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DCT BOARD APPROVES $17 MILLION IN RECOMPETITION; ASKS SOME BE SWITCHED TO COOPERATIVE AGREEMENTS

NCI's Div. of Cancer Treatment Board of Scientific Counselors has approved recompetition and sole source renewal of DCT research and resource contracts which will total an estimated $17 million in the first year of the new awards.

The Board balked at only a handful of the recompetitions and renewals proposed by DCT staff: (Continued to page 2)

In Brief

ACS ASKS REMOVAL OF DOLLAR AUTHORIZATION LEVELS; FDA MAY OVERRULE ADVISORS ON ESTRAMUSTINE

AMERICAN CANCER Society has asked the Senate Health Subcommittee to remove the authorization levels from the bill renewing the National Cancer Act. The ACS Board of Directors approved the recommendation "in anticipation of major opportunities for action against cancer in the next three years." Some ACS Board members and staff feel that authorization levels in the Cancer Act have tended to limit appropriations rather than serve as targets as they did in the early years after the Act was passed in 1971. Ironically, the Nixon Administration tried to get the dollar figures removed when the Act was up for renewal in 1974 because Nixon's budget strategists felt they were leading to higher appropriations than were justified. Cancer Program advocates fought to retain the authorization levels; many now will continue to do so despite the ACS action, seeking instead of dropping them to get Congress to set levels high enough to cover major new initiatives. . . . **FDA BUREAU** of Drugs staff is seriously considering overruling the Oncologic Drugs Advisory Committee's recommendation against marketing estramustine for treatment of prostatic cancer (***The Cancer Letter***, Oct. 19). The committee's 5-4 vote against approving an NDA was based on lack of evidence from controlled trials demonstrating an increase in survival, although most committee members agreed that the drug did appear to benefit many patients. . . . **TERESE LASSER**, founder of the Reach to Recovery program which helped an estimated 500,000 women with breast cancer, died recently of a heart ailment. She was 75. . . . **A. HAMLIN LETTON**, president of the Atlanta Medical Center; Charles Ebersol of Litchfield, Conn.; and Paul Williams of North Palm Beach, Fla. have been made Honorary Life Members of the American Cancer Society. . . . **THIRD INTERNATIONAL** Conference on Integrated Cancer Management, sponsored by Good Samaritan Hospital of Phoenix, has been scheduled for Feb. 20-22. The program includes discussion of lung, breast, head and neck, CNS, and genitourinary cancers, malignant melanoma and soft tissue sarcoma, immunotherapy of cancer and complications of cancer. Contact Secretary, Div. of Oncology, Medical Staff Services, Good Samaritan Hospital, 1033 E. McDowell Rd., Phoenix 85006.

DCT BOARD DELAYS RECOMPETITION OF PROTECTED ENVIRONMENT CONTRACT

(Continued from page 1)

• Three large clinical study projects—in lung cancer, gastric and pancreatic cancer, and the Brain Tumor Study Group—involving 25 institutions, all presently financed by contract, should be converted to the cooperative agreement mechanism as soon as that mechanism is available, the Board said.

• Action on renewal of the $765,000 a year contract with M.D. Anderson on quantitative evaluation of protected environment (laminar air flow room) was tabled until the Board's spring meeting.

• Action on the nearly $300,000 a year contract with Hazleton Laboratories for preclinical canine bone marrow transplantation was deferred until after a scheduled site visit has been completed, with temporary extension of the contract for three months approved.

• The $150,000 a year contract with Health Research Inc. (Roswell Park) for liposomal encapsulation of antitumor agents will not be recompeted when the contract expires next year because, Board members felt and NCI staff agreed, there now is enough work going on in that area to make that project unnecessary.

• The Board first voted down recompetition of the $200,000 a year contract with Pfizer for preparation and purification of viral components required by Robert Gallo's Laboratory of Tumor Cell Biology. The Board later reconsidered, determining this was an important resource for some important intramural research, and approved recompetition of the contract.

For projects approved for recompetition, new RFPs will be issued and any qualified institution or organization may submit proposals. Most current contractors are expected to join in the competition, but some of them may lose out in the process.

Approved for recompetition were:

—Adjuvant trials in resectable and partially resectable non-oat cell lung cancer. Present contractors are UCLA, Fred Hutchinson Cancer Center, Mayo Clinic, Ontario (Canada), M.D. Anderson and Vanderbilt Univ. Estimated first year award will total $1.1 million. Recompetition was planned for five years, but with the Board's decision this should be changed from contracts to cooperative agreements, a new contract period of three years or less will be considered while the new mechanism is being implemented. The DCT description of the project said:

Current protocols include Protocol 771 (stage 1 resected lung cancer—placebo vs. intrapleural BCG); Protocol 772 (stage 2 and 3 resected adeno and large cell lung cancer—BCG plus levamisole vs. CAP), and Protocol 773 (stage 2 and 3 resected epidermoid lung cancer—control vs. RT vs. RT plus levamisole). "The performance of the group has been excellent with over 300 patients randomized to Protocol 771 in the past two years. Protocols 772 and 773 have had slow but steady patient accrual. We anticipate an enlargement of this group's work scope to include therapy in partially resectable lung cancer and the group has begun drafting a protocol in this area which would compare RT vs. CAP vs. CAP plus RT. We also anticipate this group playing a major role in the Biologic Response Modifier Program and designing a stage 1 protocol in non-oat cell lung cancer employing biologic response modifiers. Included in the $1.1 million estimate for FY 80 are funds for statistical support in data analysis."

—Therapy of patients with gastric and pancreatic cancer. Also recommended for change to cooperative agreements. Present contractors are Roswell Park, Mayo, Univ. of Miami, Mt. Sinai Hospital, Sidney Farber Cancer Institute, Univ. of Southern California, and Yale Univ. Estimated first year awards would total $1.2 million. Recompetition was to have been for five years but may be reduced while cooperative agreements are being phased in. The DCT narrative said:

The Group has completed a trial (GI 8274) of chemotherapy alone vs. chemotherapy plus radiation therapy in locally unresectable gastric cancer. Early results of this study suggested that the more toxic combined modality regimen led to a shortened median survival, although later results are demonstrating that the treatment benefit of chemotherapy-alone arm is lost after two years. In a chemotherapy study in advanced disease (8375) the Group demonstrated the activity of adriamycin alone, with prolonged survival in the combination chemotherapy arms of the study (5FU+adriamycin+MeCCNU, 5FU+ARA-C+MeCCNU).

In phase 2 trials in pancreatic cancer, adriamycin was also identified as an active agent. GI 9273 demonstrated that 5FU +6000R could be safely given to patients with locally unresectable pancreatic cancer, with more impact on survival than 5FU+4000R or radiation alone.

Current studies include: 5FU+MeCCNU vs. surgery alone in surgically curable gastric cancer; phase 2/3 trials in advanced gastric cancer (5FU+adriamycin vs. 5FU+adriamycin+MeCCNU vs. 5FU+adriamycin+mitomycin-C). These studies continue to demonstrate that survival of patients with advanced disease is prolonged with current combination chemotherapy regimens; phase 2 antifol therapy in previously treated patients with advanced gastric cancer or patients ineligible for GI 8376 because of heart disease; adjuvant chemotherapy+radiation therapy in resectable pancreatic cancer, comparable to a surgery-only group. This is the only currently active study in this patient population); radiation therapy+chemotherapy (5FU+6000R vs. adriamycin+4000R) in locally unresectable pancreatic cancer; ongoing phase 2 trials of 8 single agents and combinations in advanced measurable pancreatic cancer.

Future plans for the Group include: 1) replacement of the gastric adjuvant study within the year with an adriamycin-containing combination; 2) completing the phase 2/3 trials in advanced gastric cancer and evaluating new single agents and combinations; 3) completing the study to establish the activity of antifol therapy in gastric cancer; 4) continuing to accrue patients to the pancreatic adjuvant study. Although accrual is low, significant differences are being observed even at this stage of analysis; 5) developing replacement arms for the radiation-chemotherapy and phase 2 single agent trials in pancreatic cancer, as significant results occur.

The future of these trials depends on the ability of the Group to continue to be able to develop therapies in all stages of disease, with an emphasis on developing approaches for surgically curable patients. This Group has demonstrated that it can perform meaningful combined modality studies with high levels of quality control and with attention to the natural history of these malignancies. The concept of encouraging multimodal therapists to approach the treatment of gastric and pan-

creatic cancers is important, since few previous attempts by single institutions or single modalities have provided satisfactory answers. Gastrointestinal malignancies account for almost one-quarter of all human cancers. Although colon cancer is far more frequent than gastric or pancreatic cancer, the low surgical curability rate in those two cancers makes further studies in the treatment of these tumors imperative. The scope of these trials and the future plans of these investigators make the gastric and pancreatic contracts within the GITSG a unique resource within the clinical trials program.

—Brain Tumor Study Group. Existing contractors are Bowman Gray School of Medicine, Clinica Neuro. del Universita, Duke Univ., Indiana Univ., Univ. of Kentucky, Memorial Hospital, Montefiore Hospital, New York Univ., Ohio State Univ., St. Louis Univ. and Univ. of Tennessee. Estimated first year awards would total $1 million. Recompetition was proposed for five years but that period probably will be shortened in favor of cooperative agreements. The DCT narrative said:

During the past five years, BTSG has conducted clinical trials in malignant gliomas, utilizing multidisciplinary treatment protocols developed to test the efficacy of promising modes of therapy and to provide scientific information which is relevant to the natural biology of malignant brain tumors. Seven four-arm treatment protocols, four phase 3 and three phase 2, were conducted during this period, three of which are still actively accruing patients. Approximately 400 new patients are randomized yearly to the BTSG protocols by the 11 participating institutions. This excellent rate of accrual provides sufficient patients so that the protocols can be completed and treatments evaluated in the shortest possible time.

The results of the BTSG protocols have provided valid data from well controlled studies, data which have been reproducible and have received acceptance as a "standard" against which the results of other trials are compared. The data accumulated by the BTSG during the course of the clinical trials have resulted in the following accomplishments:

—Provided adequate testing of new drugs and/or multidiscipline approaches for the treatment of malignant brain tumors in phase 2 trials.

—Screened potentially effective new drugs for efficacy in the treatment of malignant brain tumors in controlled phase 2 trials.

—Extended the survival of the patient with malignant brain tumor more than three-fold.

—Demonstrated the effectiveness of radiotherapy in this disease entity.

—Identified the factors which are of prognostic and therapeutic importance in clinical trials with malignant glioma patients.

—Demonstrated the dose-effect relationship of radiotherapy and established the efficacy of high-dose radiotherapy.

—Examined the effect of corticosteroids as a major modulator in the conduct of clinical trials of brain tumor and specifically their oncologic effect.

—Established a central Neuropathology Reference Center.

—Demonstrated the value of the nitrosoureas in the treatment of malignant gliomas.

Future plans for the BTSG include a continuing effort to test in randomized, prospective clinical trials new drugs, drug combinations, multimodality approaches and/or adjunct treatment or techniques which may be effective in extending the survival of the patient with this disease entity. The BTSG will continue to provide information both relevant to the basic nature of the disease it treats, as well as to the specific modalities of therapy. Attention will be directed to evaluating the CT scan as a means of assessing the effectiveness of therapy, drug pharmacology, treatment toxicology, drug interactions and the undesirable treatment side effects that are now being observed because of the treatment-associated increased life span of the brain tumor patient.

—Multimodal treatment of primary breast cancer. Present contractor is Istituto Nazion, Milan. Estimated first year award, $200,000. Ordinarily, DCT would have renewed this as a sole source contract, but to do that would have prevented the addition of new studies to the program. The narrative said:

This contract has supported some of the most productive clinical research in the decade of the 1970s. Studies of multimodal treatment of breast cancer have been the major emphases, but the contract also has supported studies in small cell carcinoma, colon cancer, and gliomas. The progress made in treating stage 2 breast cancer has been dramatic in the last seven years and has resulted in improved disease free survival in premenopausal breast cancer patients. The CMF studies done under this contract have provided much information both on the worth of postmastectomy chemotherapy and also on prognostic factors of importance in certain patient subgroups.

Less than one-half of stage 2 breast cancer patients are cured by surgery alone. Although administering chemotherapy after surgery has prolonged disease free status and survival in premenopausal women, in postmenopausal patients benefit is minimal. Also, 30% of stage 1 patients are not cured by surgery alone and the usefulness of adjuvant chemotherapy has not been tested in this group of patients. Less than 10% of stage 3 patients are cured of their disease with current treatment, and thus there is a great need to evaluate innovative therapy in this group of patients. NCI plans to recompete this contract so that the results of multimodal treatment obtained in stage 2 disease can be tested in stages 1 and 3. There will be continuation of stage 2 studies to define the optimal drugs, doses, and schedules of postmastectomy chemotherapy.

—Assessment of radiation therapy equipment needs. Present contractor is WSA Inc. Estimated first year award is $75,000, with the contract to be recompeted for three years. The narrative said:

The purpose of this contract is to provide technical assistance to the Radiotherapy Development Branch concerning radiotherapy equipment and related matters. Tasks are assigned by the project officer. In the first 18 months of the contract eight tasks have been assigned with four completed and three more scheduled for completion of the second year. These include: overview of particle therapy equipment; operational characteristics of conventional radiotherapy equipment; CT scanner applications in radiotherapy; and neutron leakage from high energy equipment.

This task order contract with WSA has proved to be very useful. The expertise developed is a substantial resource to the Radiotherapy Development Branch.

—New lead development in solid tumors. Present contractors are Mayo, Memorial Hospital, Sidney Farber, M.D. Anderson, and Wayne State Univ. Estimated first year awards would total $1.2 million. The narrative:

These contracts, previously designated as phase 2/3 contracts represent the endpoint of the drug development program, involving prospective development and evaluation of new chemotherapeutic agents in the therapy of metastatic malignancies. These also represent an attempt to provide an efficient system for the timely and accurate evaluation of agents identified as high priority by DCT. These institutions have developed therapies in a wide range of tumors, utilizing single agents, combination therapies and multimodality therapy.

Although there is similar work in the Cooperative Groups, these studies represent investigator interests which are not always responsive to the multiple needs of DCT. By utilizing program-directed contracts, the resources initially expended to develop new therapies will not be wasted because the final evaluations of the roles of these therapies are not performed.

The tumors which have been selected for study include cancers of the lung, breast, prostate, bladder, kidney, testicle, ovary, endometrium, cervix, head and neck, stomach, pancreas and colon, as well as lymphomas, melanomas, bone and soft tissue sarcomas. Institutions will be encouraged to submit proposals for those tumor types for which there is significant institutional expertise, facilities and capabilities. Although substantial input will come from the DCT concerning the evolution and design of studies, the investigators involved will be encouraged to design and submit protocols for approval by NCI.

—Synthesis of radiosensitizing agents. Present contractors are Institute of Cancer Research and Stanford Research Institute. Estimated first year awards are about $200,000 each. The narrative:

Objective is to design, synthesize, and develop unique compounds as potential radiosensitizers primarily of the electron-affinic type. The project will not be limited to the synthesis of novel nitroheterocyclics, but will focus on the synthesis and development of structure-activity relationships of new structural types, for example, the sulfonate and sulfonamide substituted imidazoles. The synthesis of compounds that might act as radiation modifiers through mechanisms different than the electron-affinic hypoxic cell radiation sensitizers may also be undertaken. The compounds will be evaluated for electron-affinity, lipophilicity, in vitro sensitizing efficacy and cytotoxicity.

—Preparation of novel antineoplastic compounds using biotransformation and co-oxidation. Present contractors are Bristol Labs and Univ. of Iowa. Estimated first year awards total $360,000, with recompetition planned for three years. The narrative:

The importance of biotransformation is that a microbe can carry out 18 types of known transformation reactions, many at the same time, and has a high selectivity while carrying out these reactions. Most of these are reactions which the chemist cannot carry out selectively or easily. The importance of biotransformation is the modification of a structure to make it more active, less toxic, more soluble, etc. Co-metabolism is the technique of feeding in unusual compounds and hopefully converting them to active antineoplastic agents or to short circuit the metabolism of an organism to have it produce a new active compound. Co-metabolism (co-oxidation) techniques are now being explored in the pharmaceutical chemical industry to see if new antimicrobial agents can be produced. Under the current contracts more than 30 novel compounds have been isolated and one (olivomycin-like) is now in the tumor panel. Many of the other novel compounds that have been isolated are undergoing comparison studies with the parent compound or are being produced in sufficient quantity for tumor panel evaluation. Twenty different compounds are being used in co-metabolism and biotransformation studies. The compounds which are selected for this work have not been acceptable for clinical use because of limited activity, toxicity, solubility, etc. but are of interest due to their good animal antineoplastic activity and have structures of interest. NCI hopes to attain novel materials from this work which are greatly superior to the parent and which will have clinical efficacy.

—Preparation of bulk chemicals and drugs. Present contractors are Aldrich Chemical Co., Ash Stevens Inc., Cordova Chemical Co., Pharm-Eco Laboratories Inc., Starks Associates Inc., and Warner-Lambert/-Parke-Davis. Estimated first year awards would total $2,165,500, with recompetition for three years. The narrative:

The chemical preparation laboratories are, in the strictest sense, service laboratories, and are designed and selected to prepare known chemicals and bulk drugs which are needed by the program. The compounds selected for preparation are not readily available in the quality or quantities needed from the original supplier or on the open market.

The laboratories are used to obtain data for the preparation of the necessary quantities of clinically important chemicals and to develop the most economical means for their preparation. It should be pointed out that many methods of synthesis which are practical for small quanity are not technically feasible or economically practical when used for a large-scale synthetic operation. The conversion of small-scale to large-scale production often requires developmental studies which are conveniently carried out by the preparation laboratories.

The preparation laboratories, taken collectively, provide the means of obtaining nearly any type of chemical compound, regardless of structure, and the ability of providing large quantities of very high purity drugs. A wide variety of chemical structures has and is being prepared and most preparations involve multi-step sequences. All materials prepared are fully characterized. The quantity of a given material to be resynthesized may vary from 10 grams to 200 kilograms. Factors governing the amounts depend upon use, ease of preparation, stability and cost.

—Pharmacology of antitumor agents. Present contractor is Arthur D. Little Inc. Estimated first year award is $725,000, with recompetition for three years. The narrative:

This contract has been directed towards the study of the physiological disposition of new antitumor agents. It has also encompassed autoradiographic studies of the localization of selected labeled drugs in mice. This latter activity has now terminated. The work involves the development of methodology for the measurement of drugs in biological materials; the characterization of the pharmacokinetic profiles of the agents in rodents, dogs and monkeys; the detection, isolation and identification of metabolites of the drug and investigation of the biochemical pharmacological properties of drugs and their metabolites. The contract is essentially a preclinical pharmacology effort, but interaction has occurred on several occasions with clinical groups studying the same drugs, to the mutual benefit of both.

The possibility is being explored for converting their resources from this contract into a task-order type mechanism for accomplishing pharmacological studies of new drugs. If this does not prove feasible, it is anticipated that the contract would be recompeted as an individual project.

—Pharmacological studies of antitumor agents. Present contractor is Southern Research Institute. Estimated first year award is $322,000, with recompetition for three years.

Purpose of this contract is to obtain basic quantitative pharmacologic information in rodents, dogs and monkeys which will indicate the requirements of drug dosage and scheduling necessary to produce maximum tumor cell kill while minimizing toxicity to the host's normal cells. The work involves the development of highly sensitive analytical methodology to measure drugs and their metabolites in body tissues and fluids. The methods range from specific microbiological assays to mass spectrographic assays and include techniques needed to accomplish separation and assay of the drugs in vivo. This contract is a preclinical effort, but whenever possible cooperative relationships have been set up with clinical programs working with drugs of mutual interest.

The possibility of converting this contract's resources to a task order mechanism for pharmacology is currently being explored. If it does not appear feasible, the contract would be subject to recompetition as an individual project.

—Application of the subrenal capsule assay to drug testing and development of new in vivo tumor systems. Present contractor is Mason Research Institute. Estimated first year award is $215,000, with recompetition for three years.

Purpose of this contract is to develop new in vivo tumor systems with predictive value in selecting drugs which will be active against human solid tumors and to establish and maintain in serial transplantation human tumor cell lines in nude mice as assay systems. In addition, the contract is to determine whether human tumor xenografts in the subrenal capsule assay respond to drugs in the same manner as the tumor in the patient.

—Prime contract for performance of protocol toxicology studies. Present prime contractor is Battelle Memorial Institute. Estimated first year award is $2,244,000, with recompetition for three years.

For ease in management the prime contract is divided into four tasks. Task I—All new agents intended for clinical use are administered by the proposed clinical route to animals in order to assess the quantitative and qualitative toxicologic properties of each agent. The data developed are needed to provide suggested clinical starting doses and to alert the clinician to potential organ specific toxicities that may be encountered in phase 1 trials. These studies are also done to comply with FDA requirements for IND filing. The protocol of the Laboratory of Toxicology is currently being revised. Although the guidelines for these studies are still being refined, it is expected that single dose and daily times 5 doses in the mouse and dog will satisfy both requirements. The LD10, LD50 and LD90 will be determined from the mouse studies. The mice will be observed for a minimum of 28 days; the observation (recovery) period would be extended if the animals were not fully recovered from any toxic effects. Dogs would be initially treated with 1/10th the mouse LD10 dose expressed in mg/sg m. Clinical chemistries, hematology and gross and histopathologic examination of tissues will be monitored in the dog. Four dogs will be used for each dose level—two to be held for a two month observation period to observe for possible delayed toxicity and/or irreversible toxicity.

Task II—Under this segment of the prime contract, abbreviated studies (any portion of the LT protocol—i.e., mouse x 1, dog x 1) are done. Agents which have had limited clinical use or inadequate preclinical testing are generally subjected to testing under this task. Task II is also used to aid in the preselection of agents for further protocol studies. For example, two analogues of actinomycin D and the parent compound have been studied to develop the data needed to select the least toxic analogue for a more thorough workup prior to its introduction into clinical trials.

Task III—This element is primarily concerned with developing and implementing screens to test and evaluate organ-specific toxicity. Organ-specific toxicity screens have been developed for the following systems: 1) heart (rabbit and mouse); 2) kidney (rat); 3) lung (mouse); 4) GI tract—emesis (dog); 5) nervous system (rat); and 6) vascular (rabbit). Second generation adriamycin analogues are being evaluated in the mouse for their cardiotoxic potential; a number of platinum-containing drugs are on test in the GI toxicity screen. The rabbit vascular screen has been used to assess the vasotoxic potential of PMM vs HMM and several tricyclic nucleosides.

Task IV—Under this portion of the prime contract, computer programs have been developed to assist in the following areas: report writing (tables in final reports are totally computer generated); anomalies detection (deviations from 'normal' of hematologic and clinical chemistry values, etc.), scheduling of testing (an effective mechanism of cutting down the necessity of overtime and preventing overloading of any particular subcontract), and helping in the standardization and adherence to the protocol as required by the Good Animal Laboratory Practice Regulations which became effective June 20, 1979. The computer programs which were originally developed could handle only pairs of animals (i.e., dog, monkey). They have been updated so that any species and number of animals can be handled.

—Preparation and purfication of viral components. Present contractor is Pfizer Inc. Estimated first year award is $200,000, with recompetition for three years.

This contract provides Gallo's lab with 50 liters per week of mammalian type -C RNA tumor viruses, including primate viruses suitable for the isolation of reverse transcriptase, viral antigens, high molecular weight RNA and for the preparation of complementary DNA. The contractor also analyzes human leukemic cell specimens by radioimmunoassays for antigens (p30) related to the major core protein of simian sarcoma virus, Rauscher murine leukemia virus, baboon endogenous virus, feline leukemia virus and RD114.

"You must be embarrassed to present this to us," said Board member Harris Busch, chairman of the Dept. of Pharmacology at Baylor Univ. "This has nothing to do with cancer treatment. It's a huge amount of money to give to one investigator. This is a serious question. This project has been overblown from the beginning. It's another contract for a program even the Virus Program people (in the Div. of Cancer Cause & Prevention) don't support anymore. It's a grant application from within the institute."

Busch's comments reflected the longstanding concern of many in the scientific community over the practice of some NCI scientists extending and expanding their work through use of contracts.

Some Board members questioned why Gallo's lab was located in DCT rather than DCCP, and DCT Director Vincent DeVita explained that Gallo—who has been cited for outstanding contributions—began the work primarily as it related to hematologic malignancies.

Although Board Chairman John Ultmann noted that following the Board's review of Gallo's lab last year, its recommendations "have been implemented to the letter," the Board voted to oppose recompetition of the contract (and thus to let the support it provided Gallo die when the Pfizer contract expires). Only Board member James Holland backed recompetition.

That was late on the first day of the two day meeting. The next day, Board member Charles Heidelberger, director for basic research at the USC Cancer Center, reopened the issue.

"With considerable indignation and on an empty stomach, yesterday we disapproved the support for

Dr. Gallo," Heidelberger said. "The site visit was made to his lab, and great economies have resulted. Our indignation was aimed not at Gallo but the fact that he is in DCT. That's not his fault. It is not up to us to determine whether he is in one division or another. He got high marks from us."

Holland's motion to approve recompetition of the contract was approved without dissent (Busch did not attend the second day of the meeting).

"Dr. Gallo's work is oriented to acute leukemia," DeVita said. "Sometimes it leads to viruses, sometimes elsewhere. I'm not apologizing for having him in our division. I'm proud to have him."

Board members were not convinced that extremely intensive, high dose chemotherapy, the key to effective use of protected environment, has been shown to offer much if any improvement over conventional doses.

While laminar air flow rooms do protect against infection, Board members pointed out, so do antibiotics. The expense of installing and maintaining such facilities is a significant factor, they said.

The DCT narrative describing the protected environment-prophylactic antibiotics (PEPA) program summarized:

The PEPA program has been shown to reduce the risk of infection due to neutropenia from high dose combination chemotherapy. Additionally, larger doses of chemotherapy have been possible in patients treated in the PEPA program. The question as to enhanced response or survival with this program must be regarded as unsettled. However, data from the older sarcoma study and the current oat cell study appear encouraging in this regard. The question of the value of extremely intensive chemotherapy is an important one that will remain unsettled for some time after the expiration of this current contract. Protected environments and prophylactic antibiotics appear to be an important tool in the evaluation of such cancer chemotherapy programs. The currently active (but slowly accruing) DHL study is worth completing, If the promising results in the current oat-cell trial continue, a subsequent trial utilizing intensive chemotherapy plus or minus chest radiation in limited oat cell would be a rational step. Median survivals in this disease are currently approaching two years and the potential for success could be greater than with extensive oat cell. Additionally, the PEPA program lends itself perfectly to the potential evaluation of the use of autologous bone marrow implantation and high dose chemotherapy. The use of this procedure in patients with solid tumors has been limited to date, but the use of protected environments and prophylactic antibiotics has shown to reduce complications. Autologous marrow rescue had not been studied in the current contract but is a potentially interesting prospect to be included in any future recompetition.

The significant question of high-dose chemotherapy bears further investigation and the PEPA program will be a valuable tool in delivering such intensive therapy. It is in the best interest of the Div. of Cancer Treatment to maintain such a resource in its extramural contract program as this will allow performance of the next generation of protocols mentioned above, and give the division the capability to quickly evaluate intensive administration of any new regimens that are promising. For these reasons, recompetition of this project for an additional five years, to begin April 1, 1981, is recommended.

This is an undeniably expensive program because the protected environment is a labor intensive operation and the nature of these studies require prolonged hospitalizations. It is, however, the only project in our clinical contract program evaluating intensive chemotherapy. In that regard it is unique and a resource worth maintaining.

"It's interesting that you say there have been positive results," Board member Philip DeSaia, Univ. of California (Irvine), commented. "With Hodgkin's and other lymphomas, there has been no advantage."

"The scientific results are negative," agreed Board member Sydney Salmon, Univ. of Arizona. "It has not been shown that greatly increased doses have had any positive results."

"The question is, is it time for us to get out?" DeVita said. "Can we say we have a device that protects against infection but has not increased survival? There does seem to be a trend to buying laminar air flow rooms."

DeVita explained that, since there are a number of other institutions with LAF facilities, it is now possible to recompete the contract instead of continuing it as a sole source renewal with M.D. Anderson. John MacDonald, director of DCT's Cancer Therapy Evaluation Program noted that there probably are only three places which could compete—Fred Hutchinson Cancer Center and Wayne State Univ., as well as M.D. Anderson.

Since the contract will not expire until April, 1981, the Board agreed to delay a decision until its spring meeting, hoping additional results from present studies will be available by then.

The Board approved sole source renewal of contracts with:

—Primary Breast Cancer Study Group, Univ. of Pittsburgh, $1,126,000 estimated first year award.

—Therapy of patients with colorectal cancer, Univ. of Pittsburgh, $752,600 estimated first year award. (Above two contracts support in part the National Surgical Adjuvant Breast and Colorectal Cancer Project.)

—Clinical studies by the Veterans Administration, $745,000 first year award. This will be renewed only for one year because the group will be reviewed after that by the Clinical Cancer Investigation Review Committee.

—Collaborative program for clinical investigation, Veterans Administration Medical Center (The NCI-VA Medical Oncology Branch), $2.5 million first year. Approved for one year. This is being phased out and will be replaced by a similar agreement with the Naval Medical Center in Bethesda. DeVita praised the VA for its role in this longstanding program and said the change was being made primarily because of the savings that are possible due to the fact that the Naval Center is across the street while the VA hospital is several miles away.

—Development of cell sorting and analysis systems, Los Alamos Scientific Laboratory, $75,000.

—Operation of cancer chemotherapy research collaborative office, Institut Jules Bordet, Brussels, $100,500.

UPTON MAY BE UNDER PRESSURE TO TELL DECISION AT NCAB MEETING NEXT WEEK

The day is fast approaching when Arthur Upton will have to make known his decision to give up his job as director of NCI and the National Cancer Program—if in fact he has made such a decision.

Upton has been under orders, presumably from HEW Secretary Patricia Harris, not to discuss the situation. She apparently would like to (a) have the new director lined up by the time an Upton resignation is announced, which is unlikely, or (b) give herself and the President more time to determine what to do about the situation.

The job is a Presidential appointment, although Carter left it up to then Secretary Joseph Califano the last time, and he chose Upton.

With the election less than a year away, some prospects might hesitate to take a job which, although it is not supposed to be a political one, still is one in which they serve at the pleasure of the President. It could develop that naming an acting director is the only choice the Administration will have.

If no permanent director is hired by the time Upton leaves, NIH Director Donald Fredrickson would name an acting director, although he undoubtedly would confer with Harris on that decision.

It is almost certain that an acting director would come from within the ranks of NCI. Although there are a number of NCI executives who could handle the job, the most likely prospect would be Vincent DeVita, director of the Div. of Cancer Treatment.

Several sources (not including Upton) have told ***The Cancer Letter*** that Upton will leave NCI Dec. 15 and take over his new position at New York Univ. shortly after the first of the year. If that is his plan, he probably will feel some pressure to announce that decision to the National Cancer Advisory Board at its meeting next week (Nov. 26-28).

CONGRESS SETTLES ABORTION ISSUE, HEW FUNDS APPROVED FOR ENTIRE YEAR

The long congressional fight over HEW appropriations has ended. Congress last week approved a continuing resolution providing funds for all agencies which do not yet have regular appropriations bills for the rest of the fiscal year, which ends Sept. 30, 1980.

The resolution provides funds in the exact amounts as established in the HEW appropriations bill which had been approved by the House and Senate. The only difference between the two bodies was in the language of the provision for Medicare and Medicaid funding of abortions.

That difference was settled in the continuing resolution, with the compromise language essentially the same as it has been for the past few years.

The $1 billion in the appropriations bill for NCI will now be available for disbursement as required, and grant and contract funding may now proceed.

SOURCES SOUGHT

Title: *Analysis of internally deposited radionuclides during atmospheric nuclear weapons testing, 1945-1962*

Deadline for submission of statement of qualification: *Nov. 30*

The Dept. of Defense is considering a two-year effort to: (1) determine which groups, if any, of 250,000 DOD participants in atmospheric testing may have had the opportunity for significant internal contamination, (2) reconstruct data and estimate associated long-term, internal dose commitments, (3) calculate resulting cumulative dosages to appropriate internal organs, and (4) predict late somatic (and possibly genetic) biological effects.

The effort is envisioned in two phases. Results of the first phase will determine whether the second phase is necessary. Phase one, which will last about six months, is designed to determine the magnitude of the problem by accomplishing two major tasks. One of the tasks will be to determine the number of DOD participants which may have been subjected to internal contamination. This will involve reviewing a large number of test reports and extracting descriptions of fallout directly on personnel, dusty conditions of fallout or induced radiation fields, and personnel activities likely to have caused resuspension of radionuclides if present.

The second task will be to reconstruct internal dose and predict effects for several groups likely to have experienced the most harmful internal contamination.

Phase two, which may last an additional 1½ years, will continue the dosage reconstruction process until all groups of significance have been addressed. Extensive experience in the area of inhalation toxicology experimentation is required. Knowledge of ingestion toxicology and internal dosimetry is also important. The radionuclides of interest are the radiologically and biologically long-lived isotopes among the actinides, the transuranics, fission products, and neutron-induced radioisotopes. Extensive knowledge of the biological uptake, distribution and elimination mechanics for critical elements is necessary.

Complete familiarity with current risk estimates presented by BEIR, NCRP, UNSCEAR, ICRP and other appropriate nationally and internationally prestigious organizations will be required. Intimate knowledge of the results of animal studies conducted during atmospheric testing and fallout particle size distribution phenomenology will be necessary. Additionally, experience at the test site(s) and a knowledge of the organization for testing will be helpful. The source selected for this program must have a history of producing highly prestigious, related work considered absolutely credible by the public, the Congress, and the scientific community.

This effort is an integral part of a larger program

and must eventually form part of the whole. The prime contractor will be expected to coordinate and exchange information with other DOD components and several other contractors which are working on other parts of the larger program. Ideally, subcontracts for this particular effort will be at the discretion of, and completely managed by, the prime contractor. A second, but possibly acceptable choice may involve fractionating the effort among several organizations with overall management responsibility retained by the DOD contracting officer. Interested organizations may respond individually or in concert with other complementing organizations.

Organizations having interest are invited to submit (in not more than 20 pages) information in the following categories: (1) Evidence of commitment to this type of work, as shown by past performance; (2) management capability; (3) sufficient administrative and support structure to permit development of the effort; (4) personnel expertise; (5) experience in communicating complex situations and results to government personnel; (6) related ongoing work that could contribute or be reoriented to the development of this effort; (7) sustained objectivity, independence, and absence of conflict of interest.

Respondents should also provide in not more than five pages what their general approach to the effort would be. Contractor personnel must be cleared for access to secret/RD information. Some personnel may require additional clearances. Include in response a statement regarding industrial security clearance if previously granted; standard form 129 and DD form 1630 available through local DCAS offices.

N.C. Myers, OAAM
Defense Nuclear Agency
Washington, D.C. 20305

Title: *Electron accelerator*
Deadline: *Approximately Dec. 18*

One that will be used for industrial radiography, medicine radiography, neutron radiography, and photon activation. The machine should have an output energy adjustable from 10 MeV to 50 MeV; a photon dose rate ranging from 2,000 rad/min to 10,000 rad/min at a meter, an electron focal spot at 20 MeV no greater than 0.5 mm, a pulse repetition rate of between 1,000 and 100 per sec., and a pulse width at 1,000 pulses per sec of 1 us. Firms responding to this announcement should indicate whether they are or are not a minority business enterprise.

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ACS ASKS FTC, FDA, CONGRESS ACTION AGAINST HIGH TAR-NICOTINE BRANDS

The American Cancer Society has called on the federal government to move forward more aggressively with an action program against cigarette smoking. It recommended that:

–The Federal Trade Commission seek voluntary agreements with cigarette companies to eliminate advertising of all high tar, high nicotine, high carbon monoxide cigarette brands, eliminate the use of models in advertising, and stop cigarette promotions aimed at the under 19 age group.

–FDA be given authority to examine potential health hazards of all substances contained in tobacco products, such as tobacco, tar, nicotine, gases, additives, filters and cigarette paper.

–Congress institute a graduated federal cigarette tax based on tar, nicotine and carbon monoxide content as an inducement to move smokers to lower tar and nicotine cigarettes, or at least to establish maximum acceptable levels for the tar, nicotine and other noxious agents in cigarettes, subject to successive reduction year by year.

A national advertising campaign in all media against cigarette smoking, to be underwritten by the federal government, also was recommended.

NCI CONTRACT AWARDS

Title: Carcinoembryonic antigen and related tumor associated antigens in the diagnosis of cancer and as an adjuvant in the management of cancer patients
Contractor: Health Research Inc., $36,130.

Title: Retroaldol type fragmentation of B-hydroxy-nitrosamines which may be environmental carcinogens
Contractor: Univ. of Missouri, $36,256.

Title: Primary genetic center for rodents in bio-containment environments, increased funding
Contractor: Charles River Breeding Laboratories, $499,000.

Title: In vitro malignant transformation, continuation
Contractor: Pennsylvania State Univ. (Hershey), $40,000.

Title: Holding facility for small laboratory animals, continuation
Contractor: Litton Bionetics, $322,896, and $172,817 (two contracts)

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