on serum and other biological fluids: The contractor shall perform double antibody radioimmunoassays for AFP on 5,000 samples in duplicate yearly. Since standard curves, quality controls and periodic evaluation and upgrading of the sensitivity and specificity of the assay are required, this part of the work will require processing of 15,000 individual tubes annually. The contractor shall log in samples, radiolabel the alpha-fetoprotein, perform the double antibody assays and analyze the data using the Rodbard computer program or its equivalent. NCI will provide the purified antigen, standard displacer and antibody to alpha-fetoprotein. The contractor shall produce the second antibody system (antibody to rabbit IgG) required for this and following assay procedures. The contractor will complete the assays described above as well as assays for hCG-β discussed below, within two weeks of submission of the samples.

Task IB—Purification of alpha-fetoprotein: The contractor shall purify 30mg of alph-fetoprotein yearly using materials and techniques provided by NIH. The procedure developed for this purification shall provide undamaged material that is at least 95% pure and is satisfactory for metabolic turnover studies. To be satisfactory for metabolic turnover studies, the alpha-fetoprotein should be unaggregated, non pyrogenic and should have the same biological survival in experimental animals as alpha-fetoprotein present in unfractionated serum.

Task II—Radioimmunoassay for the beta chain of human chorionic gonadotropin hCG-β: The contractor shall perform double antibody radioimmunoassay of hCG-β on 5,000 serum samples per year (15,000 tubes). NCI will provide the purified hCG-β and the antibody to this material. The requirements for other reagents and analysis of data are the same as those indicated in Task IA for alpha-fetoprotein.

Task III—Additional immunodiagnostic tests for cancer: As new tests are developed, the project officer may require that an additional test be set up and

that up to 1,000 additional double antibody radioimmunoassays be performed. The purified antigen would be provided by the project officer and the contractor would be expected to produce antisera to the antigen and to make the antisera specific by absorption with solid phase immunoadsorbants and to assist in the development of radioimmunoassay procedures with these materials.

Task IV—Handling of samples: The contractor must document the availability of facilities for long term storage of 30,000 frozen serum samples and must have the capacity to provide a means of identifying and retrieving the sample, as well as a program to produce a means of correlating different test results on the same sample with each other and with patient diagnosis.

Task V—Tests for humoral immunocompetence of patients with cancer and immunodeficiency disease: Patients with various malignant and immunodeficiency diseases who are entered into NIH immunotherapy and chemotherapy protocols will be assessed for their capacity to make a humoral immune response. Assays for the detection and quantitation of serum antibodies will be performed. The contractor shall perform approximately 2,500 assays (exclusive of controls) by already developed, simple microtitration techniques to be stipulated by the project officer, which include passive hemagglutination assays using soluble antigens coupled to human type O erythrocytes by chromic chloride or gluteraldehyde for detection of antibodies to keyhole limpet hemocyanin (KLH), diptheria toxoid, tetanus toxoid, types I, II, and III pneumococcal polysaccharide, and Serratia marcessans. Bacterial agglutination assays will be used to detect antibody to Brucella abortus and salmonella typhosa. Within the total 2,500 assays, assays of one or two additional antigens by techniques of similar difficulty may be added during the course of the contract year at the discretion of the project officer.

The project officer will provide the antigens and standard positive and negative control sera. The contractor shall provide for pick-up of serum samples at the NIH Clinical Center as well as to provide the microtitration equipment (Cooke Engineering Microtiter system), buffers, and erythrocytes and shall perform the requested assays within 30 days of receipt of the samples from the project officer.

Task VI—World Health Organization reference preparation: The contractor shall serve as a distributor of international reference preparation as established by WHO or other appropriate agencies. Approximately 500 samples will be mailed each year.

In order for the contractor and the project officer to meet and confer an estimated two or more times weekly and for the requirements of Task IV to be met, the contractor must be located within a one hour driving radius of NIH Bethesda.

Contract Specialist for the above three RFPs: Robert S. Townsend, Biology & Diagnosis, 301-496-5565

RFP NCI-CP-VO-53523-63

Title: *Studies to determine a viral involvement of mammary carcinoma of animals (excluding the human and the mouse)*

Deadline: *April 15*

(A brief summary of this RFP appeared last week)

At this time, the mouse mammary tumor virus MMTV represents the only proven etiologic agent involved in mammary carcinoma in animals. Two other agents have been found associated with breast cancer: (1) Mason-Pfizer monkey virus (MPMV), an agent isolated from a rhesus monkey mammary carcinoma and (2) the type-C R35 rat virus. Recently, a type-B virus has been isolated from guinea pig embryo cells after induction with IuDR.

The objective of these studies is to elucidate a possible viral involvement in mammary carcinoma of a given species other than mouse and human. This may be accomplished primarily by the use of techniques of virus detection, isolation, cell culture, immunology and/or biochemistry.

The contractor shall undertake one or more of the following tasks using any given species (with exception of the human and the mouse):

1. Isolation from breast tumor cells or milk an agent with the morphological, biochemical and/or immunologic properties of an RNA tumor virus.
2. Demonstration of any relationship between the agent found in task 1 and either MMTV or MPMV by immunological biochemical techniques.
3. Demonstration of the oncogenic or transforming potential of the agent found in task 1.

Adequate facilities and an expertise in the techniques being applied, for these studies should be demonstrated.

Offerors should make their independent assessment of the level of effort required and develop their proposals accordingly. It is anticipated that the project will require approximately 42 man-months of effort per year.

Contract Specialist: Jacque Labovitz, Cause & Prevention, 301-496-6496

The Cancer Letter —*Editor* JERRY D. BOYD

Published weekly by The Cancer Letter, Inc., 1411 Aldenham Ln., Reston, Va. 22090.