THE CANCER LETTER

Vol. 12 No. 28
July 11, 1986

Subscription $150 year North America
$175 year elsewhere

P.O. Box 2370 Reston, Virginia 22090 Telephone 703-620-4646

Groups Accepting Need For More Collaboration, NCI Backs Away From Drastic Structural Changes

Cooperative groups, prodded by NCI's insistence that the way they manage clinical trials will have to be improved, are forestalling possible drastic changes in the structure

Continued to page 2)

In Brief

Bristol Dedicates New Research Center; MSK Presents Awards To Sen. Moynihan, 10 Others

BRISTOL-MYERS has dedicated its new, $160 million pharmaceuctical research center in Wallingford, CT. The company said it is the largest capital project in its history. More than 100 PhD and MD investigators are involved in anticancer, anti-infective and central nervous system research in the center's 120 labs. . . . **SEN. PAT MOYNIHAN** was among 11 to receive awards at Memorial Sloan-Kettering Cancer Center's seventh annual academic convocation. The senator was presented with the center's medal by Benno Schmidt, chairman of the board of overseers and managers, in appreciation of Moynihan's "outstanding leadership in dealing with critical issues of our times." Other awards: **GEORGE BOSL** and **PAUL O'DONNELL**, Louise and Allston Boyer Young Investigator awards; **CHARLES RUBIN**, cochairman of molecular pharmacology at Albert Einstein College of Medicine, the Aaron Bendich award; **JOSEPH BERTINO**, professor of medicine and and associate director of the Yale Comprehensive Cancer Center, the Chester Stock award for significant contributions to the advancement of knowledge about cancer; and **ROBERT WEINSTEIN**, professor of biology at Massachusetts Institute of Technology, the Katherine Berkan Judd award for investigators who have made major advances toward the control and cure of cancer. . . . **JOHN LANDON**, president of Bioqual research firm, has been named president and chief executive officer of Diagnon Corp., the publicly held biotech firm in Laurel, MD, that recently purchased Bioqual. . . . **PAPERS** are being solicited for a new quarterly publication of the American Assn. for Cancer Education. To submit journal manuscripts, contact Richard Bakemeier, MD, Editorial Office, Journal of Cancer Education, 4215 E. Third Ave., Denver, CO 80220. Subscriptions are $45 for individuals, $75 for institutions, and may be ordered by contacting the journal at Pergamon Press, Maxwell House, Fairview Park, Elmsford, NY 10523.

Wittes Says Groups Already Making Changes, May Drop CTEP Proposals

(Continued from page 1)
of the system by voluntarily implementing some of the less traumatic of NCI's proposals.

"In the last few months, we're seeing vast increases in collaboration among the groups, a vast increase in intergroup communication, and a growing realization that business as usual is not the way to go," Robert Wittes, director of the Div. of Cancer Treatment's Cancer Therapy Evaluation Program, told **The Cancer Letter** this week.

The result, Wittes said, probably will be that CTEP will not press for the proposals it had developed which would have made fundamental changes in the cooperative group structure.

Two of CTEP's more significant proposals were replacing institutional grants with per case reimbursement, and use of "strategy committees" to develop protocol priorities. Per case reimbursement had been strongly opposed by group members, except on a limited basis, and Wittes indicated that he has all but abandoned the concept. Groups still may include some per case reimbursement proposals in their renewal applications, a policy already in effect (two groups--National Surgical Adjuvant Breast & Bowel Project, North Central Cancer Treatment Group--have been using such a program for years).

As for strategy committees, Wittes said he did not care whether national planning is carried out through spontaneous coordination of the kind he is seeing develop, or through formal committees convened in Bethesda. "What we're going to see is some kind of planning. That's fine, as long as it works."

Another CTEP proposal, for looser affiliations between groups and institutions, was strongly opposed by group members. "We had anticipated that opposition, but did not anticipate the strength of their feeling," Wittes said. Scratch that idea.

Cooperative group chairmen, meeting in Bethesda June 30, spent most of the day discussing the range of issues with Wittes and CTEP staff members. They asked that CTEP send out written summaries of information presented and a new statement on NCI's position.

That will include "various models for per case engraftment on institutional grants," Wittes said, "and then we will formulate another iteration (of CTEP's proposals for changes) which will be more like the present system." Group chairmen will meet again, in about six weeks, for what should be a final discussion of any changes.

The DCT Board of Scientific Counselors committee appointed to look at any proposals for change is waiting for the group chairmen to take their position, Wittes said. It is possible the committee may be able to take the proposals and its recommendations to the full board at its October meeting.

Flexibility "Tax"

One issue on which CTEP and group chairmen agreed was that the present grant (actually, cooperative agreements) system does not leave much room for moving money around to meet new priorities between review cycles, nor to take advantage of capabilities of the better producing members at the expense of the non or low level producers.

During noncompeting years, the only way money can be freed up for new initiatives or priorities is to drop members for poor performance. Even then, that money returns to CTEP, which then is free to redistribute to any of the groups, not necessarily the one from which it came.

"The (overall cooperative group) budget depends on the return of some money from groups to help fund competing awards," John Killen, deputy director of the Clinical Investigations Branch, said.

"Sort of like overbooking by the airlines," Southwest Oncology Group Chairman Charles Coltman added.

Wittes made this "solid commitment:" if in the future money is freed up by groups weeding out poor performers or by other streamlining, it will be returned to that group.

NSABP Chairman Bernard Fisher, the current chairman of the Chairmen's Committee, suggested that considerable flexibility could be achieved merely by having the authority to carry over funds from one fiscal year to the next. Recent administrations have required most NIH programs to return unexpended funds to the government at the end of each year.

NCCTG Chairman Charles Moertel expressed concern about "scientific credibility" vs. CTEP's coordination role. "There was a lot of concern at first about the fundamental nature of the cooperative agreement (when the mechanism for funding groups was changed from grants to cooperative agreements, which give NCI staff more leeway in coordinating efforts of extramural investigators). "Most of us

recognized that some control was needed. At the time, the understanding we were given was that beyond good housekeeping, science would not be taken over by CTEP. I would rather be responsive to peer review. Could you distinguish between the functions appropriate to CTEP and those not, in regard to science?" Moertel asked Wittes.

"The cooperative agreement is vague on staff involvement," Wittes said. "If we set up a system with ample opportunity for abuse, we've failed. I don't know how to assure you that the present CTEP staff is not interested in government control of science. The only thing I can say is we imagine this as a cooperative group effort, with CTEP as a coordinator."

"Where do you draw the line between protocol approval, which I see as total involvement in science, and coordination?" Moertel asked. "How do you draw the line and interrelate with peer review?"

Coordination or Interference?

Wittes noted that CTEP has other responsibilities than the cooperative groups, notably its role in drug development. "There are special considerations we have to be aware of, not just patient safety, but also the efficacy of the drug under development. The CCIRC (Cancer Clinical Investigation Review Committee, the initial review body for cooperative groups) looks at independent groups. No other group in the country is charged with looking at the overall group system but CTEP. There is a fine line between overall coordination and interference with science. We have to have some standards on drawing the line, but we try to be reasonable. Your question has to do with the enhanced role of the chairmen of the groups."

"There is a need for continued dialogue between CTEP and the CCIRC, so their criteria for evaluating an institution would be valid and up to date," Childrens Cancer Study Group Chairman Denman Hammond said. "You have been forcefully separated in recent years (when the major NCI reorganization in the late 1970s moved program staff and review bodies into separate divisions). How can that dialogue be brought about?"

Wittes noted that Mary Ann Sestili, who has been working in the Chemoprevention Branch of the Div. of Cancer Prevention & Control, had just been appointed executive secretary of the CCIRC. "We look for a very productive dialogue with the CCIRC," Wittes said. He added that while CTEP is not permitted to have input into review of specific grant proposals, it has made presentations on broad policy and budget matters.

"The CCIRC in the past has made major mistakes," Hammond insisted. "Program staff is not permitted to make corrections."

"We can call attention to major deviations," Killen said. "It is difficult to draw the line. It can be as dangerous as helpful."

"I hope the dialogue can be as effective helpful," Coltman said. "With only one of eight surviving (groups reviewed by the CCIRC during the past year), I hope we don't have an organization run amuck. If we're talking about one issue and they another, we'll continue the abolition of groups."

"No one is watching the store," Radiation Therapy Oncology Group Chairman Luther Brady said. He cited one case, in which "information presented to the CCIRC had no relation to the facts."

Some Clear Inequities

"Everytime we have a site vist and one of our institutions is evaluated, there is a gross difference between my opinion and what the pink sheets say," Hammond argued. "Once a site visit and report are made, there is no further attempt to validate the report. There are some clear inequities."

Clinical Investigations Branch Chief Michael Friedman brought the discussion back to the issue of flexibility and the "tax" to achieve it. That is the plan which would levy a certain percentage from all members in a group and place it in a reserve which would be available as a developmental fund--for urgent new, high priority studies, to support new or off cycle investigators coming into the group, and for other expenses which otherwise would have to await competitive review. Friedman listed as examples of administrative requests submitted by groups, much of which could not be paid out of cycle: changes in a university's salary support, "an unexpected administrative crisis which could not be factored into the original grant;" move of offices; increase in office rent; computer purchases or rentals ("the argument we often hear is, give us the money now, it will save us money in the long run," Friedman said); and workshops and meetings.

With no additional money expected in the FT 1987 budget, "groups will have to function on their own money (current budget levels)," Friedman said.

Friedman concluded that "ideally the system should permit dynamic matching of

resources to needs" but that is not possible with the present system which ties group budgets to infrequent peer review and the unlikely prospect that mid-cycle supplements may be obtained from CTEP, given the present state of the NCI budget.

Potential solutions Friedman offered were:

*A net increase of money would become available to CTEP, through larger appropriations from Congress to NCI. "Our assessment is that that is unlikely to happen," Friedman said.

*An increase of money would be available for surviving groups through more disapprovals by the CCIRC, with no new groups being funded.

*Assuming that wholesale group disapprovals do not occur, with no additional money available for existing groups, they would either be smaller with fewer institutional members, they would have to operate with reduced central costs for operations and statistics, or they would have to fractionally reduce awards to their institution members.

Friedman asked the group chairmen for their ideas on potential solutions.

"Squeaky Wheel"

"I'm not convinced that all of these are legitimate needs," Moertel said. "I would rather have money available through peer review. We would rather do these things within our budget and have any additional money available through peer review, than try to be the loudest squeaky wheel. The overall need is for more money."

"What I mean by flexibility," Friedman said, "is, for example, you find you need another data manager between reviews, due to a major increase in case accrual." Without some mechanism to provide those funds, "you're stuck" until the next cycle.

"We need some system to increase the chairman's flexibility," Douglas Tormey, Eastern Cooperative Oncology Group, said. Intergroup activities are expensive, quality control is becoming more detailed and costly, the audit system is expensive, and the protocol review system "is becoming extraordinarily expensive," Tormey said.

"We're interested in more flexibility for those things," Wittes said. "But if we stick with the grant based system, I'm not sure we can free up more money."

Carmack Holmes, chairman of the Lung Cancer Study Group, said his problems are due less to a lack of flexibility than to the fact "we're functioning on 20-30% less than our recommended funding. If we had that, that would meet our major needs."

"Even if you had all the money you thought you needed (at CCIRC review), you will need more control over some portion of it as new needs arise," Friedman insisted.

Holmes asked how the sudden emergence of needs brought on by the decision to expand interleukin-2 studies was met.

"That was a decision by the NCI director that money would be taken from other sources outside of CTEP," Friedman answered. But suppose you want to try IL-2 alone for lung cancer? You should have the flexibility to start that on your own."

"In a $50 million program (total NCI budget for cooperative groups), you should have the flexibility to do that," Wittes added.

Moertel suggested that part of the problem is caused by "a review system that is so slow. I think that is because science is being debated at CTEP. The monitoring required of our institutions is way beyond anything FDA requires. Your protocol review system frequently requires two or three submissions. It seldom is completed in less than two months. There is a lot of money you are losing there."

"The time interval could do with some improvement," Wittes admitted. "But the median for protocol review is not two months."

"There has been three and a half weeks between your decision and when the typing (of the notice of the decision) was done," Moertel argued.

That is one result of the forced cuts in support staff positions imposed on NCI, Wittes indicated.

"Then cut down on your nitpicking and reduce those problems," Moertel said.

Band Aids and Bailing Wire

"We're talking about band aids and bailing wire," Emil Frei, chairman of Cancer & Leukemia Group B, interjected. He suggested that a more costly problem, with greater impact on budgets, is an unnecessary emphasis on certain studies. There may be enough trials on leukemia and lymphoma, work is "well along and will continue anyway. . . More money should go into the major tumors."

Frei noted that cooperative groups "are set up to do phase 3 studies, while the LAK cell studies (which some groups are doing) are essentially phase 1 and 2. Also, we have

the monoclonals coming along. I'm not sure that this organization as a whole is set up to make these decisions. If we're going to do these things, we have to make the case upstairs that we need more money."

As the meeting wound to a close, Wittes said, "We're not getting a clear reading from you. We need guidance from you. We've gone down the track as far as we can in planning."

"I would like to see if my group would accept getting 95% of their budgets, with 5% going back to the chairman for development funds," Teresa Vietti, chairman of the Pediatric Oncology Group, said.

"I also would like to take this back to my group," Frei said, "particularly to discuss funding by case accrual. I don't like downward adjustments, I prefer that it be upward."

"There has been a lot of material presented," Hammond said to Wittes. "If there had been rampant discord, you would have heard it." He suggested that Wittes send summaries of the discussions and various proposals and ask for responses. "You might get a good response, maybe some good ideas."

Fisher agreed with that suggestion and added, "We can then have one more meeting, to end it, by the end of summer. Then let the whole thing rest."

Groups Fight To Keep CGOP Alive As DCPC, DCT Argue Over Who Pays

Cooperative group chairmen were appalled to learn that NCI has considered dropping the Cooperative Group Outreach Program, which they consider a vital part of NCI supported clinical trials.

CGOP (not to be confused with CCOP--Community Clinical Oncology Program) has supported with about $4 million a year from the Div. of Cancer Prevention & Control efforts by six groups to bring physicians and patients from community hospitals into clinical trials. That effort began about 10 years ago, well before the advent of CCOP.

CCOP, also funded and managed by DCPC, costs about $10 million a year. Its participants usually are larger hospitals than those working through CGOP, with a requirement for at least 50 patients a year going onto research protocols. CGOP hospitals for the most part enter smaller numbers of patients.

There are other differences, and one of them is that the cooperative groups control CGOP money, while the lion's share of CCOP money goes to the community participants.

DCPC now is pressing the Div. of Cancer Treatment, where management of the cooperative group program is housed in the Cancer Therapy Evaluation Program, to take over CGOP. DCPC has proposed that the cost of funding the third and final year of current CGOP contracts be split equally between the two divisions.

DCT doesn't mind taking over CGOP but is not enthralled with the prospect of squeezing another $2 million out of its already desperate budget situation.

DCPC, arguing that CGOP can no longer be considered pure cancer control research, would like to retain as much of its line item cancer control funds as possible for cancer control research. Somewhere down the road, that same argument might be made for CCOP. Meanwhile, NCI executives are considering dropping CGOP entirely and going solely with CCOP as the community clinical trials vehicle.

Bernard Fisher commented at the cooperative group chairmen's meeting that both CCOP and CGOP "have helped us get patients from different sources, and increased accrual. They have been wonderful. They are terribly critical to us who have these network programs. It is important to get them into DCT."

"CCOP has been a resounding success," Denman Hammond said. "However, they have brushed pediatric oncology only slightly. Most of our community participation is through CGOP." If CGOP is phased out, and CCOP dollars remain the same, the two pediatric groups would be severely hurt, Hammond said.

Jerome Yates, DCPC associate director for centers and community oncology, argued the case for his division. "The issue is, is it appropriate to support CGOP out of cancer control funds after 10 years?" Yates acknowledged that DCPC did not want to make any commitment for CGOP beyond the $2 million it plans to commit for the last year of the current contracts, which starts December 1986. "If it is to continue beyond that, it will have to go to some board this fall (for concept approval)," Yates said.

"Our budgets go on whatever the source," Charles Coltman said. "You (DCPC) peer reviewed and approved CGOP for three years," implying DCPC was now welching on that commitment.

"That program is more appropriate for DCT," Yates insisted. Dr. (Peter) Greenwald (DCPC director) would like to transfer it without any money. The issue is, if it is to continue past the third year, there needs to be some planning, on whose commitment it is."

"In effect, you're defaulting on a commitment," Hammond said.

"You're leaving us out on a limb," Coltman said. "There is no precedent for this."

"Oh, I'm sure there is a precedent," Yates responded.

Charles Moertel, who served a term on the DCPC board, said, "That board is not constituted to oversee treatment programs. I would not give CGOP a ghost of a chance there (at a concept review to continue it). It belongs in DCT. The question is, is it a program strong enough to continue? We have to make a strong enough case to the NCI Executive Committee (which was meeting this week and may have reached a decision about it). But if this stays in DCPC, we're in trouble."

Coltman noted that cancer control research is being added to CCOP in the upcoming recompetition, which makes that program more appropriate for DCPC. "The potential exists for cancer control in CGOP, which can be just as productive for cancer control. The reason it is in trouble with DCPC is that there is no cancer control for it now."

Yates suggested that if a cooperative group cancer control committee wrote in cancer control projects for CGOP members, "we could award support for it."

"Not without money," Coltman said.

"CCOPs have been necessary, have gotten us into the community, and have increased patient accrual," Fisher said. "Now you say they need cancer control. In view of the budget problem, where does that leave us? You're making it mandatory for CCOPs to add cancer control. Suppose our group decides it does not want to do cancer control, at least not as our top priority? Where does that leave us? That's just another worm dangled before us. I've nibbled at so many worms in the last 20 years, most of which have not caught a fish."

"You're the fish, Bernie," Coltman needled.

"Worms taste differently to different people, or fish," Yates said. "Groups are doing protocols you could call cancer control--markers, quality of care, etc. If we offered the option not to do cancer control, I think most wouldn't do it. You think of yourselves as clinical trials groups."

"You've heard how strongly DCPC feels about cancer control," Robert Wittes said. "They have discussed this with us all along. There are some irreconcilable differences."

"The science of cancer control will be dealt with primarily by the protocol review committee," Yates said. "I don't see large applications coming in from research bases on cancer control."

Fisher, addressing a question to Moertel, asked "Do you feel DCPC will be more sympathetic to our (CCOP) cancer control than they were with CGOP?"

"I can assure you that CGOP is not Dr. Greenwald's favorite program," Moertel answered. "If we are going to continue to sell this to Dr. Greenwald, we have to convince him we have an interest in the primary mission of DCPC. They have a congressional mandate for cancer control."

"What if I have a protocol for cancer control and they (the review committee) don't like it. I have 25 CCOPs in my research base. Just because the protocol review committee doesn't like it, 25 CCOPs would be left without NSABP as a research base."

Promissory Notes

"Most of the applications will be promissory notes," Yates said. "The emphasis in review will be on the multidisciplinary capabilities of the research bases. There will be no requirement for CCOPs to do cancer control with every research base."

"Are you eliminating cancer centers as primary research bases?" Theodore Phillips, chairman of the Northern California Oncology Group, asked.

"No, centers can be research bases for cancer control alone, or for both cancer control and clinical research," Yates answered."

Moertel suggested that the CCIRC, constituted primarily for clinical trials review, might treat some groups with heavy cancer control involvement unfairly. He mentioned in particular CCIRC's limit of $300 per case. "Cancer control requires new types of personnel, it is an entirely new program."

"DCT and DCPC have to have some agreement, on who does what," Yates said.

"My main concern is the review," Moertel said. "How can you assure us of fair review from CCIRC if we go down the cancer control road?"

Yates noted that Mary Ann Sestili, newly appointed CCIRC executive secretary, "just

came from DCPC. I'm sure she will continue these discussions with Bob (Wittes) and Mike (Friedman).

"An important issue is that you are asking us to take on more responsibility without more money," Fisher said. "That is not reasonable."

"We're counting on the wisdom of the review committees," Yates said.

"I have heard that there will be 50 CCOPs, with $9 million," Coltman said. "Also, that somehow you will fund an additional five in year 2 if the cancer control works."

"The best guess is that there will be 200 applications," Yates said. "Some existing CCOPs may elect not to recompete because of the cancer control requirement. I"m not as concerned about the problem, 'Here you are asking us to do something else but the budget is the same.' Show us what you can do and what it will cost. There are some holes in the budget. The RFA has to show an estimated number of grants, but those are ball park figures."

"My question was about year 2," Coltman said. "If it is successful in year 1, will there be more CCOPs in year 2?"

"I can't answer that," Yates said.

"On the issue of review," Wittes said, "it seems the best way would be to expand the mandate of CCIRC to include review of cancer control activities. Expand the membership to include the expertise needed. I think review (of cooperative groups) should remain with one body."

Program Announcements

Determination of the therepeutic usefulness of maturation, differentiation and antigrowth factor substances in cancer models

Deadlines for applications: Oct. 1, Feb. 1, July 1

The Biological Response Modifiers Program of NCI's Div. of Cancer Treatment invites grant applications for basic and applied studies on areas described in the title above.

Studies are encouraged to develop transplanted or spontaneous animal tumor models to determine the therapeutic efficacy of anticancer agents which act by specifically blocking the actions of specific peptide growth factors. These factors might include both normal and tumor cell products. Of particular interest are animal tumors shown to be responsive in vitro to a peptide growth (for example, epidermal growth factor) and agents shown to specifically block this same factor. In similar fashion an animal tumor model may be developed which can demonstrate the anticancer activity of maturation and differentiation factors which are capable of inducing terminal differentiation of various transformed cell lines in vitro. Examples of cell lines previously shown to be responsive to such agents include PC-12 pheochromocytoma cells and HL-60, Kg-1 and K 562 myeloid leukemia cells. Transplantable tumors of these, similar or newly developed cell lines might form the basis of a suitable animal tumor model focusing on therapeutic application.

Preclinical studies of LAK phenomenon

Deadlines for applications: Oct. 1, Feb. 1, June 1

The Biological Response Modifiers Program invites grant applications for basic and applied studies described in the title above.

Recently, systemic administration of a BRM therapy to patients with cancer has resulted in consistent and reproducible antitumor effects. The preliminary results from NCI's Surgery Branch using lymphokine activated kill (LAK) cell therapy has led to the development of a comprehensive plan in DCT, including plans for both intramural and extramural clinical trials. In addition, considerable intramural work is underway preclinically. Some preclinical research is underway, but in order to bring this approach to more rapid clinical application, additional research should be encouraged.

This program announcement is intended to encourage new extramural, investigator initiated preclinical research in the LAK phenomenon. Following is a list of areas felt to be potentially fruitful for new investigation: (1) therapeutic studies in additional experimental animal tumor systems; (2) combinations of LAK cells, IL-2 and standard therapy in established experimental animal tumor systems; (3) identification of the target on tumor cells that is recognized by LAK cells, and the receptor on the LAK cells which recognizes the target; (4) studies to optimize LAK cell generation in experimental animals in vivo, after administration of IL-2, or other BRMs; (5) studies on human or experimental animal cells to optimize the ex vivo generation of LAK cells; (6) identification and purification of the LAK cell cytotoxic effector molelule; and (7) further study of the process by which LAK precursors are rendered cytotoxic. These are only a sampling of the areas in which research efforts may prove fruitful. The aim of this program announcement is to encourage highly innovative research initiatives evaluating these, or other other, promising leads. Eventually, concepts arising from these studies will be tested in clinical trials.

Determination of the therapeutic usefulness of purified cytokines in cancer models

Deadlines for applications: Oct. 1, Feb. 1, July 1

The Biological Response Modifiers Program invites grant applications for basic and applied studies described in the title above.

Cytokines are proteins and glycoproteins in the 5,000 to 100,000 molecular weight range. The cytokines obtained from lymphoid tissues or supernatants of mononuclear cell cultures are celled lymphokines. Some have been shown to have direct cytocidal or antiproliferative activity, some modulate and exert selective regulatory effects on various components of immune responses and others affect bone marrow proliferation, or ossification or vessel proliferation. Production and purification of cytokines have been a problem in the past. More recently, means have been developed to obtain cytokines from lymphoid lines in culture and use of genetic engineering technology to transpose genes into microbial organisms, thus helping to resolve the problem. Administration of cytokines that can selectively activate or suppress certain components of the immune system may produce a beneficial antitumor effect in vivo.

Studies to be proposed should evaluate the therapeutic value of defined cytokines in antitumor immunity. Currently available cytokines, purified to near homogeneity, may be used in both in vivo and in

vitro studies to evaluate and monitor specific effects on the various cellular components of the antitumor response. A further stage of analysis could involve testing the therapeutic efficacy of various cytokine preparations in transplantable and spontaneous animal tumor models. Investigators may restrict their study to a single cytokine or may wish to perform comparative studies on various cytokines. A goal of the studies should be to provide information relevant to the choice of a cytokine for preliminary clinical testing and the type of tumor host relationship most amenable to effective biological modification using cytokines.

Use of oncogene related products for cancer therapy
Deadlines for application: Oct. 1, Feb. 1, June 1

The Biological Response Modifiers Program invites grant applications for basic and applied studies described in the title above.

This program announcement is intended to stimulate research that will develop and utilize oncogene products or reagents made against these products for therapy in animal model systems. Development of oncogene or oncogene related products for therapeutic evaluation may involve use of tumor associated membrane antigens for monoclonal antibody production and development of vaccines, use of monoclonal antibodies directed against growth factors or growth factor receptors controlled by or encoded by oncogenes or analysis of factors that inhibit the action of oncogene products that control cell division. Other reasonable approaches directed toward cancer therapy employing oncogene or oncogene related products or related reagents with antitumor potential may be proposed. Studies may involve the isolation and characterization of these products for the purpose of evaluating their ability to modify or alter tumor initiation, growth and/or metastases as well as stimulating cytotoxicity in vivo or in vitro through activation of macrophages, cytotoxic T cells or natural killer cells. Additional proposals involving studies on how oncogene or oncogene related products may interfere with specific immune functions will also be considered. Therapeutic potential may be evaluated in the treatment of transplanted, induced or spontaneous animal tumors or human tumor xenografts in nude athymic mice or rats.

For further information on these BRMP program announcements, investigators may contact Dr. Carl Pinsky, Chief of the Biological Resources Branch, BRMP, DCT, NCI, Bldg 426 Rm 1, Frederick, MD 21701, phone 301-695-1098.

The original and six copies of the application, on form PHS 398, should be sent to Application Receipt Office, Div. of Research Grants, NIH, Westwood Bldg Rm 240, Bethesda, MD 20892.

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 NO1-CP-41017-77

Title: Record linkage studies utilizing resources in population based tumor registries (master agreements)
Deadline: July 26 for statement of qualifications

NCI is seeking qualified firms to contract with population based cancer registries in the U.S. and other countries in order to collaborate in the conduct of record linkage and subsequent analytic studies.

The master agreement currently consists of 22 master agreement holders, under a five year master agreement which expires on March 14, 1988. Interested firms should identify their interest and capability by responding to this notice. To be considered responsive, a firm must submit a capability statement which demonstrates similar or related capabilities, experience and knowledge to support the following areas:

1. Cancer incidence data for all patients diagnosed within a defined geographic locale at a minimum during the previous decade.
2. Collection of cancer data from a variety of medical sources and multiple institutions.
3. Obtain information on vital status of cancer patients years after initial diagnosis.
4. Legal authority to collect medical data within the geographic area or else be able to demonstrate the willingness of all medical facilities within that area (including hospitals, clinics, private pathology laboratories, private facilities, and nursing homes with diagnostic services).
5. Participate in data collection and patient followup activities.
6. Ability to obtain access to existing population based registries of exposed groups of individuals in the geographic areas covered by the cancer registry.
7. Willingness to conduct collaborative research studies and analyses with the Environmental Epidemiology Branch of the Div. of Cancer Etiology and permit the pooling of data with other cancer registries for combined analyses.

Master agreements will be awarded to all firms whose technical proposal is considered acceptable. Each master agreement holder will be eligible to compete for award of master agreement orders to carry out specific record linkage and subsequent analytic studies. The above requirements, along with resumes of key personnel, must be submitted to NCI by the deadline above. Respondents should limit their responses to 15 pages and 10 copies of this document.
Contract Specialist: Donna Winters
RCB Blair Bldg Rm 114
301-427-8888

NCI Contract Awards

Title: Development and production of pharmaceutical dosage forms
Contractor: Univ. of Iowa, $1,125,214.

Title: Record linkage study of cancer risk following chest fluoroscopies during heart catherization in childhood
Contractor: Israel Center for Registration of Cancer and Allied Diseases, Jerusalem, $47,213.

Title: Operation of a registry of tumors in lower animals
Contractor: Smithsonian Institution, $1,183,099.

The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams
Published forty-eight times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter.