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DCT CONTRACT FUNDS TO BE 20 PERCENT LESS IN FY 1986 THAN IN 1985; TO ELIMINATE 'LOW PRIORITY' CONTRACTS

Funding for contracts in NCI's Div. of Cancer Treatment will be 20% less in fiscal 1986 than last year, DCT Director Bruce Chabner told the division's Board of Scientific Counselors Feb. 6. Although the division had planned to cut back support for the program this year, it hadn't planned on having as large

(Continued to page 2)

In Brief

NCI SEEKING INDUSTRY SUPPORT AGAIN FOR SUMMER PROGRAM; CONGRESS OKs SMOKELESS TOBACCO BILL

NCI AGAIN is asking industry to help support its summer student research training program. The popular and successful program, which provides about $1,000 each to students to work at NCI for two months, was saved by industry contributions last year after the Administration refused to exempt those positions from the ceiling imposed on NCI. About eight firms contributed around $3,000 each, and when the contributions hit $25,000, another company matched the total .... **CONGRESS PASSED** the bill banning smokeless tobacco advertising from radio and television and requiring health warning notices on the packages. The tobacco industry supported the bill to head off similar but varied actions by states .... **NOMINATIONS ARE** being accepted for the 1986 Bristol-Myers Award for Distinguished Achievement in Nutrition Research, which includes a cash award of $25,000. Contact Bristol-Myers, 345 Park Ave., Rm 43-38, New York 10154, phone 212-546-4319. Meanwhile, the winner of the ninth annual Bristol-Myers Award for Distinguished Achievement in Cancer Research will be announced Feb. 25. That prize includes an unrestricted award of $50,000.... **TWO MEMBERS** of NCI's Biological Response Modifiers Program received 1985 awards at the joint meeting of the International Leukocyte Culture Conference and the Reticuloendothelial Society. Elisabetta Blasi received the Presidential Award and Craig Reynolds the Young Investigator Award.... **FRANCIS RUZICKA**, chief of the Diagnostic Imaging Research Branch in the Div. of Cancer Treatment's Radiation Research Program, on the fate of one of his concept proposals: "It was declared not a contract, which we had hoped it would not be; it was also declared not a grant, so therefore it had to be a cooperative agreement. Then it went over to NIH (headquarters), and sort of disappeared." The concept for diagnostic imaging research was approved by the DCT Board of Scientific Counselors last June, and probably will not be on the street before this June. DCT Director Bruce Chabner said that "it generally takes 12 months" for concepts to go through the NCI-NIH process after they are approved by the BSCs before they show up as RFAs or RFPs, and sometimes longer.

FEDERAL PANEL FINDS BALANCED BUDGET LAW UNCONSTITUTIONAL

(Continued from page 1)
a reduction in the contracts budget, he said. The cut reflects the 4.3% decrease from the 1986 appropriation mandated by the Gramm-Rudman-Hollings balanced budget act.

DCT plans to eliminate $800,000 of its lowest priority contracts, and make a major reduction in the level of effort for its drug development contracts, and early drug trials in its Cancer Therapy Evaluation Program and Biological Response Modifiers Program. The cutback is one of the major constrictions in the current year's budgetary outlook for the division.

Funding for cooperative groups will be about 6% less in FY 1986 than in fiscal 1985, down 4.3% from the fiscal 1986 appropriation. Last year, the cooperative groups program received about $51 million. NCI had planned to give about $50 million to cooperative groups this year, but that figure will be cut to about $48 million in funding. DCT does not expect to fund all of the groups competing for funds this year. Two groups, prostate and bladder, have already been disapproved and will not be funded (**The Cancer Letter**, Oct. 11). Cooperative groups under review include the Piedmont regional group, Mid Atlantic Oncology Program (MAOP), Northern California Oncology Group (NCOG) and SEG.

There will be a 5% reduction in funding of non competing groups. Cooperative agreements are also absorbing $1 million in costs associated with the division's stepped up efforts involving LAK (lymphokine activated killer) cell and interleukin-2 therapy.

Overall, grants, contracts, intramural activities and cooperative group funding is 4.3% less than the 1986 appropriation. The 4.3% reduction from the fiscal 1986 appropriation is due to cuts mandated by the GRH legislation.

For grants, the revised 1986 amount is still 7% higher than funding in FY 1985. Built-in increases in noncompeting grants, however, will result in fewer new grants being funded, Chabner said.

Intramural cuts will include a 25% reduction in DCT's ambulatory care program, which pays for expenses of patients who come to NIH for treatment. Institute officials are uncertain at the present time whether a major laboratory or branch within DCT will have to be curtailed or even eliminated due to the budgetary restraints.

DCT's new personnel ceiling is 586 full time equivalents (FTEs) compared to 650 two years ago, Chabner said. That ceiling includes 14 new positions for AIDS (acquired immune deficiency syndrome) and 20 for LAK (lymphokine activated killer cell) research, so "by comparison we are down more than 100 positions," he said. The division currently has 603 on board. While the cuts will be shared, DCT could face the elimination of a branch or laboratory.

Overall, NCI has reduced its number of FTEs by 400 positions to 2,080 in the past two years.

The GRH cut of $54 million in fiscal 1986 leaves NCI with $1.177 billion. President Reagan's proposed rescision would cut another $6.8 million from the institute in FY 1986, leaving NCI with a budget of $1.170 billion. The rescision must be approved by Congress, which had appropriated $1.231 billion for NCI in fiscal 1986. The President's budget presented to Congress last week would give NCI $1.158 billion in fiscal 1987 (**The Cancer Letter**, Feb. 7).

The above amounts exclude some administrative costs, $4.5 million for construction of the Mary Babb Randolph Cancer Center in West Virginia, and more than $28 million for AIDS research. All funding for AIDS activities was transferred to the Surgeon General's office for administrative purposes.

While the cuts called for by the GRH legislation are being treated as if they are an unavoidable fact, the constitutionality of the law remains in question.

Late last week, a special three judge panel ruled that the automatic budget cutting provision in the budget balancing act is unconstitutional. The panel stayed the effects of its ruling until the law is reviewed by the Supreme Court, however. If it decides to hear the appeal planned by the Senate and comptroller general, the Supreme Court will probably hear the case in April or May, with a ruling expected before July.

NCAB VOTES TO "KEEP ALIVE" STAGE 2 BREAST CANCER LOW FAT TRIAL CONCEPT

The National Cancer Advisory Board has voted to accept a recommendation by outgoing board member Rose Kushner that it "keep alive" the concept behind the institute's low fat adjuvant trial for stage 2 breast cancer. The board voted unanimously to accept Kushner's recommendation that "the concept that reducing fat calories in an attempt to reduce recurrence rates in breast cancer is a valid one, disregrading the persons and problems the trial has encountered."

The recommendation also calls for consideration of the return of the Nutrition Adjuvant Study to the appropriate NCI staff so that a new concept for an RFA could be rewritten if the current investigators

of the study do not accrue the required number of women. In a letter addressed to NCAB Chairman David Korn, Kushner specifically suggested the study be turned over to Elizabeth Anderson, program director for the Breast Cancer Working Group of the Organ Systems Program.

An effort by Kushner two days earlier to convince board members to continue the trial for another six months on a "cost free" basis was unsuccessful.

NCI's Executive Committee had determined that the Nutrition Adjuvant Study for stage 2 breast cancer should be closed when funding for its feasibility phase ends April 30. The Div. of Cancer Prevention & Control's Board of Scientific Counselors voted at its January meeting to accept the recommendation that will be made by the study's policy advisory committee in April. That group will base its recommendation on the April 15 report from principal investigator Ernst Wynder. (**The Cancer Letter,** Jan. 31).

The feasibility study was delayed for several months because of controversy over whether patients should be given chemotherapy. Following the NIH consensus conference on adjuvant therapy for breast cancer, NCI and Wynder agreed to give tamoxifen to both arms of patients in the study.

As of Jan. 20, the group had randomized only 12 patients, with an additional 28 cases entered as eligible while awaiting dietary assessments. Investigators in the trial were to have accrued 250 patients for the feasibility study by April 30. Noting that two investigators had entered no patients into the study by late January, the PAC agreed with NCI's Executive Committee that patient accrual was not likely to reach the required level of 250 patients for the feasibility study. The PAC found no evidence that the trial should be funded beyond April 30, but will keep the issue open until the April 15 report from Wynder.

Wynder has expressed confidence that he will be able to demonstrate in April that the necessary 250 patients for the study can be promptly accrued.

The study is designed to test the hypothesis that cutting fat intake in half would reduce the recurrence of breast cancer.

DCPC Director Peter Greenwald told the NCAB that NCI's Executive Committee does not want to encourage continued accrual of patients in the trial, even on a "no cost" basis. "There is a cost to it," he said, adding that the obligated funds would be returned to NCI. If the study is terminated April 30, most of the $700,000 awarded in the cooperative agreement would be returned to the institute.

"The groups did have good reason not to accrue, because until the consensus conference, PIs couldn't get medical oncologists to refer patients who weren't getting chemotherapy," Kushner noted. She also questioned NCI's role in constructing the study. In addition, she emphasized the importance of studying the effect of dietary reduction of fat in women with stage 2 breast cancer. "If we're going to find out if a low fat diet is going to" affect breast cancer, then the best study population is stage 2 breast cancer patients, she said.

Following the board's endorsement of the related 10 year breast cancer low fat prevention trial, Kushner said, "I am not going to let the Nutrition Adjuvant Study just drop dead like this." Asserting that the trial will yield data on the role of dietary fat in breast cancer more rapidly than the prevention trial, Kushner said, "We need to give the concept another chance."

"I believe firmly that data regarding the effects of high fat or low fat diet would be more quickly discovered in this very, very high risk group than" the women to be studied in the Women's Health Trial, she said.

"I don't object to further consideration of the concept," Greenwald told the board, adding that two investigators have expressed interest in submitting regular grant applications for low fat trials.

Patient accrual has not been a problem for investigators involved in NCI's breast cancer low fat prevention trial entitled the Women's Health Trial. That trial completed its feasibility study, and issued a report calling for implementation of a greatly expanded study that could cost more than $100 million over 10 years. The trial has received the enthusiastic support of NCI's Executive Committee, DCPC's Board of Scientific Counselors and the PAC.

The feasibility study involved 303 women. Of 250 randomized early enough for six month followup, 150 were placed in an intervention group, and the remaining 100 women were controls. group, and the

Investigators hope to involve 30,000 women in the full scale trial: 12,000 in the intervention group and 18,000 to serve as controls. Subjects will be age 45 to 69, with one or more conventional risk factors for breast cancer, with fat contributing 38 percent or more to dietary intake. As designed, the trial has an 8 percent probability of detecting an overall 18 percent reduction in breast cancer incidence.

Investigators in the trial plan to involve 20 to 30 centers. Three sites are currently operational. Each of the three centers will be required to recruit 300 women into the trial and identify at least 800 in the next year and a half, Greenwald told the board. The trial will then add an

additional 10 clinics.

The possibility of studying a greater number of patients through a cost sharing mechanism with the National Heart, Lung & Blood Institute was discussed as an area to be examined in the future.

ADDITION OF TWO NEW ORGAN SYSTEMS PROGRAMS APPROVED BY NCAB

The National Cancer Advisory Board has approved the addition of two new organ systems programs to NCI's Organ Systems Program. The two new systems are neurooncology and cancers of the upper aerodigestive system.

The board made no funding recommendations for the new programs, but approved a report by its Organ Systems committee that recommends "appropriate funding."

NCAB member Enrico Mihich questioned the timing of the addition of the two new systems, in light of both the current budgetary situation and a full review of the entire Organ Systems Program planned by NCI for this fall.

Organ Systems committee Chairman Robert Hickey pointed out that the programs are to be funded only "when appropriate."

Discussions have been ongoing between NCI staff and representatives from disciplines of the two areas for more than a year and a half, Jerome Yates told the board. "We have identified potential sources of support for these activities," and examined the issues involved in establishing the two new programs, he said. "I think if appropriate, and funding is available, we should move forward." Yates heads the Div. of Cancer Prevention & Control's Centers and Community Oncology Program.

DCPC Director Peter Greenwald, however, told the board that he felt important issues regarding the establishment of the two new programs had not been adequately addressed at the division's Board of Scientific Counselors meeting this fall. Such issues included the criteria for why a particular site was chosen, he said, questioning whether the board should vote to add the two systems at this time. The rationale for the classification of tumors in the upper aerodigestive system was questioned by some board members at DCPC's Board of Scientific Counselors meeting last fall (**The Cancer Letter**, Oct. 4).

Following Greenwald's remarks, NCAB member Helene Brown offered an amendment to not approve the two new systems. Hickey, however, urged immediate approval of the two new systems. "We've taken the scientific community here and asked for their advice," he said.

NCI Director Vincent DeVita told the board that he was not opposed to establishing the two new programs prior to the full review of the entire OSP in the fall. The two new programs would be funded as part of the system's headquarters, and would be unlikely to have issued an RFP by the time of the fall review, he said. NCI will probably form a committee to meet before the fall's "full dress review" of the program, he said.

Brown then withdrew her earlier amendment, and the board voted unanimously to approve the two new systems.

A recommendation that the OSP be upgraded to the same status of cancer centers, clinical trials and training programs was withdrawn by its sponsor William Powers. The recommendation was part of an amendment adopted by the committee last week that also called for funds to be set aside for the OSP to support grants generated by the system's various working groups. The amendment also called for grants review by a chartered committee, and the establishment of a separate Board of Scientific Counselors (**The Cancer Letter**, Feb. 7).

Prior to withdrawing the amendment, Powers told the board that the amendment was necessary for the program to proceed in a constructive way. He cited evidence "indicating erosion of support" for the OSP back to 1982 and 1983. Powers withdrew the amendment in recognition of NCI plans to review the program in the future, and in the interest of allowing further efforts by the institute to improve the program.

A report presented by Hickey summarized the history of the Organ Sites-Organ Systems Programs and the needs described by working group chairmen in December. The report offered a series of recommendations that were approved by the board.

In addition to the establishment of the two new organ systems, the report recommended that the OSP be continued, and that the "thread and recommendations of prior reviews be recognized." It also advised that the Organ Systems Coordinating Center be continued as a single headquarters, with periodic reviews and recompetition.

The report also called for a grant review process of approved concepts to be "relevant to the program and not cancer in general."

It also advised that the "time flow be studied to shorten concept to activation." In addition, the report recommended that "the NCAB/OSC recommend funding to the NCAB Planning and Budget Committee."

NCAB COMMITTEE OPPOSES PHASE OUT OF CLINICAL EDUCATION PROGRAM

The National Cancer Advisory Board's planning and budget committee has recommended that NCI retain a minimal level of funding for its Clinical Education Program. The committee recommended in closed session last week that NCI not completely phase out the program, but try to retain some degree of funding so that the mechanism will remain available should NCI's budgetary outlook improve in the future.

NCI's Executive Committee had planned to phase out the program altogether, before meeting in closed session with the NCAB members, NCI Director Vincent DeVita told a meeting of the Div. of Cancer Treatment's Board of Scientific Counselors Feb. 6.

The Clinical Education Program is a good program that has been very useful for medical schools wanting to upgrade their curricula, DeVita said, but added, "the sentiment at our level was that it was the kind of thing one might expect medical schools to do themselves in this time" of budgetary constraints, he said.

Last month, Div. of Cancer Prevention & Control Director Peter Greenwald told his Board of Scientific Counselors that NCI planned to transfer $1 million in anticipated savings from the program to its Cancer Communications Network (**The Cancer Letter**, Jan. 31).

The NCAB committee's recommendation followed a short, but intensive lobbying effort by George Hill, president of the American Assn. for Cancer Education. Hill is director of surgical oncology at the New Jersey Medical School in Newark. He was a member of NCI's Clinical Education Program committee from 1976 to 1980, and served as chairman of the committee from 1978 to 1980.

Approximately 40 institutions currently receive grants from the Clinical Education Program, which has funding of about $4.7 million this year. During Hill's tenure as chairman of the committee, NCI spent about $10 million per year on the program, he said.

Hill maintains that medical schools will be unable to take over funding for the program, which emphasizes the importance of teaching students about the total spectrum of cancer, including such areas as prevention, detection, multidisciplinary management of patients, and rehabiliation, he said.

Originally oriented toward fellowships and training, the Clinical Education Program (R-25 grants) has focused on curriculum development for medical and dental schools in recent years.

CEP is designed to encourage the development and implementation of methods to help students in the health professions learn the skills necessary to apply state of the art knowledge in cancer care. The program is also intended to encourage multidisciplinary teaching in medical and dental schools.

It also provides stipends to student assistants for experience in cancer research or cancer service. Hill estimates that about 40 schools currently have clinical assistants programs that fund medical and dental students, usually in the summer between their first and second year of medical or dental school. Many of the programs have no other source of funding besides the CEP and would probably be dropped if NCI discontinues the program, he said.

"There has been a very persistent need to remember to remind [NCI staff] what this relatively small program has accomplished in relation to medical and dental education," he said. The program has led to a tremendous upgrading of cancer education in medical and dental schools, he asserted. "The structure of medical education has been enormously enhanced" by the program, specifically the multidisciplinary teaching of cancer, he said. Hill cited the development of programs to evaluate cancer education and the overall upgrading of methods of multidisciplinary education as well. "I don't think any program has the intensity of evaluation in a way comparable to what" is required by the program for oncology, he said.

Schools in the program must develop specific goals and objectives in both the preclinical and clinical aspects of cancer education, he said. For example, schools have developed methods to assess a medical student's actual experience with specific types of cancer to ensure that they gain clinical experience and exposure to specific types of cancer, such as lung, or ovarian cancer. Prospective analysis of patients encountered in a medical clerkship may reveal that some medical students have no exposure to certain types of cancer, and an overabundance to others, he said. Preclinical curriculum and lectures are also analyzed to determine whether any gaps or redundancies exist. The grants serve as a stimulus to cancer educators in medical schools, leading them to develop grant applications, discuss the applications with their deans, and move their own cancer education programs forward in order to be competitive, he said. Without the program, the stimulus would be diminished and in some cases, disappear completely.

Hill also said that language in the reauthorization of the National Cancer Act requires NCI to maintain a cancer education program.

DCT BOARD APPROVES PHASE 2/3 STUDIES OF LAK-IL-2: COULD COST $100 MILLION

NCI revealed plans last week for additional phase 2 studies and for phase 3 trials of the lymphokine activated killer cell-interleukin-2 therapy which could cost as much as $100 million over five years for research and patient care costs.

The Div. of Cancer Treatment Board of Scientific Counselors approved the concept for the two contract supported studies, although neither Board members nor NCI staff have any concrete idea where the patient care money will come from.

These studies will be in addition to those conducted in the six centers announced last week as having been selected to carry out confirmatory trials of the LAK-IL-2 protocol developed by Steven Rosenber (**The Cancer Letter**, Feb. 7). Those six will administer the Rosenberg protocol precisely as it is now being given by Rosenberg and his NCI colleagues. The additional phase 2 studies will test modifications of that protocol, and the phase 3 studies will test regimens coming out of the phase 2 trials.

Rosenberg briefed the BSC on the status of his program, and described some modifications in the protocol that are being developed. One adds steroids to the regimen which prevent body fluid retention, the most serious toxicity of LAK-IL-2. Since there were no responders among those receiving the steroids, there is concern that they may have aborted the antitumor effect, Rosenberg said.

LAK-IL-2 as Rosenberg has developed it is very expensive, and the most costly segment is the generation of LAK cells in vitro, a labor intensive process. Rosenberg said the Fenwal Corp. is collaborating with NCI to develop an automated system for LAK cell generation "which will reduce substantially the labor required." The system should be ready for use in four to six months.

The phase 2 and 3 contract studies will be conducted by the Cancer Therapy Evaluation Program. In trying to arrive at an estimate of the costs, CTEP staff developed two levels of effort for each. For the phase 2 study, the first level was based on use of regimens with toxicity and complexity comparable to Rosenberg's. For those, 10 trials conducted with 40 patients each will cost $4 million for research and $17.6 million for patient care. The second level, with less toxicity and simpler methods of LAK cell generation, 30 trials will be conducted, with 40 patients each. Research will cost $6 million and patient care $12 million. The total phase 2 cost will be $39.6 million.

Modifications to Rosenberg's regimen are being developed by the Biological Response Modifiers Program extramural and NCI intramural investigators. These modified regimens will be the initial regimens tested in the new phase 2 studies. Subsequent modifications will be developed through phase 1 BRMP contracts. BRMP also will sponsor grants to stimulate further basic research in this area and provide additional leads to modify the IL-2 treatment protocol or regimen for LAK cell generation.

Any modification to Rosenberg's regimen must be tested for antitumor activity and compared to response rates established for the original regimen.

From eight to 12 institutions will be funded under the contract to conduct the phase 2 studies which will be designed to (1) determine the antitumor activity of modified regimens in malignancies where the activity of Rosenberg's original regimen has been previously established (renal cell carcinoma, malignant melanoma, colorectal carcinoma); (2) determine the antitumor activity of Rosenberg's regimen in other malignancies; and (3) determine the feasibility and antitumor activity of regimens modified to treat pediatric patients.

All protocols will be open to multiple institutions.

Regimens with response rates which approximate the response rate of the original regimen will be studied further in phase 2 trials against Rosenberg's regimen to further confirm that antitumor activity has been maintained. These contractors also will determine the response rate for other target malignancies as they are identified.

The phase 2 study will be conducted over three years.

The five year phase 3 trials will cost from $32.4 to $43.2 million at the high toxicity, complex LAK level, staff estimated. That includes $6-8 million for research and $26.4 to 35.2 million for patient care in three to four trials with 200 patients each.

With the less toxic, simplified LAK regimens, 15-20 trials will be undertaken, with 200 patients each, costing $15-20 million for research and $30-40 million for patient care, or a total of $45-60 million.

The scope of the phase 3 program will depend on the toxicity and complexity of the regimen developed in phase 2. Highly toxic, very complex regimens would be used to treat only patients with metastatic disease or at high risk for relapse such as stage 2 melanoma, stage C colon carcinoma, or patients with renal cell carcinoma and extra capsular spread. Thus, only three or four large scale phase 3 trials might be indicated.

If the treatment is less toxic and LAK cell generation less complex, patients with less risk for recurrence could ethically be treated in the adjuvant setting, palliation might be a reasonable therapeutic endpoint, and more institutions would be capable of participating. Metastatic trials would be

carried out in sensitive malignancies and adjuvant trials might be justified in resistant as well as sensitive tumor types. Fifteen to 20 phase 3 trials might be indicated scientifically.

"In the harsh reality outside our Clinical Center, there is a whole new set of problems," CTEP Director Robert Wittes said. "Developments are going quickly. We will try to hit a moving target."

DCT Director Bruce Chabner said the budget problem facing NCI and the expected cost of these studies makes them "almost prohibitive." The LAK-IL-2 studies are CTEP's highest priority, Chabner said. NCI intends to ask the Administration and Congress for more money to support them. Failing that, money will be taken from other clinical trials, and if that still doesn't do it, funds will be moved from BRMP and the Radiation Research Program.

Board members asked whether industry and the American Cancer Society could help with the costs. Wittes pointed out that Cetus Corp. is providing recombinant IL-2 at no cost. As for ACS and other non federal institutions, Chabner said he would try.

Chabner said that third party payers would be asked to cover patient care costs but was not optimistic about it.

"I don't think the medical community ought to allow the third parties not to cover this," Board member Lawrence Einhorn said. But Board member Robert Goodman responded, "I'm not optimistic we'll be able to lay off these costs." Wittes noted that some insurance companies are paying for bone marrow transplants but most are not, despite the demonstrated efficacy with many tumors.

The Board also gave concept approval to switching BRMP phase 1 and 2 from master agreement orders to standard contracts; and approved the recompetition of the contract for the study of clinical pharmacokinetics of anticancer drugs. Details of those concept proposals follow:

Study of the clinical pharmacokinetics of anticancer drugs. Recompetition of a contract currently held by Ohio State Univ. Five years, estimated annual cost, $138,815.

The principal objective of this contract is to collect pharmacokinetic data on new and established antitumor agents used either as single agents or in combination in patients undergoing treatment of malignant disease during phase 1, 2, or 3 studies. The data are analyzed for individual variability which can be correlated with clinical response or some other pharmacologic parameter including toxicity. In some studies, the patients may have compromised organ function to better define the dose limiting toxicities. Specifically, these studies will be primarily concerned with the measurement of drug and/or metabolite levels in the plasma with time after a standard dose of the drug. Apparent volume of distribution and plasma protein binding should be determined. These studies may also require measurement of urinary, biliary, and fecal excretion of drug and/or metabolites. Measurement of other fluids (e.g., cerebrospinal fluid) and tissues may be necessary. Approximately 30 patients per drug per six months will be required to provide adequate statistical documentation of individual variability in pharmacokinetic behavior. It is expected that two drugs will be evaluated annually and these are to be selected by the project officer in consultation with other investigators of DCT, and with the consent of the contract's principal investigator. The contractor should have the necessary expertise to develop analytic methodologies for new and established agents and to serve as a resource to phase 1 contractors in resolving problems with the methodology, application and any discrepancies.

The contractor will continue to study two drugs a year. Studies are currently under way with flavone acetic acid and will be initiated with merbarone and ara AC.

Additionally, the future studies carried out under this contract should be those which require considerably more flexibility than is available through the present phase 1 contract mechanism which, by necessity, employs a relatively rigid protocol. This will allow for more in depth studies on the metabolites of each agent. These studies may involve combinations of established anticancer agents to determine the appropriate dose and schedule to limit toxicities and maximize activity. The contract should also be capable of assaying samples and providing results on studies performed at other institutions.

Phase 1/2 clinical trials of biological response modifying agents. Several contracts will be awarded, each for five years. Estimated annual cost will is $2 million for BRMs and $2 million for monoclonal antibodies.

BRMP currently generates about six new agents or agent combinations per year for testing against human malignancies. Since its inception BRMP has had 30 master agreement contractors who recompete for the MA contract every three years. MA contracts are not funded. Of these, approximately 13 successfully competed for clinical trials under a funded master agreement order contract. Most MA holders have never applied for a funded contract, while only eight have performed more than one MAO clinical trial. The evaluation of biological response modifiers requires an institution to perform many standardized trials which require experienced laboratory and clinical personnel.

The uncertainty concerning the availability of funded contracts makes it difficult for an institution to stay geared up. Furthermore, the MA/MAO mechanism was origially devised for relatively small procurements in the $25-50,000 range. In practice, this mechanism is ill suited to relatively large clinical trials costing from $200-300,000. It has been determined that there is

virtually no advantage in staff time and effort, and relatively little savings in overall time from conception to implementation, of this mechanism over the standard RFP/contract mechanism. Full time phase 1/2 contractors, as employed by the Cancer Therapy Evaluation Program, offer the advantages of ease of administration, rapid development of compounds and significant savings in staff effort. In order to allow time to adequately review the proposals, and to provide a mechanism for clinical

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CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY; RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

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phase 1 trials in the interim, current MA holders will be extended one more year at an estimated cost of $1.2 million for four awards.

Specific goals of the contract will be (1) to define the acute toxicities and maximum tolerated dose (phase 1a) of new biological response modifiers in defined cancer populations; (2) define optimal biologic dose at which the agent may be most successfully administered, either alone or in combination with other anticancer treatment modalities (phase 1b); (3) evaluate the effects of the agent on immune system (phase 1 b); and (4) evaluate the distribution, metabolism, and bioavailability of the selected biological agent (phase 1b).

BRMP anticipates evaluating six to eight new agents or agent combinations annually. Each contractor will be expected to test a minimum of two agents during this time period. Each agent will be tested in 25-40 patients, on average. For most new agents, maximum tolerated dose and optimal dose, route and schedule for biological response modifying effects will be determined. The end point of phase 1a/1/b will be to recommend a program for phase 2 testing. Combinations with cytotoxic therapies also will be optimized for BRM effects.

While the major objective of this contract is to accomplish phase 1 testing, a few institutions may be selected to perform initial, and limited, phase 2 testing. It is unlikely that more than one institution per year will be asked to perform this function.

John Antoine, director of the Radiation Research Program, presented a concept proposal which had been prepared as an RFA, soliciting grant applications, for specific cell diagnosis by imaging employing radiolabeled substances. The proposal called for awards with an estimated total of $1 million a year, for three years. However, because of the limits placed on DCT's budget by the various cutbacks, it was decided that this concept would be changed to a program announcement, with no set aside funds. NCI still is encouraging applications in this area, but investigators will have to compete for RO1 grants. The objectives include multidisciplinary efforts to improve existing monoclonal antibodies for imaging purposes and to investigate basic biologic mechanisms and localization. DCT does not generally ask its Board to vote on program announcement concepts, so no vote was taken.

RFPs AVAILABLE

Requests for proposal 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 Blair building room number shown, National Cancer Institute, NIH, Bethesda, Md. 20892. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CP-61019-60
Title: Transplancental carcinogenesis and tumor promotion in old world monkeys
Deadline: April 28

NCI has a requirement to support the intramural research program of its Laboratory of Comparative Carcinogenesis located at the Frederick Cancer Research Facility. The contractor selected will provide space for housing 185 patas monkeys (Erythrocebus patas) and 100 cynomolgus monkeys (Macaca fascicularis)as well as their feeding and care, and provide technical assistance in the form of carcinogen or promoter administration to animals, monitoring the animals, administration of medication were appropriate, maintenance of records and assistance in performing surgical and necropsy procedures.

This acquisition is for the recompetition of two contracts currently held by Meloy Laboratories Inc. One award covering a four year period is anticipated.

Contract Specialist: Thomas Porter
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