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First Test of Cooperative Groups' Willingness To Change Coming In New Colorectal Trials

For much of this year, Robert Wittes, director of NCI's Cancer Therapy Evaluation Program, has been trying to sell the clinical cooperative groups on making changes in the way

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In Brief

NCI Holds Paylines To 160, 165 For Now While Anticipating Another OMB Rescision Request

NOW THAT the 1987 fiscal year appropriations legislation has established $1.402 million as NCI's total, Institute executives must contend with possible White House attempts to cut back on that amount. If NCI receives that entire amount, the priority score payline for grants will be about 175. To accomodate an expected rescision request by the White House Office of Management & Budget, NCI is paying type 1 (new) grants only to the 160 level, and type 2 (competing renewals) to 165. A decision on a rescision is expected sometime in January; if none is requested, NCI will proceed with awards based on the full appropriations. Congress is almost certain to reject rescisions on any part of the NIH appropriations, so the effect will be only to delay some awards a few months. . . . **THREE CANCER** researchers who have had a major impact on cancer treatment and diagnosis received awards this week at the 30th annual Clinical Conference at M.D. Anderson Hospital & Tumor Institute. Charles Moertel, first director of Mayo's Comprehensive Cancer Center and chairman of the North Central Cancer Treatment Group, received the 21st Heath Memorial Award. Lawrence Einhorn, professor of medicine at Indiana Univ. Medical Center, received the Jeffrey A. Gottlieb Award. Robert Riddell, chief of anatomical pathology at McMaster Univ. Medical Center in Hamilton, Ontario, received the Joanne Vandenberge Hill Award. . . . **CORRECTION:** NCI Deputy Director Peter Fischinger was incorrectly quoted as saying that an experimental AIDS vaccine had induced neutralizing antibodies in chimpanzees at the Frederick Cancer Research Facility (**AIDS update**, October). What he said was that the vaccine had induced neutralizing antibodies in rhesus monkeys and had been administered to chimps. "We probably will get the antibodies in chimpanzees, since we've seen them so far in all other species which have received the same material, but we have no data yet from the chimps," Fischinger said.

DCT Board Says New Adjuvant Trials In Colorectal Cancer High Priority

(Continued from page 1)

they establish priorities for clinical trials, develop means for allowing more flexibility in changing directions, and in improving collaboration among themselves for development of more effective intergroup studies.

The Div. of Cancer Treatment Board of Scientific Counselors, after hearing at its meeting last month reports from a variety of studies that "there is something interesting and promising happening in colon and rectal cancer" approved a motion encouraging DCT to pursue new, appropriate adjuvant therapy studies in those diseases.

Reports from investigators who have headed trials which have produced those promising results, chiefly Bernard Fisher of the National Surgical Adjuvant Breast & Bowel Project and Charles Moertel of the North Central Cancer Treatment Group, prompted the Board to reach that conclusion.

Wittes followed with a summary of the problems facing CTEP and the cooperative groups which are funded out of CTEP in carrying out broad based, national clinical trials. At the heart of the problem is how the groups are organized and have traditionally operated, characteristics which have made it difficult at times to quickly mount new studies, accrue sufficient patients and find the answers in a reasonable span of time.

"There are three things we could tell them (the groups) to do in a formal sense," Wittes said. "We could tell them what to do; we could let them do what they want; or we could work together with them, to increase the amount of coordinating that goes on and, just as importantly, to maximize the input from all relevant sources. Not just from within the cooperative groups, but from wherever, so that the best ideas get a fair hearing."

Earlier this year, Wittes had presented several somewhat radical suggestions for reorganizing the cooperative groups, most of which were greeted with considerable skepticism. He settled for assurances that the groups would embrace more collaboration, flexibility and efforts to improve intergroup studies.

"How do you increase collaboration?" Wittes said to the BSC. "First of all, CTEP needs credibility of its own because CTEP will not be regarded as a credible collaborator and a credible coordinator unless we are regarded as credible individuals. I am not terribly worried about that now. I think we have the requisite amount of credibility although one wonders from month to month.

"Number two, we need good communication within the extramural community and that is sometimes a problem but is getting better. We need funds to support consensus development (which) just doesn't happen spontaneously. Probably more important than of those three things, there needs to be a commonality of interest in the cooperative groups."

Wittes said obstacles include too infrequent meetings among group members ("It is really hard to create a consensus among people who don't meet very often"); the "conflict between the need for patient numbers and speed on the one hand vs. tight quality control on the other;" the fact that "intergroup studies are a nuisance, the way the groups are organized. Because they have evolved independently they have a lot of different procedures for doing things. To get groups together doing things the same way is sometimes a real nuisance. But we are working on that and we are also working on (another obstacle) the fear of many investigators of being penalized by peer review for participating in intergroup studies rather than evolving their own ideas in a particular area. These obstacles are fixable, but they have to be dealt with intelligently."

"Significant Magnitude"

Wittes described as "positive" results of the adjuvant studies presented by Moertel and Fisher, along with a "meta-analysis" of all colorectal cancer adjuvant trials by the European Organization for Research on Treatment of Cancer. "Are they of significant magnitude? Yes. I think the magnitudes are both statistically significant and they are also medically significant.

"Are the studies concordant? Not clear. Not clear whether the studies agree with each other or with previous studies done in the past. . . Do the trials have simple clearcut implications for what to do next? I think the answer to that has to be no, they don't."

Moertel's presentation (made by videotape since the BSC meeting conflicted with an NCCTG meeting) described a trial in which 408 patients with stages Dukes B and C colon cancer were randomized to no treatment after surgery, levamisol alone or lemamisol plus 5-FU.

"Toxicity was no problem," Moertel said. "Levamisol alone was a piece of cake. Levamisol plus 5-FU simply gave the characteristic toxicity of 5-FU used alone. Because of this, treatment compliance was excellent."

All patients have been followed in excess of two and a half years, and the median followup is five and a half years. Recurrence free survival with both treatment arms is significantly superior to untreated controls, at P values of .02 and .03, Moertel said. For the Dukes B patients, a therapeutic effect was seen, particularly for 5-FU plus levamisol, but it was not statistically significant. "In Dukes C patients, however, the differences are more striking and are significant in spite of the smaller patient numbers."

A larger confirmatory study has been undertaken by the Eastern Cooperative Oncology Group and the Southwestern Oncology Group, chaired by Moertel. Patients with Dukes C lesions are randomized to the same three arms. For Dukes B, patients are randomized to either untreated control or the 5-FU-levamisol combination. Moertel said accrual of Dukes C patients should be completed early next year, but the Dukes B protocol will require another year because of slower accrual.

"Each protocol will then require some two to three years of followup before we begin to develop meaningful results. We are not sneaking peaks along the way. If nothing else, this study has demonstrated that it is possible to conduct a large intergroup study and to do so efficiently and to do so with high quality."

Moertel said this required intense, close monitoring. "I have investigators mad at me from coast to coast, but it works. Knowing the amount of meticulous effort that this requires, I frankly would be very cautious about undertaking an intergroup study more complex than this or larger than this (600 patients in Dukes C, 300 in Dukes B). I feel you would lose in quality what you gain in numbers."

Fisher described the NSABP study, also for Dukes B and C patients and including rectal cancer patients, with three arms--no treatment after surgery; 5-FU, methyl CCNU and vincristine; and BCG.

After cautioning that the results had not yet been published and therefore should be considered "non final," Fisher said "at the present time, chemotherapy vs. control, the event free survival is significant. There is a significant difference both in event free survival and survival for all patients."

Breaking the results down by subset, Fisher said that patients with left colon tumors did better than those of the right colon or sigmoid cancers, and that the rectal tumors did worse. "I think this is terribly important and is one of the reasons why we feel that there should be separate studies evaluating colon and rectal cancer, rather than lumping all tumors together as if they were a common entity."

BCG did not provide any advantage, in any subset, Fisher said. "When one compares BCG with chemotherapy, chemotherapy comes out on top in every group overall and in subsets."

He concluded that "chemotherapy has altered the natural history of Dukes B and C colon cancer and there has been a significant prolongation in disease free survival."

Noting that methyl CCNU is considered a potential leukogenic agent, Fisher said that eight cases of nonlymphocytic leukemia have been seen among 2,000 patients who received the drug.

Fisher said that NSABP has proposed a new trial comparing the methyl CCNU-vincristine-5-FU combination (the acronym is MOF, using vincristine's trade name, Oncovin) with 5-FU plus leucovorin. He cited phase 1 and 2 studies of the latter combination which have shown promise.

"Some people feel one should dissect the MOF effect and find out whether you could get rid of the methyl CCNU and get the same results, or compare MOF with CCNU and 5-FU, and with 5-FU alone, or some various other kinds of perturbations to dissect out what is of value. Should there be protocols for right sided or non right sided lesions? We believe not. Since the results are due to a quantitative interaction we feel that it is appropriate to combine all of the colon patients."

Fisher pointed out that in the NSABP study, "most of the treatment failures are abdominal throughout. In colon cancer, the first site of treatment failure is rarely anything but abdominal." Bone and brain scans after treatment thus "are not very cost effective for picking up first treatment failure since most of them occur in the liver alone or at some other (abdominal) site," Fisher said.

DCT Director Bruce Chabner suggested that "in choosing the next regimen, it seems to me

it would be most logical to take your best regimen and add something to it you think will be better. I am concerned that if you try FU and leucovorin vs. MOF that you may just get equivalent results because although leucovorin and FU is more effective than FU alone, you are losing something by dropping the other two drugs. Have you considered just using MOF plus leucovorin?"

"Yes, that was a consideration," Fisher answered. "The FU-leucovorin results I think are so compelling that that was why we felt this was worth putting now into the adjuvant setting. If leucovorin and 5-FU is better than MOF, then all the business about dissecting out the MOF is unnecessary and would be relegated to history. . . There will be pharmacologic investigations to try to more clearly define the mechanisms of FU-leucovorin effect. That would be a major part of the trial."

NCI Director Vincent DeVita asked why NSABP did not consider adding the North Central group's protocol as a third arm in the proposed new study. "Then you would have a good comparison of all therapies that work."

Fisher said that was considered, but "our own feeling about three armed studies is a very negative one. I just think the problems one has with two armed studies are exponentially increased by a three armed study."

Mystery of BCG

Commenting about the "puzzling effect" of BCG in the NSABP study, DeVita pointed out that it had no effect on relapse free survival "but in fact has some effect on overall survival. It really doesn't make any sense biologically. It happened in ovarian cancer, and lymphoma. It happened in breast cancer and now you have got it in colon cancer. I have a feeling that Mother Nature is trying to tell us something but we can't quite figure out what it is."

Another point DeVita said he wanted to make, "a point Dr. Bailar and I agree on in his 'New England Journal' article, is that there has been a long and steady decline in mortality from colon cancer. He said he doesn't understand why it is happening. I can think of two reasons now. One is colonoscopy and earlier diagnosis, although there has been no change in incidence; and the second one would be the widespread use of 5-fluorouracil in practice now. It is about the same magnitude as you might expect from the effects that you see in adjuvant studies. This certainly is another unexplained observation in colon cancer."

Moertel cited previous studies for adjuvant treatment of rectal cancer, including the Gastrointestinal Tumor Study Group study with 5-FU, methyl CCNU and radiotherapy. "The combined modality arm shows a significant advantage over the untreated control arm in recurrence free time and now in survival," Moertel said. "Combined modality, however, was not significantly superior to either radiation alone or chemotherapy alone."

Chemotherapy was not initiated until three to four months after the surgical procedure and was not given full dose until five or six months after surgery. A number of patients never received chemotherapy at all because they recurred earlier or had persistent leukopenia after radiation," Moertel pointed out.

In NCCTG's recently completed study, Dukes B-2 and C rectal cancer patients were randomized to radiation alone as the control arm following surgery to radiation plus methyl CCNU and 5-FU. "For our combined modality, we elected to move chemotherapy up front and give a full cycle at full dose before initating radiation plus 5-FU. . . Following radiation we then gave only one additional cycle of methyl CCNU and 5-FU. . .

"In recurrence free time our combined modality arm shows a striking and highly significant superiority," Moertel said. Looking at subsets, however, the entire treatment advantage was for patients who had received anterior resections, with no apparent advantage for those who had undergone AP resections.

The next North Central study proposes to compare 5-FU alone with 5-FU plus methyl CCNU, with further randomization comparing 5-FU via bolus injection with constant infusion.

"In 30 years of treating the common gastrointestinal cancers, this is the first time that I have been willing to conclude that chemotherapy is effective," Moertel said.

Fisher described the NSABP study comparing controls, chemotherapy and radiation therapy. Chemotherapy has produced better event free survival, Fisher said, but no significant difference so far on overall survival.

Looking at subsets, Fisher said that males receiving chemotherapy had "a highly significant event free survival difference" over the control group. For males under age 65, "the differences are truly great. . . With

females, this is in the opposite direction. This is something that one has to come to grips with."

Use of postoperative radiation produced "no benefit either in event free survival or survival," Fisher said. Radiation did reduce local recurrence. "There is reason to consider a reassessment of chemotherapy plus radiation. . . Certainly in our study, overall, we have not shown a very remarkable benefit from radiation therapy."

Paul Sugarbaker of NCI discussed his study using intraperitoneal infusion of 5-FU for treatment of GI malignancies. "You can get twice the dose of drug with less hematologic toxicity," he said. After second look surgery following intravenous 5-FU, 10 of 11 patients with poor prognosis had disease on peritoneal surfaces. In only two of 10 similar patients given intraperitoneal 5-FU was any disease seen on peritoneal surfaces.

Moertel and Fisher described studies using portal vein infusion of drug to combat liver metastasis. Moertel said drug toxicity has been no problem, accrual has almost been completed, and that in line with North Central policy, no results will be reported until after all patients have completed therapy.

Fisher also had no data to report from his study which has accrued 750 patients, with a goal of 400-500 more.

Other New Studies

Further presentations were made on new or impending studies with various combinations including methotrexate, PALA, thymidine, allopurinol, cisplatinum and others. Various early studies with mouse monoclonal antibodies and the phase 1 trial with human MABs were metioned briefly.

"I have heard several times today that we can only expect modest results," DeVita commented after the presentations. "If you only expect modest results, that is all you are going to get. "If you keep backing away from regimens to find out what might be taken out of them you are not going to get anywhere. I wonder where you draw the line between modest and good? I saw data today that suggests that 20 out of every 100 patients treated on the best adjuvant programs might be surviving five years free of disease, compared to an untreated control. That comes to about 20,000 patients a year in colon cancer, which by my standards is not a modest effect. It is a rather sizeable effect."

No Big Change Seen In Senate Cancer Policy; Kennedy Opts For LHR Chair

Last week's victory by Democrats in capturing control of the U.S. Senate will result in one major change with a potential impact on the National Cancer Program. Sen. Edward Kennedy, the original author of the National Cancer Act of 1971, will resume the role he was forced to give up when the Republicans took over six years ago, as the most powerful figure in the Senate on health matters.

Kennedy announced that he will pass up the opportunity to chair the Judiciary Committe and instead will take over the Labor & Human Resources Committee, which has jurisdiction over most health programs (other than those related to Medicare). Kennedy is the top ranking Democrat on both committees; Senate rules prohibit members from holding more than one major committee chairmanship.

From 1971-1980, Kennedy was chairman of the Health Subcommittee of the Labor Committee. His version of the National Cancer Act would have given NCI even more independence and flexibility than the eventual legislation, a compromise with the House which retained more control by NIH over NCI than cancer program advocates had sought. Kennedy remained a strong backer of the cancer program in three renewals of the 1971 Act.

When Orrin Hatch (R.-UT) assumed chairmanship of the Labor & Human Resources Committee following the Republican victory in 1980, he abolished the Health Subcommittee and brought all health related legislation before the full committee. Whether Kennedy will retain that format remains to be seen. If he reestablishes the Health Subcommittee, he probably will assume the chairmanship himself. Otherwise, that post would go to either Claiborne Pell (RI), who will become chairman of the Foreign Affairs Committee, or Howard Metzenbaum, who would have headed the full committee had Kennedy opted for Judiciary.

The change in party control is not likely to produce any major changes in congressional support of the National Cancer Program, which has been a truly bipartisan program from the start. The battle has not been between Republicans and Democrats but rather between Congress and the White House, no matter which party has controlled either.

Hatch, after a shaky start, turned out to

be an extremely effective leader and advocate for cancer research, along with other biomedical research programs. It was his determination that persuaded Senate Republicans to vote with Democrats in overriding President Reagan's veto of the biomedical research reauthorization act last year.

Another key position changing hands is that of chairman of the Labor-HHS-Education Appropriations Subcommittee, and again, a strong GOP friend of the cancer program, Lowell Weicker (CN), is stepping down. He will be replaced by William Proxmire (WI), who has voted consistently for increased funds for NCI, although he had been a critic of the cancer program in the early days following adoption of the National Cancer Act.

John Stennis, the conservative Mississippi Democrat, will become chairman of the full Appropriations Committee, replacing the comparatively liberal Mark Hatfield of Oregon.

Since Democrats retained control of the House, no committee or subcommittee chairmanship changes affecting the cancer program are expected there. Henry Waxman (CA) remains as chairman of the Health Subcommittee of the Energy & Commerce Committee; and William Natcher (KY) is still chairman of the Labor-HHS-Education Appropriations Subcommittee.

Loeb ACS President, Eyre President Elect; Fisher, Potter Honored

Virgil Loeb, professor of clinical medicine at Washington Univ., was elected president of the American Cancer Society last week at he annual meeting of the ACS Board of Directors. He succeeds Charles LeMaistre, president of the Univ. of Texas System Cancer Center-M.D. Anderson Hospital.

Harmon Eyre, associate professor of medicine in the Div. of Hematological Oncology at the Univ. of Utah, was elected vice president and president elect.

Loeb, a current member of the Board of Scientific Counselors of NCI's Div. of Cancer Prevention & Control, said he plans to stress a message of hope concerning cancer during his tenure as president. "Half of all cancer patients today are being cured. We have made remarkable progress in detecting and treating cancer and in understanding the biology of cancer. We have even greater prospects of preventing cancer by making careful choices in our lifestyles. We in the American Cancer Society call such choices 'Taking Control' and we have designed a program by that name to guide people in making value wise decisions relating to cancer risk."

ACS presented its prestigous Medal of Honor to Bernard Fisher, Univ. of Pittsburgh, for his "persistent, courageous action which changed attitudes so that women could receive less extensive treatment for early breast cancer and for determining the role adjuvant chemotherapy plays in controlling metastases;" to Lynn Smith, Minnesota publisher, for his impact on antismoking efforts; and to Van Rensselaer Potter, Univ. of Wisconsin, for his "groundbreaking work in biochemistry."

The Society's Distinguished Service Award was presented to Ruth Abrams, Boston, former clinical supervisor of the Social Service Dept. of Massachusetts General Hospital; Harold Amos, chairman of the Div. of Medical Sciences at Harvard and former member of the President's Cancer Panel; Oscar Auerbach, senior medical investigator at the VA Hospital in East Orange, NJ; and Jean Fergusson, nursing director of the Pediatric Nurse Practitioner Program of the Children's Cancer Research Center in Philadelphia.

RFAs Available

RFA 87-CA-09

Title: Modification of eating behavior in the community

Application receipt date: Jan. 21; letter of intent, Dec. 1

The Div. of Cancer Prevention & Control of NCI invites applications for studies to design, test, implement and evaluate procedures and materials for the modification of eating behavior in community settings. The purpose of these studies is to generate materials and strategies for use in communities with interests in improving and/or sustaining eating practices consistent with cancer risk reduction and health promotion. The studies should be targeted at specific adult audiences in discrete settings and may utilize the resources of public, private or voluntary organizations. Audiences and settings should have national applicability and interest.

The intent is to fund up to five awards, each of three years duration. Total costs for all projects are estimated at approximately $750,000 for the first year. This level of activity is dependent on receipt of a sufficient number of applications of high scientific merit.

Proposals are requested in one or more of the following areas: (1) development and testing of innovative procedures and materials for modifying dietary behavior in the community; (2) adaptation and testing of existing, efficacious procedures and materials to encompass diet and cancer risk reduction objectives; and (3) development and testing of evaluation strategies and instruments that can be used to assess the effectiveness of interventions such as those described above.

Research projects shall include practical ways to reach specific target audiences with eating behavior

modification guidance and assessment of the impact on knowledge, attitudes and practices. The research should have the long term objective of contributing to the NCI goal of reducing cancer deaths 50 percent by the year 2000. Projects contributing to this goal should address changes in dietary fat and fiber within the context of the seven Dietary Guidelines for Americans.

Some examples of the types of projects that will be considered are listed below. Offerors may propose one or more of the studies listed but are not limited to these examples:

1. Studies of the effectiveness of various approaches with defined groups of adults in specified settings, such as worksites, clinics, primary care sites, libraries, churches, worksites of private or voluntary organizations, shopping malls, restaurants and markets.

2. Studies to develop instruments and evaluation procedures that can be used by professionals or lay volunteers to assess intervention effects on eacting behavior.

3. Adaptation and testing of existing community procedures and materials for dietary modification in communities to encompass diet and cancer risk recommendations.

4. Studies on the effectiveness of various approaches to recruit, train and utilize volunteers to promote eating behavior changes in line with cancer control objectives.

5. Effectiveness of alternate communication and behavior change strategies on the knowledge, attitudes, practices and propensity for change in eating practices of hard to reach, high risk groups.

6. Studies of efficient methods to reinforce and sustain modifications in eating behavior over time.

7. Cost/benefit analyses of various models for promoting dietary change at the community level.

8. Development and testing of the effectiveness of social marketing strategies for promoting changes in eating behavior commensurate with cancer control.

The conceptual development, study design, methodology, data collection instruments and analysis plans, and implementation of the project is the responsibility of the applicant. However, staff of cooperating organizations may be coinvestigators, and may be involved in preparation of the grant application.

It is expected that investigataors will share ideas, experiences and knowledge to facilitate mutual goals. Funds should be budgeted to permit travel of senior staff to Bethesda for an annual two day meeting for the duration of the study, to refine evaluation plans, coordinate procedures to allow comparisons among projects and review progress.

Letters of intent should be sent to and complete copies of the RFA and further information obtained from Dr. Louise Light, Program Director, Health Promotion Sciences Branch, DCPC, NCI, Blair bldg Rm 416, Bethesda, MD 20892, phone 301-427-8656. Applications must be sent to NIH, Div. of Research Grants, Westwood Bldg Rm 240, Bethesda, MD 20892.

RFA 87-CA-05

Title: Integrating tobacco education into the school system

Application receipt date: Jan. 20

The Div. of Cancer Prevention & Control invites applications for research on ways to increase effective tobacco education programs in middle and intermediate schools (grades 6-9), and to assess effectives of these programs on the tobacco related knowledge, attitudes and practices of students in these grades.

Interventions that will be developed, implemented and evaluated in this research are expected to identify the strategies that are most effective as part of the total school curriculum. As a secondary objective, this research is expected to determine the effects of school based tobacco education programs on the knowledge, attitudes and practices of students.

Research should focus on geographically defined population areas. Specifically, interventions should target as many of the school districts in a state as possible. In large states or in states where there are numerous small school districts, investigators can propose that the intervention be introduced into a defined geographical area.

Funding under this RFA is limited to a maximum of four years. NCI expects to make three awards, with a total estimated cost the first year of $1.2 million, and a four year total of $6 million.

A copy of the complete RFA and further information may be obtained from Dr. Barry Portnoy, Health Promotion Sciences Branch, DCPC, NCI, Blair Bldg Rm 416, Bethesda, MD 20892, phone 301-426-8656.

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 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-CM-87207-29

Title: Pathology and veterinary support services for protocol toxicology studies

Deadline: Feb. 2

The Developmental Therapeutics Program of NCI's Div. of Cancer Treatment is seeking organizations to provide pathology and veterinary support services for protocol toxicology studies.

DTP is responsible for discovering and developing new antineoplastic and antiviral agents. The final step in the developmental process centers on toxicology studies to define the safety of initial human doses and the primary organ toxicity induced by the new agent. The critical evaluation step in the toxicology studies is histological characterization and diagnosis of lesions produced by the new agents. Three areas of pathology support are desired by the Toxicology Branch to meet the requirements of DTP: Repository and archival storage capabilities; pathology quality assurance; and general pathology services including necropsy supervision, tissue trimming and blocking, slide preparation, and pathology evaluation. In addition to the above, support is also required in the area of veterinary services. These services are envisioned to include development of surgical procedures for placing drug administration materials and general veterinary medical care to rodents and dogs.

The principal investigator should have a degree in veterinary medicine with several years experience in the pathology specialty. The other members of the proposed team should have education and experience reflecting their abilities to carry out the assigned tasks.

One contract will be awarded and it will be administered on a task managed basis. Task orders will be issued under a funded cost reimbursement, level of effort contract resulting from this RFP.

It is anticipated that the contract will be awarded for five years and will be incrementally funded.

This will be a 100 percent small business set aside. For the purposes of this contract, a small business is defined as one that is independelty owned and operated, is not dominant in the field represented in this work, and with its affiliates does not exceed 500 employees.

Contracting Officer: Clyde Williams
RCB Blair Bldg Rm 224
301-427-8737

RFP NCI-CM-87205-29

Title: Performance of protocol toxicology studies

Deadline: March 2

The Developmental Therapeutics Program is seeking organizations to conduct preclinical toxicology studies of oncolitic agents. The data from these studies must be suitable for filing with FDA as part of investigational new drug applications. The organizations should have the facilities and staff to carry out such studies and the management expertisue to analyze and evaluate the data.

As a minimum requirement, the contractors must perform all toxicology studies in accordance with FDA's good laboratory practice regulations. Contractors must be in compliance with GLPs at the time of proposal submission. One or two contracts will be awarded and each will be administered on a task managed basis. Task orders will be issued under funded cost reimbursement, level of effort contracts resulting from this soliciation. Annual workload estimated for the described studies are 8,000 technical staff hours per compound satudied. Assignments are estimated to involve one to two agents per year. The objective of the task orders to be issued are:

*Determination and safety assessment of an initial dose for clinical use.

*Determination of the primary organ systems adversely affected by the drug administration.

*Determination of schedule dependent toxicity.

*Acquisition and use of pharmacokinetic information to permit extrapolation of toxic effects across species by relating plasm drug levels to time of appearance and severity of toxicity.

The principal investigator should have a doctoral degree in toxicology/pharmacology or a closely related discipline and several years of diverse experience in directing, implementing and evaluating preclinical drug toxicity studies in experimental animals. The pathologist and analytical chemist should similarly have credentials demonstrating competence and accomplishments in serving as critical team members in the conduct of such studies.

It is anticipated that contract awards will cover five years and will be incrementally funded. This represents recompetition of work done in part under a prime contract held by Battelle Memorial Institute, Columbus Laboratories of Columbus, Ohio.

This will be a 100 percent small business set aside (same definition for small business as in the previous RFP above).

Contracting Officer: Clyde Williams
RCB Blair Bldg Rm 224
301-427-8737

RFP NCI-CM-87201-29

Title: Performance of protocol toxicology studies

Deadline: March 2

This RFP is identical to the one above except that it is <u>not</u> a small business set aside. NCI expects to award two to four contracts under this RFP, and "all responsible sources will be considered." Clyde Williams is also the contracting officer for this procurement.

RFP NCI-CN-75409

Title: Multidisciplined analysis of chemopreventive agents (CORRECTION)

The announcement seeking sources for this RFP which appeard in **The Cancer Letter** Oct. 31 has been revised to correct the definition of a small business for the purposes of this procurement. The previous definition stated that a small business is one whose annual sales or receipts for the past three fiscal years have not averaged more than $7 million per year. The dollar limit has been eliminated. The definition of a small business for the purposes of this RFP is "any concern that is independently owned and operated, is not dominant in the field of operation in which it is bidding on government contracts and with its affiliates, the number of employees does not exceed 500 persons."

The deadline for statement of qualifications remains Dec. 26.

RFP NIH-NIAID-AIDSP-87-14

Title: Investigations on HTLV-3/LAV neutralizing antibodies

Deadline: Jan. 7 (tentative)

The Prevention Branch, AIDS Program, of the National Institute of Allergy & Infectious Diseases, has a requirment for the development of new or improved neutralization assays for HTLV-3/LAV and the use of those assays to investigate some important immunological issues of AIDS. In addition to the development of an assay technique, contractors will be asked to also determine the role of neutralizing antibodies in the initiation and pathogenesis of HTLV-3/LAV infections and to investigate if live virus or vaccine preparations can induce neutralizing antibodies in laboratory animals.

The NIAID sponsored project shall take approximately three years to complete. This shall be a cost reimbursement contract.

All inquiries must be in writing. Contact Sherry Orr, Contract Management Branch, NIAID, NIH, Westwood Bldg Rm 707, Bethesda, MD 20892.

RFP NIH-NIAID-AIDSP-87-18

Title: Evaluating biological response modifiers as therapies for AIDS

Deadline: Jan. 15 (tentative)

The Treatment Branch, AIDS Program, NIAID, has a requirement to ensure that efforts will be made to evaluate biological response modifiers for the treatment of AIDS in animal models and facilitate the entry of BRMs into clinical trials. Specifically, the contract aims to (1) evaluate BRMs that may be used as an effective therapy in the treatment of AIDS; and (2) evaluate identified BRMs in combination with other drugs as therapies for AIDS. The successful offeror must have the capabilities, appropriate technical approach, facilities and appropriate personnel to provide a detailed evaluation of the effect of a BRM as a treatment for a retrovirus infection in an appropriate animal model.

This project will take approximately five years to complete. It is expected that a cost reimbursement type contract will be used. To receive a copy of the RFP, send two self addressed mailing labels to Jacqueline Holden, NIAID, Westwood Bldg Rm 707, Bethesda, MD 20892.

The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams

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