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RFP TO BE ISSUED FOR TWO MORE NEUTRON THERAPY FACILITIES; WINNERS TO CONDUCT CLINICAL TRIALS

NCI's Div. of Cancer Treatment plans to issue an RFP for the development of two clinically dedicated neutron facilities with a total estimated first year expenditure of $9 million as the major effort in the

(Continued to page 2)

In Brief

FIVE INSTITUTIONS TO TEST INTERFERON; APPENDECTOMY-CANCER ASSOCIATION NOTED

FIVE INSTITUTIONS will carry out clinical trials of interferon, supported by the American Cancer Society—M.D. Anderson, Sloan-Kettering, Roswell Park, Columbia, and Stanford. Interferon will be tested against breast cancer, melanoma, multiple myeloma, squamous cell lung cancer, non-Hodgkins lymphoma, and bladder cancer. ACS has allocated up to $2 million for purchase of the material, which is being imported from Finland. . . . **PERSONS WITH** cancer of the large bowel are twice as likely to have had an appendectomy as the general population, according to a study of M.D. Anderson patient records by Birger Jansson, biomathematician with the National Large Bowel Cancer Project. The study, reported at the XIIth International Cancer Congress, considered 917 patients treated for colon and rectum cancer from 1963-73. Thirtyfive percent of the patients had had prior appendectomies, compared with 15% of the general population. . . . **LESLIE BLUMENSON**, research scientist in the Roswell Park biostatistics dept., received the George W. Snedecor Award from the American Statistical Assn. for his paper on mammography which analyzed x-ray hazards. . . . **K. ROBERT MCINTIRE** is the new chief of the Diagnosis Branch of NCI's Div. of Cancer Biology & Diagnosis, the position left vacant by the death of William Pomerance. McIntire has been senior investigator in the division's Laboratory of Immunodiagnosis, came to NCI in 1961. . . . **1977 REPORT** of the Council for Tobacco Research is now available. It includes abstracts of reports by investigators funded by the council which have appeared in scientific journals since publication of the 1976 report. Copies may be obtained from the Council, 110 E. 59th St., New York 10022. The Council has funded $46 million in research since its formation in 1954 by tobacco manufacturers, growers and warehousemen. Grant recipients work independently in their own institutions. Grants are reviewed by a 10-member scientific advisory board chaired by Sheldon Sommers, Columbia Univ. Robert Huebner, former chief of NCI's Laboratory of RNA Tumor Viruses and now retired, is a member. . . . **FRANK SCHABEL JR.**, director of chemotherapy research at Southern Research Institute, will present the Jeffrey A. Gottlieb Memorial Lecture at the 23rd annual Clinical Conference Nov. 2-3 at the Shamrock Hilton in Houston. The 11th annual Special Pathology Program will follow Nov. 4.

NCI TO GRADUALLY PHASE OUT GRANTEES UTILIZING NEUTRON PHYSICS MACHINES

(Continued from page 1)

division's stepped up Particle Therapy Program.

The DCT Board of Scientific Counselors last week unanimously approved the plan for the new neutron therapy initiative, which will support purchase of two machines at a cost of about $5.5 million, related facilities totaling $2 million and construction at another $2 million.

The winners in the open competition for the two contracts will then automatically be recipients of sole source contract awards for clinical trials when the facilities become operational.

The Board had approved last March the decision by DCT to increase funds for neutron development while continuing other particle therapy projects—protons, heavy ions and pions.

A description of the program presented to the Board by Daniel Rubin, special assistant for scientific coordination to DCT Director Vincent DeVita, said:

"The major emphasis in the DCT Particle Program will be on clinical neutron therapy research and development in FY 79 and FY 80. Therefore, DCT proposes:

"—The obligation of funds in FY 79 and 80 to develop three clinically dedicated neutron therapy facilities.

"Since NCI already has a peer-reviewed, grant supported project at M.D. Anderson for a clinically dedicated neutron machine, we propose that:

"—An RFP be issued for open competition for the development of two additional clinically dedicated neutron facilities using the M.D. Anderson project as a model.

"—Current and pending grant applications submitted to the NCI for clinical neutron projects be held and considered responsive to the RFP when issued.

"—The current neutron physics machine based projects will be encouraged to response to the RFP.

"We recommend the contract mechanism for implementation of this project because:

"—The goals of this project are clearly in sight and a targeted approach is warranted.

"—This is the only funding approach which can be initiated and have the necessary funds obligated in FY 79 and FY 80, while assuring appropriate peer review and approval.

"—This approach offers the greatest potential for acquiring the necessary capital resources at the most reasonable cost to the government.

"—A contract will allow each respondent to compete equally on the same work scope, within the same time frame, and undergo the same peer review.

"—This approach offers greater potential for stability and continuity of the project with regard to both the initial facility implementation phase, and the coordination of the clinical trials phase of this project.

"Specific advice and consultation of the radiation oncology community will be obtained for the preparation of the guidelines and criteria for this RFP."

While no new programs in other non-neutron particle therapy projects will be initiated, they will be maintained at essentially the current level ($3.3 million in FY 1978). Those are all supported by grants, and some are up for renewal this year, so that figure could change.

Ten neutron therapy grants totaling $6.3 million comprise the existing NCI effort in that field, including the M.D. Anderson project. The others use physics machines which are unsuitable for clinical trials; and DCT proposed that these be gradually phase out and the funds reprogrammed to help pay for the two new facilities. Six of those grants expire in 1978, and DCT estimated that approximately $3 million would be available for reprogramming. Not all of that would go into the neutron projects; some would be required to support the built-in increases in the other particle therapy grants.

The other four neutron therapy grants expire in 1979.

Rubin said the reprogramming of funds from the ongoing clinical neutron therapy research program would be subject to the following:

"—Gradual phaseout of neutron physics machine facilities based on the results of the proposed RFP competition, and the progress and periodic reassessment of state of the science and technology. The grantees working with the physics machines will be encouraged to respond to the RFP.

"—Advice and consultation from both the Radiation Oncology Coordination Subcommittee of the DCT Board and members of the National Cancer Advisory Board particle subcommittee."

Here's how DCT broke down the estimated first year cost in the development of each facility:

Isochronous cyclotron (42 MeV Proton)—$2.78 million.

Beam delivery system—$450,000.

Other capital equipment—$140,000.

Construction—$1.13 million.

The construction funds are already allocated to DCT and would require 50-50 matching funds from the institutions.

Rubin commented that RFP responders may consider the M.D. Anderson project "as a model but not a blueprint." Board member Sydney Salmon asked, "What's wrong with using it as a blueprint?"

"We want to permit responders to have a certain amount of freedom in what they can do," Rubin said.

"I would accept M.D. Anderson's facility as a blueprint, for the physical plant, leaving the flexibility in what they do with it," Salmon answered.

"Some physicists might come up with concepts for facilities better than M.D. Anderson's," Board

member Henry Kaplan said.

The RFP will not ask for plans for clinical trials, Rubin said in answer to a question from Board member Sharon Murphy. But Board member Philip Rubin suggested that responders would have to have "a track record" in neutron therapy. He pointed out that the Radiation Therapy Oncology Group has 10 phase III clinical trials in progress.

"There is a concern among my non-radiation oncology colleagues about the cost of the hardware," Kaplan said. "There is an analogy in the Drug Development Program. The cost is not in merely opening a vial and administering the drug. Millions of dollars go into it to reach that point. These hardware costs are reasonable, and may even be economical. We approved $25 million for drug screening alone (earlier in the meeting)."

Board member Enrico Mihich questioned the decision to phase out the physics machines. "I've heard Simon Kramer and others say the problem is to get enough patients to get the answers. Is it wise to phase out the physics machines to get more comfortable, adaptable machines? I suggest we not phase out the physics machines. Continue them to add to our knowledge, and get the new ones, too."

"We've looked at those programs in detail," DeVita said. "The consensus is that they will never give us the answers." He emphasized that the grants for other types of particle therapy machines built for physics research which are being used now in cancer research would not be phased out.

Kaplan asked if the RFP could be written to encourage regional participation. "The RFP should indicate that priority scores would take into consideration inter-institutional arrangements for treatment of patients in these trials. That would result in more progress and would help defuse the political problems we will have with only two machines for the entire country."

"There will be three machines (with M.D. Anderson's), and the trials will be very limited in size, to get the answers we are seeking," Philip Rubin said. "The original recommendation was for eight machines. The French have recently decided to develop four."

"If there were a few more in other countries, maybe we wouldn't have to do it," DeVita quipped.

"Is this truly a free competition, or is it linked to RTOG membership?" Salmon asked. "I assume it is not, but would be if the RFP limits responders to RTOG protocols."

"We will not ignore what has already gone on," DeVita said, "but I assure you, we will not limit this to RTOG membership. It will be a wide open competition."

"What about those with physics machines?" Mihich asked. "If they want to compete, could they use their existing equipment?"

"I'll tell you how I would do it (as a grantee presently using a physics machine)," DeVita said. "I would compete for this, and get my own machine in my center or hospital."

DCT BOARD APPROVES NEW CONTRACT PROJECTS, REJECTS NUTRITION PROPOSAL

The DCT Board of Scientific Counselors approved another new research contract program, a multi-institutional study of hormone receptors in endometrial cancer, but rejected a new, ambitious $2.4 million a year project to study total parenteral nutrition as an adjunct to antineoplastic therapy.

The Board accepted the concept that the role of TNP with established modalities should be studied, but objected to DCT's specific plan on how the tests should be accomplished. A subcommittee, including Sydney Salmon as chairman, Walter Lawrence and Philip Rubin, was appointed by Board Chairman John Ultmann to work with DCT staff in developing a new plan.

The hormone receptors study would involve awards totaling an estimated $400,000 in the first year, starting June 1, 1979, to six to eight institutions. An RFP will be issued seeking responders in open competition.

The narrative description of the project, to be administered by DCT's Cancer Therapy Evaluation Program:

"Specific cytoplasmic progesterone receptors that bind ^{3}H-progesterone in vitro have been demonstrated and characterized in normal, hyperplastic and carcinomatous human endometria.

"Work from Indiana Univ. has shown that specific cytoplasmic progesterone receptors can be detected in almost all normal endometria, are present in most endometrial hyperplasias and while some endometrial adenocarcinomas retain their rpogesterone receptors, as tumors become more anaplastic, a greater percent lose their progesterone receptors. This is in agreement with the findings of others.

"If progesterone acts on endometrial cells as other steroid hormones act on their target tissues, perhaps the cytoplasmic progesterone receptor system of the tumor cells limits the response of endometrial adenocarcinomas to progestin therapy.

"Young, Ehrlich and Cleary have studied 58 endometrial carcinomas using a simple, sensitive and specific dextran-coated charcoal assay. In non-irradiated tumors it was found that 16 out of 19 (84%) Grade I, 8 out of 16 (50%) Grade II, and 4 out of 13 (31%) Grade III, endometrial adenocarcinomas had significant or 'high' receptor activity. Nine out of 10 endometrial adenocarcinomas showed no significant or 'low' progesterone receptor activity after irradiation while appearing histologically viable. This lack of significant or 'high' receptor activity in irradiated tumors is in keeping with the clinical observation that the response to progestin is decreased in irradiated tumors.

"Fourteen recurrent or advanced endometrial adenocarcinomas have been assayed for progesterone binding proteins prior to therapy with medroxy-progesterone acetate (provera). Nine of these patients' tumors showed no response to progestin therapy and none of these tumors had 'high' progesterone binding activity. The other five patients showed objective responses and four of the five had 'high' progesterone binding activity. No definite conclusions can be drawn from these 14 cases, but these data suggest that endometrial adenocarcinoma with progesterone receptor activity in appreciable or 'high' quantities may be predictive of a response to progesterone therapy.

"The scope of work would seek to form a consortium of institutions with both laboratory and clinical facilities to test whether: 1) progesterone or other hormonal receptor activity and related endocrine determinators in early stages of endometrial adenocarcinoma correlate with disease free survival; 2) differentiation, stage, and site of involvement correlates with the above parameters; and 3) in a randomized controlled trial, hormone receptors predict for responsiveness to either chemotherapy and/or progestins or other hormonal manipulations.

"Statistical requirements for a two-arm trial in stage I/II disease with a projected five year survival of 75% with current surgical therapy would necessitate accrual of 250-300 patients. Projections would require 6-8 institutions with accrual capability of 25 patients/year so protocol registration could be completed in 2–2.5 years. Followup would take an additional three to four years."

The Board was ready to disapprove the nutrition project entirely, until DeVita said that the money allocated for it would have to be spent for nutrition research–by some other division, if not DCT.

The Diet, Nutrition & Cancer Program, which had been administered by the Div. of Cancer Cause & Prevention, has been broken up, with the treatment related projects assigned to DCT. Treatment related grants formerly administered by the Div. of Cancer Research Resources & Centers also have been turned over to DCT.

The proposal would have been a multidisciplinary project consisting of randomized prospective controlled clinical trials in three diseases–diffuse histiocytic lymphoma, small cell anaplastic carcinoma of the lung, and locally unresectable carcinoma of the stomach, designed to determine the value of total parenteral nutrition as an adjunct to standard therapy. The project would attempt to determine whether TNP improves toleration to therapy, response rates, duration of response and duration of survival, and whether it affects host-immune response.

The study would involve 150 patients for each of the three diseases.

Salmon said he felt the study was too big, "not entirely well conceived," and that stomach cancer as one of the three diseases "would not be useful." The plan to study acute histiocytic lymphoma patients with six monthly cycles of therapy was not adequate, Salmon said.

Rubin suggested that diseases with better survival be used.

"Are there any new leads?" Henry Kaplan asked. "People have been trying to find leads for 20 years. It is clear that drums are beating (for nutrition) in the halls of Congress, but does that inspire any new cells in the brains of investigators?"

NCI released a program announcement covering the entire nutrition program (***The Cancer Letter***, Sept. 22). The treatment portion of the announcement requested grant applications for clinical and preclinical research in anorexia, cachexia metabolism, nutritional supplementation, and nutritional complications of antineoplastic therapy.

Enrico Mihich suggested that it was premature to develop a contract program before the response to the grant request could be ascertained. He offered a motion to disapprove.

"Would this free up money for other projects?" Salmon asked.

"This money is for nutrition," DeVita answered. "If we don't spend it on nutrition, it will go somewhere else."

"In my opinion, $2.4 million is a large amount regardless of what pocket it comes out of," Board member Charles Heidelberger said. "It needs to be spent carefully." Heidelberger suggested that the proposal be disapproved as written and that a subcommittee be appointed to rewrite it, and the rest of the Board agreed.

They approved four new resources contract programs and a new research contract effort in the Developmental Therapeutics Program. One proposal, for a three year, $70,000 per year project to develop prescreens for evaluation of crude natural products, was withdrawn when Board members suggested it was more appropriately a research project than resources, as written. They also felt it might better be funded through a grant.

The new research contract proposal, which will be announced through an RFP, is for basic analog synthesis. First year award was estimated at $175,000 on a three year contract, and multiple awards will be considered. The narrative description of the project:

"Objective of the proposed contract is the synthesis of rational analogs of new leads identified in our program for activity/toxicity optimization.

"Purpose of this project is to assure through limited well-focused structure-activity studies the selection of the best compounds in a series of progression through the linear array. At present, analogs of leads identified by the data review subcommittee for followup studies are chosen for existing inventory

amounts are not needed, and a large scale production facility is not so much an asset."

"This isn't molecular oncology," Weinstein said. "It's a grabbag of activities. It is not the place to continue this kind of virology. It could be a place to expand chemical carcinogenesis. It is a hiding place for second rate virology, and doesn't compare with other intramural work."

Old disagreed. "There's some awfully good work being done there."

O'Conor suggested that the Board hold its next meeting at FCRC and plan to conduct a review of some of the programs there. "Your decision then might carry more weight."

Board member Louis Siminovitch said, "The problem may not be the individual programs, but that the whole concept is wrong. A locked in contract is not the way to do cancer research."

"What's the general feeling of the group about meeting at Frederick?" Magee asked.

"It's a bad idea. I was there six years ago," Watson said.

"If we look at the concept, we can do it in this room," Siminovitch said.

Litton Bionetics first won the contract in 1972 over about 10 other serious proposals. The terms of the contract provide for a fee, or profit, which is determined semiannually by NCI research contract and other staff members who review Litton's performance during the previous six months.

The first contract was for a five year period. It was advertised for recompetition last year, but no other organization was interested in going up against Litton and the firm received a new five year contract. The government, however, always reserves the right to terminate contracts before expiration dates. While it is possible the contract could be phased out earlier, if that is the decision, it probably would require the four years remaining for NCI and other NIH components to gear up for the takeover.

The government has other GOCO facilities—Oak Ridge, Argonne, Brookhaven, and Los Alamos, among them—which are considered to be efficient and effective operations. On the other hand, the National Center for Toxicology Research, located in a former Army chemical warfare base in Arkansas, is operated and staffed directly by the Food & Drug Administration and is not given high marks by some who are familiar with its work.

SCHNEIDERMAN LEAVES FIELD STUDIES; SIBAL NAMED ACTING DCCP DEPUTY CHIEF

Two major personnel changes in the Div. of Cancer Cause & Prevention were announced at the first meeting of the division's Board of Scientific Counselors.

Marvin Schneiderman, longtime chief of Field Studies & Statistics, revealed that he is leaving that position Nov. 1 to become associate NCI director for science policy, in the office of Director Arthur Upton.

Upton told the President's Cancer Panel that "I've been concerned about the degree to which the Office of Director is isolated from the scientific activity of NCI." He said he created the Office of Science Policy to fill that gap, and that Schneiderman also would work with him in liaison activity with other HEW offices and agencies outside the department as well as with organizations in the private sector. He also will help with legislative duties and preparing reports to Congress.

Schneiderman thus follows the path trod earlier by two of his former DCCP colleagues—James Peters, ousted DCCP director, and John Moloney, who was removed by Upton as head of the Viral Oncology Program as a prelude to dismantling that program. Peters and Moloney were assigned to Upton's office, with Peters eventually leaving the government.

"I don't feel I'm being kicked upstairs," Schneiderman told ***The Cancer Letter.*** "If I felt that way, I would leave. I look forward to the new job as an interesting and challenging one, and one where I hope I can make a contribution."

O'Conor also announced that Louis Sibal had been named as his acting deputy director. Gio Gori, still the deputy director of record, is spending part of his time pursuing master of public health studies at Johns Hopkins Univ., part of his time at NCI working with the Smoking & Health Program, and much of his time on the Baltimore-Washington Parkway.

Gori's status when he returns full time next June is yet to be determined. O'Conor did not tell the Board, as reported in the *Blue Sheet,* that Gori would not return to NCI. In all probability, Gori will not be back as deputy director, but he says he intends to stay at NCI. Upton has said Gori is welcome to stay, the dispute over Gori's article on less hazardous cigarettes notwithstanding, but has not determined what job he will have.

Sibal was deputy director of the Viral Oncology Program, and temporarily headed it after Moloney left.

ADVISORY GROUP, OTHER CANCER MEETINGS FOR NOVEMBER, DECEMBER

23rd Annual Clinical Conference—Nov. 1-3, Shamrock Hilton, Houston.

Pancreatic Cancer Review Committee—Nov. 1, Continental Plaza Hotel, Chicago, open 8:30—10 a.m.

Australian Cancer Society—Nov. 1-3, Adelaide, biannual meeting.

Clinical Cancer Education Review Committee—Nov. 1-2, Landow Room A, open Nov. 1, 8:30—9 a.m.

Practical Aspects of Cancer Management—Nov. 5-7, Williamsburg, Va.

Cancer Clinical Investigation Review Committee—Nov. 6-7, NIH Bldg 31 Room 6, open Nov. 6, 9 a.m.—12:30 p.m.

Course on Cancer Epidemiology—Nov. 6-17, Sydney.

26th Annual Meeting of the American Society of Cytology—Nov. 7-11, Bal Harbour, Miami Beach.

Progress in Head & Neck Oncology—Nov. 9, Roswell Park continuing education in oncology. Contact Claudia Lee.

French Society of Head & Neck Tumors— Nov. 10-11, Paris.

Comprehensive Cancer Rehabilitation—Nov. 10, Mt. Zion Hospital & Medical Center, Box 7921, San Francisco 94120, phone 415-567-6600.

Breast Cancer Symposium—Nov. 11, Cancer Therapy & Research Center, San Antonio 78229, phone 512-690-1111.

NCI-CROS Conference on Combined Modalities: Chemotherapy and Radiotherapy—Nov. 15-18, Hilton Head Island, S.C.

Cancer Centers Support Review Committee—Nov. 16, Linden Hill Hotel, Bethesda, open 8:30—10 a.m.

Div. of Cancer Control & Rehabilitation Advisory Committee—Nov. 16-17, NIH Bldg 31 Room 10, 9 a.m. both days, open.

Cancer & Medicine 1978—Nov. 16-18, Univ. of Kentucky, Lexington, continuing education.

Prostatic Cancer Review Committee—Nov. 17, Bethesda Holiday Inn, open 8-9 a.m.

Current Trends in Analgesia for Cancer Patients—Nov. 18, Roswell Park continuing education in oncology.

National Cancer Advisory Board—Nov. 20, 9 a.m., all open. (Previously scheduled for three days, this is now a one-day meeting, with no subcommittee meetings scheduled.)

Symposium on Nutrition & Cancer—Nov. 20-22, Adelaide, Australia.

Clinical Oncological Society of Australia Annual Scientific Meeting—Nov. 22-24, Adelaide.

Clearinghouse on Environmental Carcinogens Plenary Session—Nov. 31, NIH Bldg 31 Room 10, 9 a.m., open.

4th Congress of Medical Oncological Society—Dec. 2-4, Nice.

Seminar on At Home Rehabilitation for Cancer Patients and Families—Dec. 6, Park Plaza Hotel, Cleveland, sponsored by the Cancer Center Inc.

Endocrinologic Aspects of Cancer—Dec. 7, Roswell Park continuing education in oncology.

Large Bowel Cancer Contract Review Committee—Dec. 7-8, Prudential Bldg, Houston, open Dec. 7, 7:30 p.m.—8 p.m.

Cause & Prevention Scientific Review Committee—Dec. 8, Landow Room A, open 9—9:30 a.m.

Cooperative Group Chairmen's Committee—Dec. 11, NIH Bldg 31 Room 8, 1 p.m., open.

President's Cancer Panel—Dec. 12, NIH Bldg 31 Room 7, 9:30 a.m., open.

Clearinghouse Chemical Selection Subgroup—Dec. 12, NIH Bldg 31 Room 10, 9 a.m., open.

Tumor Immunology Committee—Dec. 13, Westwood Bldg Room 803, open 1:30—2 p.m.

Clearinghouse Data Evaluation/Risk Assessment Subgroup—Dec. 13, NIH Bldg 31 Room 10, 9 a.m., open.

Clinical Cancer Program Project Review Committee—Dec. 14-16, NIH Bldg 31 Room 6, open Dec. 14, 8:30—10:30 a.m.

Pacific Endocurietherapy Society—Dec. 15-17, Wailea Beach Hotel, Maui.

2nd International Conference on Inorganic & Nutritional Aspects of Cancer— Jan. 3-5, Univ. of California (San Diego) La Jolla 92093, phone 714-452-4463.

National Cancer Advisory Board—Jan. 15-17, NIH Bldg 31 Room 6 (schedule and agenda to be determined).

NCI CONTRACT AWARDS

Title: Reconstruction algorithms for dose reduction in x-ray computed tomography
Contractor: Mayo Foundation, $337,709.

Title: Development of topical chemotherapeutic agents for mycosis fungoides, continuation
Contractor: Johns Hopkins Univ., $94,076.

Title: Designing and implementation of computer programs and systems relating to biomedical computing
Contractors: Geomet Inc., Gaithersburg, $583,246, ORI Inc., Silver Spring, $312,741.

Title: EPA/NCI special skin cancer epidemiology study, continuation
Contractor: Geomet Inc., $81,970.

Title: Validation and standardization of in vitro techniques to assess the effect of diet/nutrition on the mutagenic/carcinogenic potential of human secretions and excretions
Contractors: Washington Univ., $351,212, and SRI International, $575,704.

Title: Reagents for characterization of human cell subpopulations
Contractors: Univ. of New Mexico, $93,580, and Univ. of Illinois, $137,411.

Title: Statistical coordinating center, continuation
Contractor: Univ. of Texas System Cancer Center, $300,000.

Title: Science program information systems study
Contractor: Enviro Control Inc., $75,000.

Title: Prototype clinical chemotherapy program in cancer control, renewal
Contractor: Cornell Univ. Medical College, $156,222.

Title: Prototype comprehensive network demonstration project in head and neck cancer, renewal
Contractor: Illinois Cancer Council, $653,496.

Title: Technical writing and telephone answering services in response to cancer related inquiries
Contractor: Biospherics Inc., $730,427.

Title: Data management support to selected treatment and rehabilitation programs
Contractor: Small Business Administration, $139,136.

Title: National Cancer Program information clearinghouse and allied services, renewal
Contractor: Kappa Systems, $262,297.

Title: National survey of public attitudes, knowledge and practices related to breast cancer
Contractor: Opinion Research Corp., $189,139.

Title: Seven additional alteration/renovation projects at Frederick Cancer Research Center
Contractor: Litton Bionetics, $1,659,056.

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and through procurement from the scientific community. This method tends to be random and does not allow for rational inputs to the design and synthesis of analogs. There is presently no contract to synthesize a selected number of basic analogs for comparative studies. The proposed project is intended to fill the gap.

"This project will serve to support the recommendations for the synthesis of congeners arising from our various analog committees. The data from the ongoing biochemical and pharmacological studies would also form the basis for the design and synthesis of analogs. It is expected that the contractor will synthesize seven to 10 analogs of each lead and there will be approximately three to four leads per year selected for this purpose. Compounds will be synthesized in amounts of 0.5 to 5 grams each as dictated by screening requirements.

"Also, it was recommended by Cancer Treatment Program staff that this effort be offered as a task order contract. The purpose will be to synthesize analogs of high priority as requested to avoid committing all funds if found unnecessary. Therefore, monies will be set aside and obligated on an as needed basis. Recommendations for synthesis will germinate in the Decision Network review."

The new resources contracts will be:

• Preparation of plant extracts from fresh plants, $150,000 first year of three year contract, multiple awards to be considered.

"The present DTP program for antitumor screening of plant extracts calls for the preparation of organic solvent extracts of dried plant materials. Some water soluble compounds and proteinaceous or unstable materials would not be identified by this procedure. Several compounds of plant origin currently under development in the program would likewise not have been recognized. It is therefore considered highly important to initiate a small program to examine the antitumor potential of water soluble extracts of fresh plant material from a variety of sources to see whether the yield of antitumor agents from plant sources could be enriched.

"The function of this proposed contract will be to prepare aqueous extracts (ambient temperature) of fresh plant material and to lyophilize these extracts for shipment to a government screening facility. The plants to be collected should be from diverse taxonomic sources and the collection area must be within a half days transport distance distance from the extraction laboratory in order to minimize deterioration of sensitive plant components because of microbial fermentation. The project will require leadership by a team of a botanist with expertise in identification of the flora to be collected and a phytochemist experienced in plant extract work."

• Computerized literature surveillance of natural products, $75,000 first year of three year award, multiple awards to be considered.

"The Natural Products Branch is responsible for acquisition of natural products for antitumor screening. It is necessary to have a resource contract to identify for the Natural Products Branch staff (1) new natural products reported in the literature (2) compounds reported in the literature which are analogs of compounds of current interest for development as antitumor agents (3) compounds which are reported to have biological activities which may correlate with antitumor activity (4) botanical, zoological, or microbial sources of specific compounds of interest to NCI staff (5) compounds which have been isolated from plant, animal, or microbial extracts active in NCI antitumor screening protocols.

"This would be a very important computer-programmed contract to keep us abreast of all new natural products isolated and reported. Several thousand new natural products a year are isolated and in some cases even are evaluated for various biological activities. A program as stated would help us determine which materials might be worthwhile evaluating in our program, give NCI insight into what plants should be collected, and help identify potential sources of supplying a compound to NCI.

"It was further agreed at the Cancer Treatment Program staff meeting that the competition should be based on specific and well defined assignments as requested by the government project officer rather than on a level of effort approach."

• In vitro and in vivo screening of radiosensitizers, $250,000 first year award, three years, possible multiple awards.

"In 1977, development of hypoxic cell radiosensitizers was added as a new dimension to the Drug Development Program. One of its chief objectives was to search for compounds which selectively increase the lethal effects of ionizing radiation on neoplasms while sparing normal host tissues. The purpose of the proposed contract is to provide selected physical-chemical properties on compounds, such as solubilities and lipid/water partition coefficients and to provide in vitro and in vivo screening tests for the development of new classes of radiosensitizers and to improve the therapeutic indices of known agents currently in clinical trial.

"NCI will supply the contractor with compounds of diverse chemical structures for evaluation for selective effects on hypoxic cells in culture. Promising materials from this primary screen and other programs will be evaluated in vivo according to the Treatment Linear Array for Radiosensitizers, which was published by the DCT in September 1977. This document contains the standards and guidelines, test systems, and criteria that will be used for the development, testing and evaluation of radiosensitizers and radiopotentiators."

• Resynthesis laboratory, $250,000 first year award, three years, possible multiple awards.

"It is of vital importance that DTP have the capa-

bility to pursue new leads which are uncovered through screening. The development of many of these active compounds is hampered because of our failure to obtain sufficient supply of compounds for confirmatory testing. The problem of obtaining larger samples for testing from the scientific community has become acute in recent years, because chemists, with the advent of HPLC, NMR and Gc-Ms, in general are synthesizing only small amounts of material. In fact, the more unique the structure the more difficult it is to procure sufficient material for testing. In addition, drastic cuts in the synthesis-contract activities no longer make it feasible to procure even contract leads in adequate quantity.

"Objective of the synthesis laboratory is the resynthesis of 50-70 compounds per year in quantities of 2-5 grams each.

"The types of compounds to be resynthesized include radiosensitizers, nucleosides and nitrogen, oxygen and sulfur containing heterocycles. The compounds will be selected from:

"—Potential radiosensitizers especially of the nonnitroimidazole types.

"—Compounds selected from the Cumulative QNS list.

"—Unique compounds not available from the grantees in sufficient quantities for complete evaluation.

"—Compounds recommended by the Analog Committees for special studies."

Existing DCT contracts approved for either recompetition or noncompetitive renewal will be described in subsequent issues of ***The Cancer Letter.***

NCI DIVISION CHIEFS RECOMMEND PHASEOUT OF LITTON CONTRACT, NIH FCRC TAKEOVER

NCI's division directors have unanimously agreed that the contract with Litton Bionetics for operation of the Frederick Cancer Research Center and conduct of cancer research there should be phased out and the space and facilities used to permit expansion of NIH intramural programs.

Div. of Cancer Cause & Prevention Director Gregory O'Conor told his new Board of Scientific Counselors that his fellow division directors felt that use of FCRC "as an extension of the NIH campus" would help alleviate the growing space and facilities crunch which intramural scientists say is limiting their growth.

O'Conor pointed out that the major impediment to such a change is the limit on the number of positions allotted NCI and the rest of NIH. Several hundred scientists, professional and support staff at FCRC are on Litton's payroll and thus are not counted against NCI's total.

Litton Bionetics, under a $25 million a year "GOCO" (government-owned, contractor operated) contract from NCI, is responsible for all of NCI's activities at FCRC, the former Army biological warfare base at Frederick, Md., located about 25 miles from the NIH campus in Bethesda.

Activities there include production of viruses, chemicals, reagents, drugs, and animals both for NCI intramural programs and for grantees and contractors, and a basic research program headed by Michael Hanna.

NCI Director Arthur Upton has had a staff committee studying the FCRC situation, and has asked the group to identify those areas that present problems and need immediate improvements, O'Conor said. The committee includes John Moloney, former director of the Viral Oncology Program; Vincent Groupe, Louis Carrese, William Payne and Henry Hearn. The latter two are NCI staff members assigned to FCRC.

"The question is, what is special about Frederick?" O'Conor asked. "Why should this work be done at Frederick and not elsewhere? (a question asked frequently by others around the country who look with some envy at the $25 million budget). When Frederick became available (and NCI was ordered by President Nixon to make use of its facilities), there was no choice. Use of a contractor was the only realistic way. It has been used effectively, but is it the most effective way to use it in the future? Space is short on campus, especially for animals. If we're going to maintain high quality intramural programs, many of us look to the use of FCRC in the future."

O'Conor said he and Upton were "urgently seeking" the advice of the new Board. One of the Board's charges is review of DCCP intramural programs, including that part of FCRC which is supported by the division. "Other parts are yours, if you are willing," O'Conor said.

The Div. of Cancer Biology & Diagnosis Board of Scientific Counselors reviewed Hanna's program. O'Conor asked his Board to review DCCP's molecular oncology and chemical carcinogenesis programs there.

"I'm delighted with the way this is going," said Board member Lloyd Old. "I hope it will be incorporated into NIH."

"There is still a major feeling outside NCI that per dollar spent at Frederick, it is not being spent as effectively as it could be," said Board member James Watson. "It needs some good review."

Peter Magee, chairman of the Board, asked if the facilities at FCRC are particularly good for carcinogenesis. Hearn replied that they were, but Board member Bernard Weinstein said, "I challenge that. The administrative structure is so fouled up, that the science could be good but would not be effective. It is not a particularly good place to do high quality carcinogenesis research. The equipment is antiquated."

Watson commented, "Seven or eight years ago, people thought that large amounts of viruses were a good thing. Now, it is not so necessary. Large