THE CANCER LETTER

Vol. 18 No. 9
Feb. 28, 1992

Price $215 Per Year US, Canada.
$240 Per Year Elsewhere

P.O. Box 15189 Washington, D.C. 20003 Telephone 202-543-7665

Program Project Payline Is 125; Budget Cuts Will Allow NCI To Fund 49 Competing P01s

NCI has set an interim payline of 125 for program project (P01) grants in fiscal 1992, and expects to make cuts in P01 grant budgets, in some cases funding only a few projects included in each application, Institute officials said this week. The budget cuts will allow the number of funded competing P01s to rise from 44 last year to 49 this year, but many P01 renewals will be lost. The pressure on P01s is the result of a

(Continued to page 2)

In Brief

Thomas Jordan Promoted At Bristol-Myers, Markison To Succeed Him In Oncology Div.

THOMAS JORDAN, vice president-marketing for the Bristol-Myers Oncology Div., has been named to the newly created position of vice president, strategic product planning for oncology. "My primary responsibility is to be the interface between our cancer research and development group and the worldwide business operations," Jordan said. "The first major task is the coordination of the launch of taxol throughout the world." **Brian Markison**, director of marketing for Squibb Diagnostics, a Bristol-Myers Squibb subsidiary, has been named senior director for marketing of the Bristol-Myers Oncology Div. Markison had previously worked in the division and was responsible for the U.S. introductions of paraplatin and ifex/mesna. . . . **STEVEN BROWN** has been appointed associate director for NCI's Radiation Research Program, replacing **John Antoine**, who left last year for Loma Linda Univ. Brown, former chief of radiotherapy at Univ. of Vermont and later a private practitioner in Los Angeles, "brings to NCI a fine background in clinical radiotherapy and the strong backing of the academic radiotherapy community," said Div. of Cancer Treatment Director Bruce Chabner. . . **JOB OPENING:** Chief of NCI's Radiation Oncology Program, to replace **Eli Glatstein,** who left this month to head radiation therapy a Univ. of Texas Southwestern Medical School after 15 years at NCI. A search committee has been formed and the job will be officially advertised in March. DCT Director Chabner said he hopes to make an appointment by July 1. Interested candidates who can ignore "the economic realities of NIH" are invited to call Chabner's office at 301/496-4291. . . . **ROBERT ENCK,** former vice president for medical affairs at Adria Labs, has been named medical director of Mercy's Regional Cancer Center in Davenport, IA. Enck left Adria last September. He was president of the Assn. of Community Cancer Centers from 1987-88.

Payline Is 125 For Program Projects; NCI Will Fund About 49 This Year

(Continued from page 1)

Congressional mandate to fund a set number of new and competing grants.

A P01 costs on average five times more than an R01 and consists of seven projects; however, it only counts as one research project grant, NCI Deputy Director Daniel Ihde told the Div. of Cancer Treatment Board of Scientific Counselors this week.

NCI plans to spend about $890 million this year--a 12 percent increase over FY91--to fund 3,254 research project grants, Ihde said. Of that amount, about $270 million will fund approximately 1,160 new and competing grants, for a 32 percent funding rate.

"We have no intention of discontinuing the P01 grant mechanism, but we will use it selectively," Ihde said. In its report on the appropriations bill, Congress said NCI should continue to support the P01, Ihde said.

He said the Institute is placing emphasis on those P01s that have the potential to "translate" basic research findings to the clinical setting.

Additional P01s may be funded as exceptions after significant budget reductions, DCT Director Bruce Chabner told the board. Chabner called the payline "stringent."

"We simply can't afford $1 million-plus grants," Chabner said. "Our strategy has been to select only the outstanding components of the P01 and to urge investigators to apply for R01s for those portions of the application that go unfunded.

"In addition, I am urging grantees to consider the alternative of the interactive R01, since each component of this type of grant is counted individually toward the grant total," Chabner continued.

"Needless to say, I am disappointed with this and am unhappy with this situation, but NCI is powerless to do otherwise this year."

Last fall, NCI established the "Interactive Research Project Grants for Cancer" as a step between the traditional R01 and the complex P01. Under an IRPG, three investigators would submit linked R01s which would be funded as a package, but still be counted as three separate grants.

Chabner said "it's too early to say" how the IRPG mechanism is working. "We will fund a couple of P01s that were naturals for the interactive R01," but whose applications came in before the IRPG RFA was released. NCI plans to break these particular program projects apart and fund the projects separately, he said.

"How can P01s be counted in the numbers game?" DCT board Chairman Ron Levy asked.

"Congress often gives us instructions that cannot all be carried out at the same time," Ihde said, referring to the grant target and the mandate to support P01s. He said NCI Director Samuel Broder has talked to the appropriations committees about the problem.

NCI will devote 23 percent of the research project grants funds to P01s this year; the average at other institutes is 15 percent. "We are in difficulty compared to other institutes," Ihde said.

"We asked for permission to count P01s by the number of projects, but we were told that's gamesmanship, and that Congress would only increase the grant target, so we wouldn't gain anything," Chabner said.

Travel Restrictions

DCT board member Lester Peters said he was "somewhat disturbed" that some P01 site reviews are being eliminated due to NCI's $1.3 million cut in travel expenses. "It seems that some attributes of P01s that make them unique can only be determined with a site visit," he said.

The cut in travel funds also was a Congressional action, Ihde said. Program and scientific travel has been cut 40 percent. "It puts real strains on site visits. We simply do not see an alternative," he said.

NCI decided to discontinue automatic site visits for P01 reviews (**The Cancer Letter,** Feb. 7). The reviews will be done by ad hoc review groups meeting in Bethesda, augmented by phone calls and teleconferences. The process was termed "reverse site visit."

Peters asked, "Does it cost more to establish an ad hoc committee and bring it to Bethesda, or to send staff on a site visit?" Ihde said the travel expenses for the ad hoc committees does not come out of NCI's staff travel budget.

THE CANCER LETTER

Editor: **Kirsten Boyd Goldberg**
Founder & Contributing Editor:
Jerry D. Boyd

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

Subscription rate $215 per year North America, $240 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter.

Chabner noted that the travel cut was made more difficult since in came three months into the fiscal year. He said one branch in DCT has about $6,000 left in travel funds, an average of about $300 per person. The annual American Assn. for Cancer Research and American Society of Clinical Oncology meetings are in San Diego this year--just the plane ticket alone will cost much more than $300 per person, he remarked.

"We will not be able to send all deserving staff members to the cancer meetings, and it is doubtful that senior staff will attend more than an average of one meeting this year," Chabner said. "These cuts are most damaging to younger staff members, whose careers depend on being able to present their work at national meetings. In addition, the restrictions inhibit technology transfer and defeat the very purpose of increases in research funding. I hope that Congress will realize the seriousness of the situation in its deliberations next year."

DCT will send only one staff member to the International AIDS Conference in Amsterdam this June, despite having a budget for AIDS research of $57 million.

NCI's total AIDS budget for fiscal 1992 is nearly $170 million, but the Institute will send a total of eight people to the AIDS meeting, Chabner said.

"Many of the important advances in AIDS research are coming from this campus," he said.

NCI Cancer, AIDS Drug Screening Contracts Ok'd For Recompetition

Four large contracts that comprise a major part of NCI's effort to screen drugs and natural products for activity against HIV and cancer were recommended for recompetition this week. NCI advisors found problems with the Institute's in vivo cancer screening capability, but approved the relevant concept in order for screening work to continue.

The Div. of Cancer Treatment Board of Scientific Counselors committed $15.8 million to fund the contracts over five years.

Michael Grever, director of NCI's Developmental Therapeutics Program, told the board that NCI's in vitro cancer screen has established 60 cell lines for testing potential anticancer agents, and the program has screened over 21,000 agents in the last year, 984 of which were referred for further evaluation. About 10 percent of those agents were given the highest priority for preclinical investigation.

Some examples of the potential agents are: bengamide A, a natural product from the Fiji islands submitted by DCT board member Philip Crews; brefeldin A, an antibiotic from penicillin; geldanamycin; imidazoacridone; nitrobenzoylurea tubulin binders; halichondrin B; and 9-deazaadenoside.

The screen does not have cell lines for breast cancer and prostate cancer, two major omissions, but the program is working on it, Grever said.

The program also is investigating the use of artificial intelligence to establish a computerized "neural network" to compare data on agents. It has also established a "fast track" group of potential cancer drugs and is trying to do in vivo studies on these agents. One problem is getting enough of the material for testing, Grever said.

One example of a fast track drug is a rebeccamycin derivative being developed by Bristol-Myers Squibb. The company has done enough work on the drug to take it into phase 1 trials.

"We really need to enhance our in vivo capacity," Grever said. "We are trying to correlate in vitro with in vivo sensitivity."

Following are the concept statements and board discussion:

Screening for agents against HIV. Recompetition of a contract held by Southern Research Institute, $950,000 per year, five years; total $4.75 million.

The Developmental Therapeutics Program instituted an AIDS antiviral screening program in 1987 involving acquisition of diverse compounds from various sources worldwide and testing the ability of these compounds to interfere with cell killing induced by HIV. The screening effort was assigned to two support contracts dedicated to the screening of pure synthetic compounds and of crude natural products, respectively. The original workscope for synthetic compounds called for the performance of 5,000 tests per year in two different human T-lymphoblast cell lines (MT-2 and CEM). It became apparent that all active compounds could be identified in CEM cells, and the workscope was expanded to the performance of 10,000 tests in duplicate per year in this one cell line. Significant progress was made in assay optimization and standardization, resulting in greater sensitivity and consistency in the screen.

In addition to the screening responsibilities for synthetic compounds, the workscope was supplemented in FY 1990 to include confirmatory assays for inhibition of production of virion reverse transcriptase, p24 antigen, and infectious virus. The contractor has continued confirmatory testing of compounds identified by the NCI and characterized as candidates for preclinical development. In connection with other contracting activities at the Southern Research Institute (SRI), the contractor has developed other second stage assays for DTP. These include (1) performance of dose response tests on serum samples submitted under the direction of the Pharmacology and Toxicology Branches of DTP, (2) testing against a panel of HIV-1 and HIV-2 isolates, (3) use of peripheral blood lymphocytes stimulated to grow in culture to characterize range-of-action of selected compounds, and (4) antiviral analysis for cross-resistance against AZT-resistant, HIV mutants. It is estimated that 25% of the

resources of the contract are currently being expended for second stage efforts and that the resources will be expanded as needed in characterization of active compounds identified by the program.

Soon after the inception of this contract, the screening of chemical compounds in two lymphoblast cell lines was evaluated. It was apparent that all active compounds could be identified in CEM cells. Changes in the testing protocol, including decreasing the time of infection from seven to six days and infecting the cell "in-well" instead of "in-bulk," have led to assay optimization and increased sensitivity. The turnaround time for retesting of active compounds has been reduced from several months to less than three weeks. The retest rate has been reduced from 31.5% in the first contract year to the present level of 8 to 12%, which is near to an optimal level since 5 to 6% of the test materials exhibit anti-HIV activity that is routinely confirmed in a retest before the supplier is notified of the test results. This reduction in retest rate is a significant accomplishment that has contributed to the overall success of the program. The SRI scientists developed high-titer viral stocks which made the in-well infection protocol feasible; for each new virus stock the multiplicity-of-infection has been optimized. The prep lab streamlined procedures for handling retests. The contractor conducted optimization studies on the length of incubation which showed a six-day assay to be more reliable than a seven-day assay. Lastly, the contractor routinely performs 24-hour delayed additions of AZT to demonstrate that at least two rounds of infection are required for optimal cell killing, thus enabling the screen to detect compounds acting at any stage of virus reproduction.

The screen has discovered over 20 new classes of anti-HIV compounds in addition to a large number of compounds in classes already recognized as having antiviral activity. Eight compounds discovered in the screen are currently in the process of preclinical development, and compounds in nine other classes are under consideration for such recommendation.

As the need for second-stage evaluation of new active compounds has become apparent, the capabilities of this contractor have expanded. The contractor has been responsive in developing assays for inhibition of virus reproduction, including virus-associated reverse transcriptase activity, p24 viral antigen, and infectious virus. SRI has developed a panel of HIV-I and HIV-2 isolates for range-of-action studies. Also, primary cultures of peripheral blood lymphocytes have been propagated along with the HIV strains that infect these cells to determine whether drugs in the program inhibit HIV infections in these cells.

It is planned to recompete the contract as a resource for the anti-HIV drug discovery and development program. It is expected that the contractor will continue to evaluate synthetic compounds submitted to the program for anti-HIV activity at or above: current level of 10,000 compounds per year. An increased percentage of effort will be devoted to second-stage evaluation of active agents. The workscope will be expanded to include (1) combination studies with AZT, and with compounds other than AZT as they become approved for clinical use, (2) testing for cross-resistance in AZT-resistant strains, (3) testing in other HIV-1 strains resistant to novel compounds of known action, (4) in vitro isolation of resistant variants to compounds of interest to the program, (5) effects on enzymatic reverse transcriptases using various template/primers, (6) inclusion of new CD4-expressing and nonexpressing cell lines in range-of-action determinations, (7) effects of varying multiplicity of infection on compound efficacy, (8) stability and activity of compounds in high serum levels and other preliminary pharmacological considerations, and (9) activity against murine leukemia viruses and use of a mouse model system for estimation of in vivo potential. Assays for other viral activities will be added as they become available.

Some of the drugs identified by this contract were Glaxo's carbovir, which was not taken into clinical trials due to cardiotoxicity, Glaxo's 3TC, UC-38, a third generation Uniroyal drug, quinobene, and michellamine, discovered by Michael Boyd, chief of NCI's Laboratory of Drug Discovery Research & Development.

John Bader, chief of DTP's Antiviral Evaluations Branch, said the HIV screen is now very sensitive and consistent, and can detect a compound that has activity against the virus at any stage in the virus' life. It can also test against AZT-resistant cell lines. The screen managed to eliminate about 75 percent of what were thought to be promising candidates because the drugs turned out to be cross resistant.

"A single mutation in the enzyme can lead to resistance to a whole range of drugs," DCT Director Bruce Chabner said. "We need new approaches to drug design. It is startling how many active drugs attack the same site and it is frightening how easy it is for the virus to mutate."

"We're trying to see what we are left with and move forward," Grever told the board. The concept requests a $260,000 increase per year over last year's level to provide more intensive review of the mechanism of action of agents, he said.

The concept was approved unanimously.

Quality control/model development in rodents and tumor cells. Recompetition of a contract held by Southern Research Institute, $1.4 million per year, five years; total $7 million.

This contract was initiated as a resource to develop appropriate models and to implement the testing of "actives" from the disease-oriented in vitro screening program. It has also been utilized to prepare correlating in vivo models from the cell lines selected for the in vitro testing panel. As information was acquired from the in vitro screen, the need for modification of the traditional approach to in vivo testing became obvious. One of the advantages of the in vitro initial screen was that testing could be accomplished with very small amounts of compound. Consequently, smaller amounts were solicited from suppliers. As actives were observed, this advantage became a problem for secondary testing. Traditional staged tumor in vivo studies require significantly larger amounts of compound than are usually available. However, further testing is usually indicated in order to confirm the observed initial in vitro activity and consequently to justify requests for additional compound. It is often necessary to perform this followup testing in multiple tumor lines in order to assure that indications of activity from the initial screen are fully exploited. It becomes increasingly obvious that at this early stage of drug development, traditional testing with established subcutaneous tumors is not the method of choice for initial in vivo studies, and that this testing must be performed in animals with minimal tumor burden that requires lesser compound amounts and provides a quicker turnaround time.

This contract has developed a model that is amenable to large-scale testing and evaluation of agents that have been determined to be of interest with the initial in vitro screen. Testing can be accomplished with relatively small amounts of compound

and offers two parameters for evaluation of activity. Further research on this screening approach may be necessary, however, in order to develop a more sensitive model. This contract performed tumorigenicity testing for all of the cell lines in the current in vitro panel. Approximately 50 of the 60 cell lines in the panel have been grown in vivo and are now available for followup testing. Candidate cell lines for future in vitro panel testing are tested in vivo for tumorigenicity by this contract. Subpanels of six human prostate cell strains and 10 human breast cell strains have been developed and are now available for in vivo testing. Most of the staged tumor testing referred by the Biological Evaluation Committee (BEC) has been performed by this contract.

It is planned to recompete this contract as a resource to be utilized to continue with the development and implementation of testing methods that reflect the needs of the drug development program at both the early stages of secondary testing where input is relatively large with smaller amounts of compound available and at later stages where smaller numbers of agents can be studied intensively using appropriate orthotopic models, schedule-dependency studies, etc., as indicated.

This project will develop and implement models that are capable of accomplishing initial followup testing of BEC referrals. Models will be adaptable to the utilization of small amounts of compound, will have a large thru-put capability, and will be sensitive enough to detect subtle differences in effectiveness between candidate agents. Diverse areas of expertise, including in vitro capacities and capabilities, will be needed for proper performance in this area. Model development and implementation for advanced studies with small numbers of compounds will be customized to meet specific requirements, e.g., orthotopic models for lung cancer studies. The rationale for an increase in funding is based on the need for significant testing of candidate agents in selected subpanels for evidence of breast and prostate activity.

"We still need to develop a better in vivo test," Grever said, anticipating board discussion. New board member Allen Oliff, head of oncology and virology drug development at Merck, Sharp & Dohme, criticized the contract for "burning a lot of the compound."

"We've had a lot of discussion about this," Chabner said. "My position is, find a sensitive mouse tumor and give it to the animal and test the compound in vivo. If it works, don't waste time on the human tumor cell lines. Everyone else in the division says that defeats the purpose."

"We're aiming at having a simple in vivo test" that is suitable for testing several hundred compounds per year, Grever said. "I thought it would be difficult to come back to the board and say, 'We're going back to animal tumor models.'"

"This is more than a million bucks a year," board member Ralph Weichselbaum said. He also questioned the rationale for 60 cell lines.

"Most pharmaceutical firms have this budget for in vivo testing," Grever said. He noted that "Nobody knows what the best [in vivo] system is. We need ad hoc review."

"The decision you are faced with is to continue this contract when what we ask it to do still needs to be resolved," Chabner told the board. "We'd like to recompete this pending advice from ad hoc reviewers."

Board member Paul Carbone noted that DCT's budget for contracts is not slated to increase this year. "Were will you get the 14 percent increase requested?"

"This is important enough to us that we have to have it," Chabner said. "We need to have in vivo activity before we go into preclinical and clinical evaluation. There's no simple way to do it."

Board member Loretta Itri suggested delaying vote on the concept until the ad hoc review can take place. But Grever said that would result in a lag between the in vitro and in vivo screening.

Chabner asked for volunteers from the board to take part in the review.

Carbone moved that the concept be approved at the current level of funding of $1.24 million per year, pending advice from the review group. The concept passed, with Weichselbaum the sole opposing vote.

In vivo testing. Concept for a new RFP, $750,000 per year, five years; total $3.75 million, multiple awards.

The evaluation of potential new cancer agents requires in vivo studies for both therapeutic and pharmacologic reasons. The capacity of DTP to perform in vivo studies in experimental tumor systems was severely curtailed during mid-1980s in order to provide funding capacity for the development of the new in vitro screen and again during 1990-91 to provide intramural space for a pharmacokinetics and metabolism laboratory. Although approximately 50 of the 60 cell lines in the current panel grow as xenografts and are available for in vivo studies, resources for this effort are severely limited. Current capacity, which includes one extramural contractor and limited resources at the Frederick Cancer Research and Development Center, allows for a performance level of no more than a 250 tests yearly using a staged tumor subcutaneous assay. The DTP Biological Evaluation Committee (BEC) has a current backlog of 950 referrals for in vivo testing from the initial in screen. The difference between current capacity and demand for testing provides a strong rationale for the early approval and implementation of this effort.

The purpose of this award is to provide the necessary capacity for secondary evaluation of current and anticipated referrals of agents from the initial in vitro screen which have been determined by BEC to merit confirmation studies. It is anticipated that at least 500 tests per year will be required to evaluate compounds referred by BEC, utilizing models developed under an ongoing contract that is scheduled for recompetition. This testing is envisioned to include a rapid and sensitive preliminary test in one or more tumor systems and followup testing of actives in other model systems.

"It's senseless to vote for the previous contract and not for this one," Weichselbaum said when board members began criticizing DTP for not having enough data to perform the in vivo testing proposed in this concept. "You ought to give him this one." He made a motion for approval.

"If you approve this, we'll come back to you and tell you what we're going to do," Chabner said.

The concept was approved unanimously.

In vitro and in vivo evaluation of combination therapy for anticancer activity. Addition of $300,000 per year to fund one additional award under this RFP.

In October 1990, the DCT Board of Scientific Counselors conceptually approved a proposed contract to provide DCT with a resource to evaluate combination chemotherapy in a preclinical setting. Restricted budgetary considerations during this period mandated a request for limited funding, $300,000 per year for a three-year period, which was approved by BSC. By outside peer review (Initial Technical Evaluation Group) and NCI staff review (Source Evaluation Group) four highly capable offerors were identified, but because of budgetary restrictions only one could be funded. A contract was awarded to Southern Research Institute in December 1991. If an additional $350,000 per year is approved at the February 1992 BSC meeting, negotiations could be reopened with the existing offerors who were not funded, and an additional contract could be rapidly awarded in the first part of 1992.

Preclinical combination modality studies are especially important with some of the newer agents: taxol/taxotere, topotecan/camptothecin analogs, pyrazoloacridine, anthrapyazole, and temozoiamide which are potentially active agents in lung, breast, and brain tumors. Although combined modalities are explored clinically, many years and many patients are required to evaluate proper timing, schedules, doses, and sequences of promising agents. In the preclinical setting, it is possible to test hypotheses rapidly. Such a resource is highly desired by the Cancer Therapy Evaluation Program/DCT to help guide their clinical trials with respect to both choice of combinations and scheduling of agents, particularly with the recent availability of cytokines, antibodies, swainsonine, antimotility agents, antiangiogenesis factors, and other potential agents best used in a combined modality arena.

When this RFP was originally competed, the primary emphasis was to be the evaluation of potential synergy using cytotoxic agents in combinations, in vitro and subsequently in vivo, with various schedules of administration, and to followup the interesting leads with similar studies in humans. However, the Statement of Work was written broadly enough to permit other combinations of interest, such as studies of a cytotoxic with a chemoprotective agent, a recombinant cytokine, or an agent that would reverse drug resistance.

In light of the capabilities of these offerors and the recent phase 1 meetings which focused on dose intensification using colony stimulating factors and reversal of drug resistance, it is felt that it would be extremely useful to conduct preliminary preclinical studies prior to such studies in humans. Such studies provide leads on appropriate combinations and schedules of these newer agents. Because of a shift in the emphasis of the Developmental Therapeutics Program (DTP) needs in 1985, no exclusive combination studies contract has been available to DTP/CTEP for several years.

This contract has developed some data on the combination of taxol with doxorubicin, but there are potentially thousands of drug combinations that should be explored, Grever told the board.

Cancer Therapy Evaluation Program Director Michael Friedman said a surge in new anticancer agents, such as taxol, topo 1 and 2, and a number of tubulin agents has resulted in the need for a larger number of combination studies.

"Everyone wants to do molecular biology, but when clinicians want to use an agent, there's little data on how it actually works in a living organism," Chabner said. "We need this kind of basic information. We're flying by the seat of our pants in designing clinical trials."

"We're getting deeper and deeper," said board member William Hryniuk. "We have an in vitro screen, we have an in vivo screen and we don't know whether it works, and now we're testing combinations."

Friedman said the other concepts were for testing new agents, while this one tests drugs with known activity for synergism. "As imperfect as it is, this is one step closer to patients. We've already seen it work with adriamycin/taxol combination."

"I'd like to see it, too," Hryniuk said, referring to release of the data. "I have a great sense of unease going past the in vivo screen."

The concept was approved on a vote of 11-5.

NCI Advisory Group, Other Cancer Meetings For March, April, Future

Generating Designer Ligands for Biological Targets--March 1-2, Holiday Inn Crowne Plaza, Rockville, MD. Contact Dr. Roy Wu, NCI, Cancer Therapy Evaluation Program, 301/496-8866.

International Conference on Monoclonal Antibody Immunoconjugates for Cancer--March 5-7, San Diego, CA. Cont act Cass Jones, Professional Conference Management, 619/565-9921.

Cancer Nursing: AIDS-Related Lymphomas--March 6, Cleveland, OH. Contact Education Coordinator, Ireland Cancer Center/Case Western Reserve Univ., phone 216/844-7858.

Controversies in the Management of Breast Cancer--March 6-7, New York City. Contact Ann Boehme, Long Island Jewish Medical Center, 718/470-8650, fax 516/352-4081.

Assn. of Community Cancer Centers--March 12-14, Washington, DC. Contact ACCC, 301/984-9496.

American Society of Preventive Oncology Annual Meeting--March 14-16, Bethesda, MD. Contact Dr. Richard Love, ASPO, 1300 University Ave., Madison, WI 53706, phone 608/263-6919.

Radiation Research Society--March 14-18, Salt Lake City, UT. Contact Radiation Research Society, 703/648-3780.

Society of Gynecologic Oncology Annual Meeting--March 15-18, San Antonio, TX. Contact SCO, 312/644-6610, fax 312/527-6640.

Society of Surgical Oncology Annual Meeting--March 15-18, New York City. Contact SSO, 508/526-8830.

NCI Div. of Cancer Biology, Diagnosis & Centers Board of Scientific Counselors--March 16, NIH Bldg. 31 Conf. Rm 6, open 8:30 a.m.

German Cancer Congress--March 16-22, Berlin, Germany. Contact Deutsche Krebsgesellschaft, Paul Ehrlich Str. 41, 6000, Frankfurt am Main 70, Germany.

NCI-EORTC Symposium on New Drugs in Cancer Therapy--March 17-20, Amsterdam, The Netherlands. Contact EORTC New Drug Development Office, Free University Hospital, De Boelelaan 1117, NL-1081 HV Amsterdam, The Netherlands, phone 31-(0)20-5487881, fax 31-(0)20-5486101.

Advances in Cancer Treatment Research & Autologous Bone Marrow Transplantation Symposium--March 18-20, New York City. Contact Office of Continuing Medical Education, Montefiore Medical, 212/920-6674.

Current Perspectives in Cancer Therapy: The Multimodal Approach--March 18, Cleveland, OH. Contact Education Coordinator, Ireland Cancer Center/Case Western Reserve Univ., 216/844-7858.

Cancer & AIDS: Integrating Science, Medical Practice & Health Policy--March 23-25, Paris, France. Contact International Society for Global Health Policy, 74 Ave., Kleber, 75016 Paris, France, phone 47.27.01.39.

NCI Div. of Cancer Etiology Board of Scientific Counselors--March 26-27, NIH Bldg. 31 Conference Room. Open 1 p.m.-adjournment March 26 and 9 a.m.-noon March 27.

Cancer Centers Support Grant Review Committee--March 26-27, Hyatt Regency, Bethesda. Open 8-8:30 a.m. March 26.

American Cancer Society Science Writers Seminar--March 29-April 1, St. Petersburg, FL. Contact ACS, 404/329-7604.

ACS National Conference on Gynecologic Cancers--April 2-4, Orlando, FL. Contact Andy Cannon, American Cancer Society, phone 404/329-7604.

Diagnosis & Treatment of Neoplastic Disorders, Medical, Surgical, and Radiotherapeutic Aspects--April 2-3, Baltimore, MD, Johns Hopkins Univ. School of Medicine. Contact Office of Continuing Education, phone 301/955-2959.

Illinois Cancer Center Conference: Issues of Cancer Management in Women & Minorities--April 8, Chicago, IL. Contact Carole Johnson, ICC, 312/986-7033, fax 312/986-0404.

J. Donald Woodruff Symposium on Gynecologic Oncology--April 9-11, Baltimore, MD. Contact Johns Hopkins Office of Continuing Education, 410/955-2959.

Regional Breast Cancer Summit--April 10, Detroit, MI. Contact Meyer Prentis Comprehensive Cancer Center, 313/745-8870.

American Radium Society Annual Meeting--April 11-15, Walt Disney World Swan, Orlando, FL. Abstract deadline Oct. 31. Contact ARS, 1101 Market St. Suite 1400, Philadelphia, PA 19107, phone 215/574-3179.

National Surgical Adjuvant Breast & Bowel Project Annual Meeting--April 12-15, Hilton Head, SC. Contact Joan Dash, NSABP, 3550 Terrace St. Rm 914, Pittsburgh, PA 15261, 412/648-9720.

Transcriptional Control of Cell Growth & Oncogenesis--April 23-24, Chapel Hill, NC. Contact Dianne Shaw, Public Information, UNC Lineberger Comprehensive Cancer Center, 919/966-3036.

Molecular Basis for Cancer Prevention--April 24, Memphis, TN. Contact Dr. James Hamner, Univ. of Tennessee, 901/528-6354.

Breast Cancer: Issues in Prevention & Cure--April 24, Minneapolis, MN. Contact Northwestern Hospital, Virginia Piper Cancer Institute, 612/863-5461.

Current Perspectives & Future Directions in Clinical Flow Cytometry--April 25-28, Baltimore, MD. Contact New York Academy of Sciences, 2 East 63rd St., New York, NY 10021, phone 212/838-0230.

Advances in Internal Medicine--April 27-May 1, Ann Arbor, MI. Contact Angela Stewart, Univ. of Michigan, 313/763-1400.

Innovations in Oncology Social Work--April 29-May 2, Detroit, MI. Contact Andrea Andrlik, Social Work Service, VA Hospital, 708/216-2100, fax 708/832-6945.

Cytometry 2000 Annual Cancer Symposium--April 30-May 1-2, Detroit, MI. Contact Dr. Alexander Nakeff, Wayne State Univ. Div. of Hematology/Oncology, phone 313/577-7923.

Future Meetings

Assn. of Biotechnology Companies International Meeting--May 17-20, San Diego, CA. Contact ABC, 202/234-3565.

Challenges & Controversies in Cancer Research--Sept. 9-12, Columbus, OH. Contact Nancy Jones, Suite 1132, James Cancer Hospital, 300 W. 10th Ave., Columbus, OH 43210.

Transrectal Ultrasound in the Diagnosis & Management of BPH and Prostate Cancer--Sept. 11-13, Chicago, IL. Contact Diversified Conference Management, 313/665-2535, or 800/458-2535.

Radioimmunodetection & Radioimmunotherapy of Cancer--Sept. 17-19, Princeton, NJ. Abstract deadline May 15. Contact Center for Molecular Medicine & Immunology, 201/456-7047.

Environmental Skin Cancer--Oct. 16-17, Cleveland, OH. Contact Kelly Ormsby, Skin Diseases Research Center, Univ. Hospitals of Cleveland, 216/844-3682.

Diet & Cancer: Markers, Prevention and Treatment--Oct. 29-30, Tyson's Corner, VA. Contact Rita Taliaferro, 202-737-8062.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-27745-44
Title: Preparation of immunoconjugates
Deadline: Approximately June 15

Presolicitation notice. This project was originally synopsized as a master agreement announcement Number NCI-CM-27731. The purpose of this procurement is to prepare various preclinical and clnical grade monoclonal antibodies/targeting agents with ligands such as chelating agents, toxins, cytotoxic agents or other targeting molecules. Although NCI wishes to be flexible in the nature of their requests, it is primarily interested in the preparation of immunoconjugates including monoclonal antibody chelates, which can bind various radionuclides, and immunotoxins. Monoclonal antibodies (or other targeting agents) supplied by NCI will be chemically conjugated to various ligands such as chelating agents and toxins using procedures that have appeared in peer-reviewed journals.

It is anticipated that the offeror will prepare milligram quantities (approximately 50 to 1000 mg) each of purified ligand conjugated monoclonal antibodies, antibody fragments, or other targeting molecules as specified by NCI under conditions of GLP and/or GMP. The offeror will evaluate these immunoconjugates for purity, stability, immunoreactivity, and other criteria as specified by NCI. These immunoconjugates will be evaluated by NCI for their potential as diagnostic and/or therapeutic agents. One or more awards may be made to qualified offeror responding to this RFP.
Contract specialist: Patricia Lightner
RCB Executive Plaza South Rm 603
301/496-8620

RFP NCI-CO-21117-13
Title: Chemotherapy and you
Deadline: Approximately April 8

Single award for a fixed price contract. Inspection of source materials will be on or about April 1 at NIH, Bethesda, MD. Book. Sixty page book with separate wraparound cover. Covers 1 and 4 print four color process, 1 PMS color and flood dull varnish. Covers 2 and 3 print one PmS solid color. Text prints two colors.

1,000,724 copies and films used in printing. Trim size, 5-7/8" x 9-1/8", bind on the 9-1/8" dimension. Four color process, PMS 325 blue, PMS 155 tan and black. Solid inks, no builds allowed. Operations include printing, binding, trimming, separation, coating, packaging, mailing and shipping. Contractor furnish paper. Material furnished: 32 mechanicals with tissue overlays, 1 reflective art color illustration and sample for style only. Quality attributes level 2 for printing and finishing.

Contracting officer: Sharon Miller
RCB Executive Plaza South Rm 620
301/496-8611

Program Announcements

PA-92-41

Title: Clinical investigator award for research on special populations

Application Receipt Dates: June 1, Oct. 1, Feb. 1

The Comprehensive Minority Biomedical Research Program in NCI's Div. of Extramural Activities announces the availability of clinical investigator awards for research on special populations. The term "special populations" refers to those population segments that may experience or are known to experience high cancer rates and are underserved in terms of: cancer prevention and control programs; diagnostic and treatment modalities; sutdy for special risk factors or underlying biological differences; and access to routine medical care. The definition of special populations includes: African Americans, Alaska Natives, American Indians, Asian Americans, Pacific Islanders, Hispanics, the elderly, and low income groups.

The award will enable candidates to undertake three to five years of special study and supervised research experience tailored to individual needs with a sponsor or sponsors who is competent to provide research guidance. This award is intended to cover the transition between postdoctoral research experience and an independent research career and to acquaint the candidate with the often unique challenges and circumstances involved in designing research protocols directed toward improving the health of groups comprising a significant and often disproportional percentage of individuals at risk from high cancer morbidity and morality rates.

Although the award is primarily for individuals with an MD degree, applications will be accepted from MDs and DOs who have a PhD or an equivalent research degree if special circumstances can be shown such as a PhD in an unrelated field or an intervening period of clinical training since the completion of the PhD. These applications will be considered on a case by case basis.

Candidates must have completed their clinical training by the time of award, have documented competence in clinical activities, and have research experience in the chosen area of interest. Candidates must provide evidence of a serious intent for research and academic careers and an interest in medical issues associated with special populations.

Applications may not submit a concurrent application for an NIH Research Career Development Award, Academic Award, FIRST award, or a research project grant. However, an awardee of this program may apply subsequently for a research project grant or a FIRST award.

The grantee institution must be a domestic nonprofit research institution, school, or comparable institution with strong, well established research and training programs, adequate numbers of highly trained faculty in clinical and basic science departments, and development of independent research careers.

Support of this program will be through the NIH Clinical Investigator Award (K08). Applicants may request three to five years of support. Awards are nonrenewable and nontransferable from one awardee institution to another. Funding beyond the first year of the grant is contingent on satisfactory progress during the preceding year.

Allowable costs may include:

--Awardees salary: a maximum of $50,000 per year for full time support; in addition, fringe benefits will be provided. Institutional supplementation is permitted.

--Research support: a maximum of $10,000 annually for years 1 and 2 and $20,000 annually for succeeding years to provide equipment, supplies, travel, and tuition, and other costs.

Indirect costs may not exceed 8 percent of the total allowable direct costs.

For information and copies of the complete program announcement, contact Dr. Lemuel Evans, Div. of Extramural Activities, Comprehensive Minority Biomedical Program, NCI, Bldg. 31 Rm 10A04, Bethesda, MD 20892, phone 301/496-7344, fax 301/402-0062.

PA-92-38

Title: Biomedical research support grant

Application Receipt Date: June 15

The National Center for Research Resources announces the Biomedical Research Support Grant program for fiscal 1992. Because the FY 1992 appropriation of $5.204 million for the program is a significant reduction in amount of funds available, awards which will be made on a competitive basis and fewer awards will be made.

The objectives of the program for FY92 have been narrowed to focus on support for biomedical research projects in ways that are not adequately or efficiently provided for by other funding mechanisms such as the traditional investigator initiated research project grant. The allowable uses of BRSG funds for FY 1992 are:

1. Pilot research. Small, short term projects that explore new research ideas (including multidisciplinary collaborations to explore new directions in biomedical research), seek preliminary findings, and establish the validity of the approach and pilot data that may provide the basis for research project grant applications.

2. New investigators. Initial research support for new investigators and investigators who have recently relocated and are in the process of applying for longer term funding.

3. Unexpected requirements and opportunities for projects supported by other NIH funding mechanisms. This includes funding to enable research programs to continue during temporary lapses in project grant support.

These uses exploit the capacity of the BRSG to respond promptly to short term, low cost needs that are essential to complement research project grant mechanisms that typically fund continuing, multi-year programs.

Institutions eligible to apply must have received a minimum of three allowable Public Health Service research grants and/or cooperative agreements, totalling $200,000 (including direct and indirect costs) awarded during FY 1991.

The grant mechanism used for this program will be the S07 grant. Awards of $50,000 for direct costs will be made for a 12 month project period. No indirect costs will be provided. Awards will be made on or before Sept. 30, 1992.

Because of the delay in the FY92 BRSG award process, NCRR plans to extend the ending date of all active FY91 BRSG awards through Sept. 29, 1992. Revised awards reflecting this extension will reach the institutions prior to the current March 31 end date of the FY91 award period.

Copies of the complete PA are available from BRS Program Office, Westwood Bldg. Rm 10A11, Bethesda, MD 20892, phone 301/496-6743.