THE CANCER LETTER

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NCI Considering Adoption Of NIGMS Guidelines To Limit Growth Of Renewals, Ensure New Grants

NCI is considering adoption of guidelines related to funding of grants which were recently implemented by the National Institute of General Medical Sciences, with the approval of the National Advisory General Medical Sciences Council. The guidelines, or some version of them, will

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In Brief

Three Patients Evaluated For Gene Therapy; Revised Program Instructions Available

"WE ARE WATCHING history being made," NCI Director Samuel Broder said of the recent FDA approval for the first study using human gene therapy to treat cancer. Addressing a meeting of the President's Cancer Panel, Broder said, "This investigation captures the imagination of the public and in that sense strengthens all of our activities." At this time three patients are under evaluation for various forms of gene therapy and about 50 patients will eventually be treated. . . . **REVISED PROGRAM** instructions on NCI's Cancer Construction Program are now available. The 143 page booklet includes details on how to apply for construction and renovation, and other information including tips on selection of architectural and engineering firms. Contact Research Facilities Branch, NCI, Div. of Cancer Biology, Diagnosis & Centers, EPN Room 300, Bethesda, MD 20892, phone 301/496-8534. Ken Brow is chief of the branch. . . . **BARUJ BENACERRAF,** president of Dana-Farber Cancer Institute, was one of 20 scientists to receive the National Medal of Science from President Bush earlier this month. He was honored for his achievements in the field of immunology. . . . **WILLIAM MOSS,** Portland, OR, has received the American College of Radiology Gold Medal at ACR's recent annual meeting. . . . **STUART QUAN,** a leading investigator in colorectal cancer surgery, has had a research fellowship endowed in his honor by an anonymous patient at Memorial Sloan-Kettering Cancer Center, where Quan is a member of the surgical staff. The Quan Fellowship will support young people in academic medicine who wish to conduct research on colon and rectal cancer. . . . **RONALD CASTELLINO** has joined Memorial Sloan-Kettering as chairman of the medical imaging department. He succeeds R. Caird Watson, who died this summer. Castellino most recently was acting chairman of Stanford Univ. Medical School's diagnostic radiology and nuclear medicine department. . . .**CORRECTION:** The drug clomesone was developed by Fulmer Shealy of Southern Research Institute, not Thomas Johnston, as reported in the Nov. 9 issue of **The Cancer Letter.**

NCI Considering NIGMS Guidelines For Making Grant Funding Decisions

(Continued from page 1)
be presented to the National Cancer Advisory Board for its consideration.

The guidelines were established by NIGMS to deal with the ever tightening budget faced by all NIH institutes. They are aimed at ensuring some measure of support for new and young investigators and continue funding the maximum number of research grants by limiting support for large grants. They also place some limits on growth of recompeting grants.

The guidelines state:

"In times of extremely constrained funding, the Institute scientific staff should take additional [to the usual criteria for funding grants of scientific and technical merit, scientific program needs and balance, and availability of funds] factors into account in making funding decisions.

"A. In determining whether or not to make an award, Institute staff should give special consideration to a highly rated application from an applicant investigator who has no other significant source of research support.

"B. Prior to considering awards to investigators whose total research support from all sources, including the pending award, exceeds $500,000 (direct costs), special analysis and justification should be required.

"C. In determining the appropriate funding level for competing continuation awards, the Institute scientific staff will consider:

--The previously committed level of support.

--Special needs for equipment.

--Whether the application is the first renewal after an initial award.

"Escalations in excess of 10 percent over the previously committed level of support will require special justification."

NIGMS reported that funding decisions made in the first two rounds of this year, after the guidelines went into effect, included these actions:

* The Institute had sufficient funds to continue its policy, established last year, of paying both new and noncompeting FIRST awards at full cost, without cuts. FIRSTs comprise 9 percent of the FY1990 competing awards.

* The Institute has applied the same reductions to program projects and centers as it has to regular research grants (12 percent reduction from the council recommended level).

* The Institute freed up funds through two actions sanctioned under the guidelines:

--Of the 15 applications from investigators who, if funded, would have had funding in excess of $500,000, only four were not paid; these applications were for new awards, not for competing continuations. and they received percentile ratings from 2 to the theoretical Institute payline; some other investigators in this category (total funding in excess of $500,000) received reduced funding on their awards.

--Thirty percent of the competing continuation applications paid after the January and May councils were cut beyond the budget driven average of 12 percent.

* Freed up funds allowed a six percent increase in the number of awards made after the January council.

* Seven percent of NIGMS awards were made to grantees who had no other significant source of research support and who also had percentiles beyond the theoretical Institute payline.

When the guidelines were discussed by the Board of Scientific Counselors of NCI's Div. of Cancer Biology, Diagnosis, & Centers, Albert LoBuglio noted that about 20 percent of the division's grantees, including those receiving FIRST awards, are new investigators. "I don't know how long you are a new investigator, but you're an old investigator for a long time," he said, suggesting that 20 percent seemed to be enough.

Ross McIntyre added that "the problem of the number of applications [record numbers of applications received by NIH, with significant reductions in award rates] will take care of itself in time, as people lose interest and the number dries up."

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Editor: **Kirsten B. Goldberg**

Contributing Editor: Jerry D. Boyd

Editorial/Subscriptions Office
PO Box 15189, Washington, DC 20003
Tel: (202) 543-7665 Fax: (202) 543-6879

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Joseph Cullen, Cancer Prevention Leader, Dead At 54 Of Brain Tumor

Joseph Cullen, director of the AMC Cancer Research Center in Denver and a national leader in cancer prevention and control, died in San Francisco on Nov. 24 of a brain tumor hemorrhage. He would have turned 54 this week.

Before moving to Denver in 1989, Cullen was deputy director of NCI's Div. of Cancer Prevention & Control and led the federal government's highly successful antitobacco campaign. His unexpected death, while on vacation in San Francisco, shocked friends and co-workers, who said Cullen had shown no symptoms of illness until last week, when the tumor was detected. AMC officials confirmed that the tumor, detected Nov. 21, was malignant and "extremely aggressive."

Cullen participated in the early development of NCI's Cancer Control Program from 1974 to 1976, leaving to direct the cancer control program at the UCLA Jonnson Comprehensive Cancer Center. He returned to NCI in 1982 to head the institute's antitobacco activities. He also was chairman of an advisory panel that helped the Surgeon General prepare a major report on the health consequences of smokeless tobacco.

"Building upon the extensive proof of tobacco risks, a nationwide network of scientists and public health specialists worked together under Dr. Cullen's leadership to conduct intervention research and develop programs to lower smoking and cancer rates in every major segment of our population," DCPC Director Peter Greenwald said last week. **"This is the best program of its kind ever developed by the government."**

Cullen always declined to take credit for the progress achieved in recent years on antismoking efforts, but it was on his watch that new and stronger warning labels were required on tobacco products, smoking was banned in federal buildings and commercial airliners, federal and state tobacco taxes rose dramatically, and smoking prevention and cessation efforts became widely disseminated.

"The only thing I can take credit for is having hired first class staff," he said last year before leaving NCI.

Many in his field thought otherwise. Cullen, Greenwald said, was "a national and international leader in cancer prevention and control. In the 1980s he played a key role in defining and building a scientific foundation for this field." Many NCI staff and cancer prevention and control scientists around the country "selected or have been influenced in their careers by the guidance and exemplary work of Dr. Cullen," Greenwald said.

Cullen left NCI last July to pursue what he said was a career goal. "I've always wanted to be a center director," Cullen told **The Cancer Letter.** At that time, he said he hoped to build AMC into a "model cancer prevention and control center."

"Our loss at AMC is enormous, both professionally and personally," AMC President Bob Baker said. Thomas Kean, director of intervention research, will serve as acting director of the center.

Cullen was born in Boston and earned his A.B. and A.M. degrees from Boston college. He received his PhD in physiological psychology from Florida State Univ. in 1968. He received many awards and honors from NIH and other organizations, including the Surgeon General's Medallion in 1987.

Cullen is survived by his wife, Katherine, of Englewood, CO; son Neal of State College, PA; daughter Jennifer of Berkeley, CA; brother Richard of Northville, NY; and sister Joan Degnan of Long Island, NY.

'Major Discovery' Reported In FCRDC Basic Research Program Report

"A major discovery this year that has had an enormous impact on human cancer research" was cited by George Vande Woude as the crowning achievement of the Basic Research Program during the past year at Frederick Cancer Research & Development Center.

Vande Woude, director of the Basic Research Program under NCI's contract with Advanced BioScience Laboratories Inc., led off the introduction to his annual report on the program by referring to discoveries by the Mammalian Genetics Laboratory, one of eight laboratories with 27 research units supported through the contract.

This research was carried out by Neal Copeland, director of the laboratory, with Nancy Jenkins and Arthur Buchberg. They collaborated with Ray White and colleagues of the Howard Hughes Medical Institute, Univ. of Utah Medical Center.

"Neal's laboratory found that a gene frequently activated in myeloid leukemia, named Evi-2, is located in a region of the mouse genome that is equivalent to the portion of the human genome that contains the neurofibromatosis type 1 (NF1) locus," Vande Woude wrote. "Neurofibromatosis is one of the most commonly inherited genetic diseases and afflicts more than one million people worldwide with symptoms that include neurological dysfunction and

nonmalignant and malignant tumors of the nervous system. Their astute observations subsequently led to the discovery of the NF1 gene. In addition to this important contribution, they have recently shown that the NF1 gene shares sequence homology with two yeast genes, IRA1 and IRA2, which are members of the recently discovered GAP (for GTPase activating protein) family of genes.

"The products of these genes are intimately involved with signal recognition by the ras G protein family as well as with growth factor signal transduction by tyrosine kinases in response to mitogenic stimulation.

"This discovery represents a remarkable advance for cancer research and provides a provocative lead for the mechanism of the disease, since GAP genes have been shown to have activity as tumor suppressor genes in ras transformed cells."

Vande Woude mentioned the name change this year of Frederick Cancer Research Facility to Frederick Cancer Research & Development Center, at least the second name change in the 18 years since President Nixon turned over most of the Army's biological warfare research base to NCI.

"This government owned, contractor operated center is the only federally funded research and development center in the Dept. of Health & Human Services," Vande Woude wrote, "and the new name reflects this distinction. "The government and contractor programs at FCRDC represent a unique association of cooperating units. There are now 27 research units within the ABL Basic Research Program and these are distributed among eight laboratories. We take great pride in our 59 postdoctoral fellows and graduate students. Together with visiting scientists, we now have 140 professionals among 215 employees."

The contract with Advanced BioScience Laboratories (a subsidiary of the Dutch firm, Orgenon Technica) represents only a fraction of NCI's activity at Frederick. Program Resources Inc., which has the contract with NCI for management and operations, has more than 1,100 employees there. This contract, costing NCI this year more than $120 million, supports cancer and AIDS drug development, NCI's supercomputer, and the intramural nutrition research laboratory among other activities.

Vande Woude described several organizational changes in his program during the past year.

"Tony Dipple formed the new Chemistry of Carcinogenesis Laboratory, which consists of the Molecular Aspects of Chemical Carcinogenesis Section, headed by Tony, and the Carcinogen Modified Nucleic Acid Chemistry Group, headed by Bob Moschel. These investigators have worked together for many years and have made exciting advances in understanding how ultimate carcinogens modify DNA. In recent years they have developed new strategies for studying DNA modifications at the molecular level. One of the new approaches has led to the recent discovery by Bob's group (in collaboration with Anthony Pegg, Pennsylvania State Univ. College of Medicine) that the modified nucleic acid base O^6-benzylguanine is very reactive toward mammalian O^6-alkylguanine DNA alkyltransferase and might, therefore, be useful in reducing the level of chemotherapeutic agent, such as chloro-ethylating nitrosoureas or other alkylating chemotherapeutic drugs, required for effective treatment.

"Three new working groups were formed this year in the Molecular Mechanisms of Carcinogenesis Laboratory." Barbara Felber was promoted to staff scientist and formed the Human Retrovirus Pathogenesis Group; Deborah Morrison, recruited this year from the Univ. of California (San Francisco), formed the Cellular Growth Mechanisms Group; and David Kaplan, also recruited from UCSF, formed the Eukaryotic Signal Transduction Group.

Vande Woude noted the retirement of Maurice Guss as executive officer of the Basic Research Program and the recruitment of John Nutter as assistant director with responsibility for administrative components of the program.

Vande Woude closed the introduction to the report with a comment on dwindling support for biomedical research at a time of unprecedented opportunity.

"Despite the many extraordinary achievements by the ABL Basic Research Program during the past year, my concern over the crisis in funding for biomedical research tempers any sense of accomplishment. This problem currently preoccupies the scientific community, but it will have a severe negative impact on the future of human health research and, therefore, should be the concern of everyone. For the 510,000 cancer deaths and the 1,040,000 new cases of cancer in 1990, the money spent in the past 20 years on basic research is inadequate, especially when compared to the projected cost of the S&L bailout.

"Describing all of the achievements in cancer research would be a major endeavor, and obviously justice to this subject cannot be achieved in one paragraph. However, in addition to the discovery of retroviruses responsible for human disease, major advancements have been made in treatments that are responsible for the cure of Hodgkins disease, testicular cancer, and more than two thirds of all childhood leukemias. Moreover, significant improvements in diagnostics have increased the sensitivity for the

detection of some of these diseases more than a thousand fold. Aside from these achievements, a whole new biotechnology industry has developed that promises to be a major economic force in the 21st Century. The issue of research funding is so serious that it cannot be neglected if we plan to make effective progress toward cures for these diseases or to maintain our leadership in biotechnology."

DCT Advisors Reject MRS Concept, Approve Radiology Group Expansion

A proposed grants program for MR spectroscopy was rejected but brought back as a program announcement by the NCI Div. of Cancer Treatment Board of Scientific Counselors.

The board at its recent meeting unanimously opposed the concept statement for the RFA, which would have provided first year funding of $800,000 for three-year research projects on phosphorus-31 MRS in the detection and prediction of early therapeutic response in cancer patients. They then gave the statement concept approval as a program announcement.

Board members and DCT Director Bruce Chabner expressed several reservations about the proposed RFA, including whether the field of MRS is advanced enough for predictive studies in humans, and possible technical and quality control problems.

In another action, the board gave concept approval to the expansion of the Radiologic Diagnostic Oncology Group to study pediatric solid tumors and ovarian cancer. The program would provide $800,000 for the first year of the three-year program, which is being called RDOG IV.

The board also gave concept approval to two program announcements for radiology training fellowships. The announcements are expected to be available early next month and will be published in **The Cancer Letter** at that time.

The concept statements and board discussion follow:

MRS/MRI and cancer therapy. In contrast to currently available imaging methodologies, which rely predominantly on changes in tumor size to evaluate therapeutic response, MR spectroscopy can detect early biochemical changes in tumor composition that precede morphologic changes in response to therapeutic interventions. Over the last few years MRS has emerged as a promising tool for early detection and prediction of therapeutic response. Indeed, phosphorus-31 (31P) MRS studies in animal tumors have clearly demonstrated spectral changes in response to radiation or chemotherapy which precede changes in tumor size. Chemotherapy of a number of tumors results in a transient decrease in organic phosphorus and increase in pH. Photodynamic therapy and interleukin-1, on the other hand, cause an increase in organic phosphorus as the tumors respond.

Although the majority of 31P spectral changes in animal models have been seen in energy metabolites and pH, changes in phosphomonoester (PME) and phosphodiester (PDE) levels have been reported in patients with tumors in response to chemotherapy. Further, changes in PME and PDE have been reported in tumor cell lines in response to cyclophosphamide, adriamycin, IL-2, LAK cells and TIL. Since MRS is one of few methods that can be performed on living cells in culture, in animal tumors and human malignancies, it may provide an opportunity to investigate the relevance of MRS studies of tumor models to human cancer....

The goal of this proposal is to conduct well focused, prospective clinical experimentation using currently available, routinely applicable methodology to begin comprehensive testing of the potential for 31P MRS to predict and/or detect therapeutic response in patients with tumors. Given the limited resources available at any one institution and the effort required to perform repeated measurements in each patient for response predictor studies, it seems prudent to coordinate such studies between several institutions. The critical issue in these studies is quality control, i.e. setting precise standards for performance and interpretation of spectroscopic studies.

Board members asked Faina Shtern, of the Diagnostic Imaging Research Branch, for clarification on many aspects of the proposed RFA. "My feeling is that we're sort of supporting a fishing expedition," said board member JoAnne Stubbe.

"This is interesting work, but one of the major questions I have is, is the field of MR spectroscopy ready for this?" Chabner asked.

Alexander Margulis, recently retired as chief of radiology at Univ. of California (San Francisco), was on hand with other MRS experts to help Shtern answer questions. "The field has made tremendous advances," Margulis said. "What is needed is training of spectroscopists. It's a very, very fast moving field. It is an ideal way of doing chemical analysis in vivo without damaging tissue. It would be smug to say this is well advanced--it's not--but this is a tremendous opportunity." Unlike PET, the equipment is already in the field, he said.

But board members were not convinced. "I detect not a lot of enthusiasm for this now," Board chairman John Niederhuber said.

Chabner suggested that the concept be rewritten as a program announcement. The board voted to reject the RFA concept statement and then approved the concept as a program announcement.

Radiologic Diagnostic Oncology Group IV: Pediatric solid tumors and ovarian cancer. Concept for an RFA, proposed first year award $800,000, three years. Planned date of announcement March 1, 1991, anticipated award date Jan. 1, 1992.

The Radiologic Diagnostic Oncology Group was formed in September 1987 in response to an RFA. Its objective is the timely evaluation of current and emerging imaging modalities in the management of patients with cancer.

RDOG findings have been important for the development of optimal imaging algorithms in the areas of prostatic and lung cancer (RDOG I), pancreatic and colon cancer (RDOG II). Four protocols are currently underway in 10 academic centers in this country. Recently, a new RFA to establish RDOG III has been issued to study musculoskeletal, head and neck tumor imaging, and five or six new institutions are expected to be funded. The results of each study should have a direct and immediate impact on patient care. Considerable cost saving is expected due to the elimination of unnecessary diagnostic studies.

RDOG has had a significant impact on clinical research in radiology. This is the first time that multi-institutional clinical trials in diagnostic imaging have been conducted in a centrally coordinated fashion with strict quality control and analysis of cost effectiveness.... The recent meeting of the DIRB expert panel identified pediatric solid tumors and ovarian cancer as the highest research priority areas in clinical radiology. The specific focus of this proposal is to expand RDOG in order to include these important areas of cancer research.

This proposed RFA would stimulate the establishment of a multi-institutional scientific group to optimize imaging algorithms for diagnosis, staging and serial monitoring of pediatric solid tumors and ovarian cancer. The successful completion of this research will offer the potential of accurate cancer diagnosis, improved patient care and reduced health care costs.

Barbara McNeil, head of the heath care policy department at Harvard Medical School, provided an update on the RDOG's comparison studies of MRI, ultrasound and CT in staging prostate and lung cancer, and comparison of CT and MRI in preoperative detection of liver metastases in colorectal cancer. In the prostate protocols, neither MRI nor US has been good, though MRI may be better with some refinements, while in the lung protocols, MRI and CT both have shown good results, she said. Colorectal and pancreas protocols are still pending. McNeil concluded that RDOG is an "effective mechanism for technology assessment for screening, diagnosing or following up patients with cancer."

"This is one of the more positive things to happen in a long time--it is so essential," Niederhuber said.

The concept was approved unanimously.

Anti-HIV Drug Development Preclinical Contract Recompetitions Approved

Recompetition of drug development contracts with an estimated total cost of $17 million over the three to five year award periods has received concept approval from the Board of Scientific Counselors of NCI's Div. of Cancer Treatment.

The contracts are all managed by DCT's Developmental Therapeutics Program. They include preclinical activities involving potential agents with both anticancer and anti-HIV activity, with funding from NCI's cancer and AIDS designated appropriations.

DTP decided that its preclinical pharmacology contracts for anti-HIV agents, which the board had approved for recompetition last February, could be combined with the contracts for preclinical pharmacology of antitumor agents, for an estimated savings of $190,000. The board approved the antitumor agent recompetition at an estimated annual cost of $560,000; the anti-HIV agent recompetition had been approved for $910,000. An RFP for the combined contracts will be issued, with the estimated total of the two figures, funded equally from cancer and AIDS money.

The concept statements follow:

Cultivation of marine protozoa. Recompetition of a contract held by Martek Corp. Estimated annual cost, $315,991 for three years, 100 percent funded by AIDS appropriations.

Protozoa represent a taxonomically diverse group of organisms which have not been extensively investigated for their potential pharmacological properties. The wide diversity of this group, as well as the lack of information on the production of secondary metabolites by these organisms, warrants their study as potential sources of novel anti-AIDS and anticancer agents. The present contract is responsible for the cultivation of 600 cultures of protozoa representing at least 50 genera and at least two orders. These organisms are axenic or monoxenic.

The contractor furnishes to NCI 100 mg of organic extracts of each cultured organism, which are stored in the Natural Products Repository at -20 degrees C. Small samples of each extract are tested for AIDS-antiviral and antitumor activity. When significant activity is observed, the active organism is regrown on a scale sufficient to provide enough extract for bioassay guided fractionation, with a view to isolation of the active components. Stock cultures of each organism are maintained, cryogenically preserved, and delivered to NCI.

During the past year, the culture collection of protozoa continued to expand and, as of July 1, 1990, 457 cultures are on hand representing 79 genera and 11 protozoan orders. Four hundred eight of the above cultures are axenic. Two hundred sixty one of the above organisms representing 43 genera and eight orders have been cultured. One hundred thirteen extracts have been delivered to the NCI repository, and 31 of the above extracts have been tested in the anti-AIDS in vitro screen. No activity has yet been observed; however, a number of extracts have exhibited cytotoxic effects and may prove to be of interest in the antitumor screen.

It is anticipated that future projects will be conducted along the same lines as outlined in the background information above. Extracts housed in the repository will be tested for both anti-HIV and antitumor activity. It is hoped that sufficient data will become available during the next three year period to permit a meaningful assessment of the worth of this area as a source of potentially useful agents.

(NCI justified funding this contract 100% with AIDS money because in the past it has been supported entirely by cancer funds).

Analysis of anticancer and anti-AIDS chemicals and pharmaceutical formulations. Recompetition of contracts held by Midwest Research Institute, Research Triangle Institute, and SRI International. Estimated annual cost, $1,234,000 (50% cancer, 50% AIDS, five year awards.

These contracts constitute a program resource responsible for

evaluating the identity and purity of bulk chemicals and formulated drug products. Reports of the analytical testing on bulk drugs and dosage forms are used as a basis for assessing the suitability of bulk drugs or finished dosage forms for use in advanced antitumor screening, toxicological studies, formulation studies, or clinical trials.

These data are also supplied to the Food & Drug Administration as part of NCI's investigational new drug (IND) filings for new antitumor agents and related compounds. Historical summaries of the data are used in preparing specifications for the various bulk pharmaceutical substances, for procurement actions, and for routine quality control of these materials.

Additionally, data on solubility and stability are developed, and selected assay methods are adapted for the quantitation of drugs in plasma. The data are also provided to other contract projects to facilitate formulation development, and to aid in the analytical aspects of pharmacological and toxicological testing.

During the past calendar year, over 100 reports were received describing the analytical evaluation of separate lots of bulk drug and formulated products. Also, during the past year, analytical data from these contractors were filed with the Food & Drug Administration in support of new IND findings and amended IND findings. Additional information has also been provided to FDA in response to requests for data following their review of various IND filings.

Data from these contractors have been supplied to other contractors responsible for formulation development, pharmacology studies, toxicology studies, dosage form production, and shelf life studies. This transfer of information facilitates the initiation of the analytical work associated with each of these projects.

It is anticipated that the major thrust of project work will continue to be as outlined in the background information above. Priority will be given to the expeditious development of analytical methods for the determination of structure and for purity assessment of new agents discovered by the new in vitro screen. At recompetition, the requirements will be structured to include the analytical evaluation of both anticancer and anti-AIDS products.

Primary rodent production centers. Recompetition of contracts held by Charles River Laboratories, Harlan Sprague Dawley, and Simonsen Laboratories. Estimated annual cost, $3.4 million (80% cancer, 20% AIDS), three year awards. Since these animals are made available to investigators outside DCT, a payback system covers about $3 million of the cost.

These contracts produce approximately 2,500,000 laboratory rodents, including nude mice, annually which are distributed intramurally to NCI and NIH investigators and extramurally to NCI grantees, collaborators, and to qualified users who have expressed a strong interest in obtaining research animals whose health status and genetic makeup are of the same quality as those used by NCI. Pedigree charts for inbred and first generation hybrids are carefully maintained and monitored by the project officer.

Essentially, the entire rodent production capacity for DCT/NCI is confined to these contracts and that at Frederick Cancer & Development Center. Although the repository for inbred strains is maintained, intramural rodent production on the NIH campus at Bethesda no longer exists. Approximately 60 rodent strains are provided through these primary rodent production centers. This program represents the sole source for several of these 60 strains. The intramural capabilities at FCRDC and the extramural production by these contracts are considered essential for the continuation of in vivo cancer research without interruption.

This resource performs a number of services that are proving very useful for investigation. For example, inquiries are often received regarding model development which requires rodent strains that are not commercially available. Such needs are met through these contracts. Intramural investigators are encouraged to use the off campus conventional facility operated by FCRDC to perform initial studies validating the usefulness of the model. After model validation, strains are rederived into a gnotobiotic condition through these contract resources and expanded to meet anticipated needs.

It is estimated that approximately 85% of the rodents used by researchers on the NIH campus, as well as a large percentage of animals required by NCI funded grantees and contractors, have been supplied from this effort. Contractor usage has included the preclinical toxicological and pharmacological testing programs and DTP's extramural in vivo model development and in vivo AIDS testing programs. These production contracts were also adjusted to assist the scientific community in meeting the needs for some strains of mice during the emergency created by the disastrous fire at Jackson Laboratories.

During recent months, efforts have been introduced for the production of quantities of the severely compromised immunodeficiency (SCID) and the triple immunodeficient (BNX) strains.

These contracts will be recompeted with a renewal date effective May 1, 1992, for a three year period. These contracts will continue to provide genetically defined, pathogen free rodents, maintained under strict barrier conditions. By renewing these contracts, the many NCI research activities will be able to continue receiving quality laboratory animals, many of which are not available from any other source. Also, these contracts supply large numbers of time mated pregnant animals and dated litters to NIH campus investigators five days a week.

Preclinical pharmacology studies of antitumor and anti-AIDS agents. Recompetition of contracts held by Mayo Foundation, Ohio State Univ., and Univ. of Southern California, for anticancer agents, and the previously approved recompetition of contracts for anti-AIDS agents, held by Arthur D. Little Inc., Southern Research Institute, and Vermont Regional Cancer Center. The total combined annual cost is estimated at $1,470,000, three year awards, to be funded 50-50 from cancer and AIDS money.

This procurement will provide a continuing resource for method development and preclinical pharmacokinetic evaluation of antitumor and anti-AIDS agents under development by DTP. Active compounds identified by the in vitro HIV and human tumor cell line screens are prioritized for further study by the DCT Decision Network Committee. Task assignments will be issued to successful applicants to perform method development, pharmacokinetic, and other defined pharmacology studies on selected in vitro active agents.

Analytical methods will be developed to quantify compounds in biological fluids at levels expected to be in the therapeutic range, as estimated in vitro. The pharmacokinetics of test compounds following bolus and infusion doses will be investigated for various routes of administration in several species. Stability of agents in plasma, plasma protein binding, and bioavailability after nonparenteral administration will be emphasized. The data obtained in these studies will be used in the planning and interpretation of preclinical therapeutic and toxicology investigations. An understanding of species similarities or differences in pharmacokinetic behavior will be useful in determining appropriate doses and schedules for detailed IND directed toxicology studies. Since in vitro screens will be used for the initial detection of antitumor activity, pharmacologic data obtained in animals in conjunction with preclinical therapeutic studies in mouse tumor models will be important for extrapolating effective in vitro and in vivo concentrations and exposure times to rational doses and schedules in phase 1 clinical trials.

NCI Advisory Group, Other Cancer Meetings For Dec., Jan., Future

European Society for Medical Oncology--Dec. 2-5, Copenhagen, Denmark. Contact Dr. H.H. Hansen, Dept. of Oncology, Rigshospital, 2100 Copenhagen, Denmark.

National Cancer Advisory Board--Dec. 3-4, NIH Bldg. 31 Rm 10, open 8 a.m. both days.

NCAB Committee Planning & Budget--Dec. 3 immediately following adjournment of NCAB.

NCAB Committee on Cancer Centers--Dec. 3 immediately following adjournment of NCAB.

NIH-DOE Subcommittee on the Human Genome--Dec. 3, NIH Bldg. 31 Rm 6, open 9 a.m.-noon.

NIH Program Advisory Committee on the Human Genome--Dec. 3, NIH Bldg. 31 Rm 6, open 1-6 p.m.

Growth Factors & Their Receptors In Cancer: Basic Mechanisms & Therapy--Dec. 4-7, Houston, TX. Westin Galleria Hotel. Contact Univ. of Texas M.D. Anderson Cancer Center, Paula Gray, phone 713/792-3030.

Neutron Capture Therapy for Cancer--Dec. 4-7, Sydney, Australia. Contact International Society for Neutron Capture Therapy, ANSTO, PMB1 Menai NSW 2234, Australia.

The Challenge of Cancer Pain: Obstacles & Interventions--Dec. 5, New York, NY. Contact Cancer Care Inc., 1180 Avenue of the Americas, New York, NY 10036, phone 212/302-2400.

Pittsburgh Cancer Conference--Dec. 6-7, Pittsburgh, PA. Hyatt Hotel at Chatham Center. Contact Univ. of Pittsburgh Center for Continuing Education for the Health Sciences, 412/647-8217.

President's Cancer Panel--Dec. 7, San Francisco, CA. Univ. of California (San Francisco), Cole Hall, 8:30 a.m.-noon.

Cancer Pain Mangement--Dec. 8, Minneapolis, MN. Contact E. Canaan, Office of Academic Affairs, 701 Park Ave., Minneapolis, MN 55415, phone 612/347-2075.

Tokyo Symposium on Prostate Cancer--Dec. 14-15, Tokyo, Japan. Contact James Karr, Roswell Park Memorial Institute, 666 Elm St., Buffalo, NY 14263, phone 716/845-2389.

Novel Strategies in Chemotherapy--Dec. 19-20, Birmingham, UK. Contact Dr. C.R. Wolf, ICRF, Hugh Robson Bldg., George Sq., Edinburgh, Scotland.

JANUARY

Colony Stimulating Factors--Jan. 10, Knoxville, TN. Contact Education Coordinator, Thompson Cancer Survival Center, 1915 White Ave., Knoxville, TN 37916, phone 615/541-1749.

Tamoxifen & ER Positive Breast Cancer--Jan. 11, Knoxville, TN. Contact Education Coordinator, Thompson Cancer Survival Center, 1915 White Ave., Knoxville, TN 37916, phone 615/541-1749.

NCI Cooperative Group Chairmen's Committee--Jan. 11, NIH Executive Plaza North, Rm C-D-E, open 9 a.m.

Insulin-Like Growth Factors/Somatomedins--Jan. 12-16, San Francisco, CA. Contact Univ. of California School of Medicine, Extended Programs in Medical Education Rm C-124, San Francisco, CA 94143-0742, phone 415/476-5808.

Transgenes, Development & Disease--Jan. 12-18, Tamarron, CO. Contact Keystone Symposia, 2032 Armacost Ave., Los Angeles, CA 90025, phone 213/207-5042.

Recent Trends in Management of Mediastinal Tumors--Jan. 13, Cairo, Egypt. Contact Kasr el Einy Center of Radiation, Oncology & Nuclear Medicine, Manial University Hospital, Manial El-Rhoda, Cairo, Egypt.

Developmental Therapuetics Contracts Review Committee--Jan. 16-18, Holiday Inn, Bethesda, MD. Open 8:30-9:30 a.m. on Jan. 16. Closed Jan. 17-18.

Self Reactivity & Its Regulation--Jan. 17-24, Keysone, CO. Contact Keystone Symposia, 2032 Armacost Ave., Los Angeles, CA 90025, phone 213/207-5042.

The Adipose Cell--Jan. 18-24, Park City, Utah. Contact Keystone Symposia, 2032 Armacost Ave., Los Angeles, CA 90025, phone 213/207-5042.

Gene Regulation & Signalling In Edocrine Systems--Jan. 19-25, Steamboat Springs, CO. Contact Keystone Symposia, 2032 Armacost Ave., Los Angeles, CA 90025, phone 213/207-5042.

Platinum & Other Metal Coordination Compounds in Cancer Chemotherapy--Jan. 23-26, San Diego, CA. Sheraton Harbor Island East Hotel. Contact Cass Jones, Professional Conference Management, 7916 Convoy Ct., San Diego, CA 92111, phone 619/565-9921.

Cancer Biology, Immunology Contracts Review Committee--Jan. 23-25, Holiday Inn, Chevy Chase, MD. Open Jan. 23 9 a.m.-10 a.m., closed Jan. 24-25.

New Drugs--Jan. 24, Brno, Czechoslovakia. Contact Cancer Research Institute, Zluty kopec 7, Brno, Czechoslovakia.

Current Status & Future Directions of Immunodiagnosis & Immunotherapy--Jan. 25-27, Key Biscayne, FL. Contact Div. of Continuing Medical Education, Univ. of Miami School of Medicine, PO Box 016960, Miami, FL 33101, phone 305/547-6716.

Oncology Practice 1991: A Perspective on Breast Cancer & Lymphoma--Jan. 27-Feb. 1, Snowmass, CO. Contact Dr. Stephen Jones, Charles Sammons Cancer Center, Rm 4800, Baylor Univ. Medical Center, 3500 Gaston Ave., Dallas, TX 75246, phone 214/820-2021.

Molecular Basis of Exidative Damage by Leukocytes--Jan. 28-Feb. 3, Big Sky, MT. Contact Keystone Symposia, 2032 Armacost Ave., Los Angeles, CA 90025, phone 213/207-5042.

Div. of Cancer Prevention & Control Board of Scientific Counselors--Jan. 31-Feb. 1, NIH Bldg. 1 Wilson Hall.

FUTURE MEETINGS

Major Advances in Oncology: Update on Hematopoietic Growth Factors--Feb. 2, Cleveland, OH. Contact Education Coordinator, Ireland Cancer Center, Univ. Hospitals of Cleveland/Case Western Reserve Univ., 2074 Abington Rd., Cleveland, OH 44106, phone 216/844-7858.

Developmental Genetics of Childhood Cancer--Feb. 8-11, San Diego, CA. Catamaran Resort Hotel. Contact American Assn. for Cancer Research, Public Ledger Bldg., Suite 816, 6th & Chestnut Sts., Philadelphia, PA 19106, phone 215/440-9300.

Physiological & Pharmacological Effects of Camellia Sinensis (Tea): Implications for Cardiovascular Disease, Cancer & Public Health--March 4-5, New York, NY. Contact Lisa Loke, Ketchum Public Relations, 1133 Avenue of the Americas, New York, NY 10036, phone 212/869-8027.

Lineburger Comprehensive Cancer Center Annual Symposium: Molecular Basis of Cancer Therapeutics--March 21-22, Chapel Hill, NC. Contact Lineburger Comprehensive Cancer Center, Univ. of North Carolina, Campus Box 7295, Chapel Hill, NC 27599-7295, phone 919/966-3036.

Fourth World Congress on Cancers Of The Skin--April 18-20, New York, NY. Contact The Skin Cancer Foundation, 245 Fifth Ave. Suite 2402, New York, NY 10016, phone 212/725-5176.

American Assn. for Cancer Research Annual Meeting--May 15-18, Houston, TX. Contact AACR, Public Ledger Bldg., Suite 816, 6th & Chestnut Sts., Philadelphia, PA 19106, phone 215/440-9300.

Aging and Cellular Defense Mechanisms--Sept. 23-27, Modena, Italy. Contact Marketing Dept., New York Academy of Sciences, 2 East 63rd St., New York, NY 10021, phone 212/838-0230.

International Symposium on Cervical Cancer--Nov. 27-29, 1991, Saint Lucia, Windward Islands. Sponsored by Saint Lucia Cancer Society and Minstry of Health. Contact Dr. Jean Paul Ryst, Ministry of Health, Chaussee Rd., Castries, Saint Lucia, W.I., phone 80945-32668.