THE CANCER LETTER

Vol. 17 No. 23
June 7, 1991

Price $205 Per Year US, Canada.
$230 Per Year Elsewhere

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

Why Did DeVita Resign MSK Post? Clash Of Style, Other Serious Issues Pointed To By Colleagues

No one in the cancer research community, especially those who know Vincent DeVita, believed for a minute that he resigned as physician in chief at Memorial Hospital "so that he may pursue his interest in clinical research. . . without the added administrative responsibilities," as the

(Continued to page 2)

In Brief

Patent For Semisynthetic Taxol Issued To FL Scientist; Simone To Chair Pediatric Group

TAXOL PATENT: U.S. Patent & Trademark Office has issued a patent to Robert Holton and the Univ. of Florida for a method of making a partly synthetic version of the promising anticancer drug taxol, which is currently available only from the bark of the Pacific yew tree. Holton's method combines the main component of taxol, baccatin III, obtained from the needles of the more common English yew, with a synthetic chain to make taxol in the laboratory. With the process, Holton said, about two pounds of needles are needed to extract enough baccatin to produce taxol for one patient. Bristol-Myers Squibb Co. has a licensing agreement with the university to use the new process, but it could take two to three years before the drug could be produced in quantity, the company has said. . . . **JOSEPH SIMONE**, scientific director of St. Jude Children's Research Hospital, has been elected chairman elect of the Pediatric Oncology Group. He will take over from **Teresa Vietti** when her term expires in the fall of 1993. Vietti has headed the group since it was established in 1981. . . . **THREE NEW INITIATIVES** for clinically related research will be presented to the Div. of Cancer Treatment Board of Scientific Counselors for concept approval: Survivors of Childhood Cancer, Solid Tumor/Correlates, and 3-D Treatment Planning for Prostate Cancer. Cancer Therapy Evaluation Program Director Michael Friedman told cooperative group chairmen last week that group members should consider competing for those grants. "It's my hope that we can add substantially to group funding with these mechanisms." The grants (or cooperative agreements in the case of the childhood cancer survivors) will be funded out of NCI's research project grants pool, not the cooperative groups budget. . . . **PUBLIC AFFAIRS** network formed by officials at the 24 NCI designated comprehensive cancer centers last year has expanded to include the 15 NCI designated clinical cancer centers. The mission of the network is to share information and resources, develop unified positions on critical issues of common concern, and to enhance public understanding of the nation's cancer research effort.

Clash At Sloan-Kettering Provoked DeVita's Resignation, Say Colleagues

(Continued from page 1)
official statement from Memorial Sloan-Kettering Cancer Center said last week.

Administrative responsibilities--and the power to shape and influence programs--are DeVita's specialty, his raison d'etre. At NCI, he relished those responsibilities and exercised them vigorously. Many of his colleagues around the country are speculating that his resignation must have been precipitated by a clash, whether of style, substance, or both, with MSK President Paul Marks.

"I wasn't surprised by this," said an NCI staff member. "What surprised me was that Vince lasted almost three years."

Said another, "It was dumb of him to take that job in the first place. Two brilliant, strong minded individuals, both somewhat arrogant, both with big egos, would never get along. This was inevitable."

Those closer to the scene in New York are not as inclined to blame Marks for the rupture as are those who have been closer to DeVita. New Yorkers, at MSK and elsewhere, who have discussed the situation with **The Cancer Letter** in general feel that DeVita brought it on himself.

Neither DeVita nor Marks would return phone calls seeking comment. Both have obviously decided that for now, at least, nothing they would say would help the situation. That may have been part of the agreement they negotiated in which DeVita stepped down as physician in chief but will remain at MSK in an endowed chair in clinical oncology and will continue as professor of medicine at Cornell Medical Center.

Information for this article was obtained from individuals in New York, Bethesda, and other points around the country. All requested anonymity, and most admitted offering as much speculation as hard facts.

'A Blowup Was Building'

Rumors that things were not going well for DeVita were circulating for two or three months before last week's announcement. "A blowup was building up," one source said. What were the problems? The complete story probably will not be known until either DeVita or Marks tells it. Until then, here are some possible scenarios:

* DeVita's management style was unsuited for academia, and he simply became frustrated. "Vince liked to do things very rapidly. At NCI, he could make up his mind that something had to be done and immediately implement change," said a source who worked with him at NCI. "In an academic environment, you can't move as quickly. It's a community. You have to do a lot of checking around, discussion with people. It's more laborious. The inability to move quickly was probably very frustrating for him."

"DeVita really ran roughshod over people at NCI," a source in a cancer organization said. "People either loved him or hated him. He is willing to break the rules, to forge ahead and do what he thinks is right, and if you disagree, too bad."

"Vince is brilliant," another source said. He sees things rapidly, and he's impatient with people who don't see it."

Those comments are all based on fact, but they don't completely describe how DeVita operated as NCI director.

It is true that DeVita made sweeping changes immediately on becoming director. He replaced every division director except Alan Rabson; moved out most of his associate and assistant directors; moved programs in and out of divisions. In his eight years in that job, he completely changed the face of NCI, put his own stamp on most programs, initiated several highly successful new programs, moved people and programs in and out of divisions.

And yet, he displayed great patience at times, and frequently delayed making a move or reaching a key decision if he did not have a consensus of his senior staff members, or when appropriate, the National Cancer Advisory Board.

The image of DeVita as bullheaded and arrogant may be difficult for those to picture who watched him charm NCAB members, Congress, and on occasion his colleagues outside government. They might wonder why he did not use that charm and the articulate

THE CANCER LETTER

Editor: **Kirsten Boyd Goldberg**
Associate Editor: **Lisa M. O'Rourke**
Contributing Editor: Jerry D. Boyd

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

Subscription rate $205 per year North America, $230 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter and AIDS Update.

persuasiveness of which he was capable on MSK staff and board members.

* DeVita's efforts to shake up the Memorial staff ran into the fact that "everyone has a little constituency of his own," a source said. "A surgeon who operated on the wife of a board member, a physician who has successfully treated a board member who thinks that doctor saved his life, are not going to go quietly. Vince dealt poorly with staff. He was arrogant. Those with pals on the board saw to it he got his comeuppance.

Another source said, "DeVita wanted to improve the clinical end of things, and the clinic needs to be improved."

It is probable that DeVita felt he was hired to make improvements, although at the time he praised Memorial as the finest cancer treatment facility in the world.

* The "Paul Marks is impossible to work with" factor. "DeVita and Marks probably got into it [argued] more than once," said an NCI executive. A source at MSK told **The Cancer Letter** that DeVita and Marks on several occasions had arguments in front of other staff members. They battled over programming and personnel, another source said. "Marks is abrasive and DeVita is a real control freak. It was a clash of titans," said one observer.

"Paul Marks is a very dynamic personality. I hoped this would make for a mutually constructive future for Memorial Sloan-Kettering. On the other hand, I also saw that two strong leaders might take opposite sides of an issue," said a former NCI executive.

One source said that DeVita had distributed memos to various Memorial staff members with orders about one thing or another. "Then Marks came right behind him and nullified the orders."

The difficulty that some people have had working with Marks is well known. After surgical oncologist Jerome DeCosse left Memorial in a bitter rupture with Marks, DeCosse was quoted in a "New York Times Magazine" article as calling Marks "an administrative Rambo." He added later that "Paul is the kind of guy who would consider that a compliment."

At the time of DeVita's move to MSK, Marks responded to his critics. "One shouldn't confuse striving for excellence and high standards with being difficult to work with. Clearly, Vince and I feel we can work well together," he told **The Cancer Letter.**

* DeVita could not get assurances that he would be Marks' successor. "I would have thought Vince had solved the problem of succession up front, that he would have gotten concessions from the board that after a few years, Marks would retire and Vince would take over, that it was only a matter of time. It could be that Marks has decided to hang on."

DeVita denied when he took the job that he considered it a stepping stone to the MSK presidency. "The job I'm getting is the one I want," he said. "I don't like the idea of being in one job while waiting for another." Marks also denied there had been any such deal between he and DeVita or between DeVita and the board.

What are DeVita's prospects for the future? Very bright, most of **The Cancer Letter's** sources said. Most agreed those prospects go far beyond a clinical professorship, although DeVita has said at every major move in his career that he most enjoyed being a doctor and working with patients.

DeVita is president of the International Coordinating Council for Cancer Research, a mostly honorary position. There are any number of nonprofit or not for profit cancer organizations who could make good use of his leadership abilities. "I would think he would be very much in demand in industry," one source commented.

"If I were the CEO of a pharmaceutical company with a major interest in cancer drugs, I would be looking over my shoulder right now," one of DeVita's former colleagues at NCI said.

"There may be some cancer center directors doing the same thing," another added.

A long time friend of DeVita's said he would not recommend that DeVita go to another cancer center. A university center director is usually under a dean, and may not have as much authority as a department chairman, he said.

There are some centers where the director is responsible only to the university president or vice president/chancellor for health, a situation DeVita probably could live with.

Some have speculated he will turn up again in Washington, perhaps next time there is an opening in the Surgeon General, Assistant Secretary for Health, or even HHS Secretary positions.

Guys Hospital Study Supports Hypothesis On Mastectomy Timing

A study published this week in "Lancet" and carried out at Guys Hospital in London provides further evidence for the hypothesis that premenopausal breast cancer patients who undergo surgery seven to 10 days following putative ovulation will have significantly better 10 year survival than those whose mastectomies were performed at either end of the menstrual cycle.

The retrospective study by Ian Fentiman looked at data on 249 patients from whom information on menstruation timing had been obtained. Similar studies in the U.S. found that survival apparently was improved five fold for those with surgery at midcycle.

"There are now four studies, involving 600 women, which clearly demonstrate the advantage for midcycle surgery," said William Hrushesky, whose mouse studies reported in 1988 first suggested that timing of surgery could be crucial to survival. Hrushesky has been studying circadian rhythm in relation to cancer chemotherapy for the past 12 years. He recently obtained an NCI R01 grant to carry out a six institution trial comparing continuous infusion FUDR to circadian administration of the same agent for treatment of advanced metastatic renal cell cancer.

Hrushesky still believes that a prospective study is needed to prove the breast cancer surgery results beyond doubt. The National Surgical Adjuvant Breast & Bowel Project has agreed to obtain menstrual period data on breast cancer patients entering its various clinical trials. However, Hrushesky thinks that the Guys Hospital data now may make it difficult to carry out a prospective trial. "Guys Hospital now has a blanket policy that all breast cancer surgery be done only in the early luteal phase," he said. "I think we'll start seeing that now in this country. It's an easy, nontoxic step that involves only some scheduling by the surgeons."

Advisors Commit $31 Mil. To Lab, Clinical Chemoprevention Studies

NCI advisors have committed more than $31 million over the next five years to fund contract research designed to move chemopreventive agents from the laboratory into phase 2 clinical trials.

The Div. of Cancer Prevention & Control Board of Scientific Counselors has approved five RFP concepts--including two new proposed RFPs--that would fund research for in vitro screening, in vivo screening, preclinical toxicology, biomarkers, and phase 2 human studies with chemopreventive agents.

The first four concepts were approved unanimously. The fifth concept for an RFP for phase 2 trials was approved after the board decided to increase the estimated funding from $1.2 million per year to $2 million per year.

Board member David Alberts said the original figure was much too low for the complex studies proposed. He said he had recently completed a budget for similar trials and found that they should be about $500,000 per study, per year. Since the concept estimates that four studies would be conducted, Alberts proposed the $2 million figure.

Following are the concept statements:

Evaluation of chemopreventive agents by in vitro screening assays. Recompetition of an RFP; master agreement orders. Five to six task orders issued annually, estimated award $900,000 per year, five years; total $4.5 million.

The primary objective of this study is the in vitro screening for efficacy of various selected chemopreventive agents in various in vitro transformation systems. The in vitro systems selected are a battery of screening systems including the following:

1) human cells (so that any activity of the chemopreventive agent that might be specific to human cell substrates can be evaluation, 2) organ cultures where acceptable systems exist so that any activity of the chemopreventive agent that might be specific to a particular differentiated organ can be evaluated, 3) cells of epithelial origin are those primarily used (because of the relevance to the human cancer prevention problem in which most of the cancers are carcinomas having epithelial histogenic origins, and 4) in vitro systems that allow screening against the different stages of carcinogenesis.

The emphasis of the activity will be to take the initial leads from the published literature and focus on the most promising chemopreventive agents for testing in the in vitro screening system. Promising data obtained from the in vitro screening assays will be used as one criteria for further testing.

This effort will improve the criteria for the selection of agents for in vivo screening, extended efficacy evaluation, preclinical toxicology evaluation and potential clinical testing, decreasing efficacy toxicology costs and accelerating the rate at which agents are evaluated.

Presently 107 agents or regimens are being studied: testing on an additional 52 new compounds, selected with the advice of extramural experts, will begin in vitro screening for inhibition of transformation this year. Twenty agents or combinations of agents are undergoing extended animal efficacy testing at present with more to be added this year and it is anticipated that several of these compounds will yield efficacy activity to justify the rigorous evaluations of their toxicity in preclinical toxicity studies as the final evaluation needed to obtain an IND from the FDA for phase 1 clinical studies.

Master agreement contracts will be issued to all investigators or institutions who are deemed via peer review to be qualified for carrying out the proposed tasks. The award will be for five years. As agents become available, applications will be requested and reviewed, and the best proposal will be selected for funding and implementation.

Up to 50 new agents will be studied per year; the number of studies and screening systems will be determined as necessary for each compound evaluated. All master agreement contract holders will be asked to submit a master protocol in their technical proposals which details all aspects of the study except those determined by the specific chemopreventive agent.

A standardized protocol was or will be developed by program for each screening system and for each chemopreventive agent including the number of experimental groups and controls, statistically valid replicates, number of doses of agents, administration of the carcinogen, standardized test for purity of the agent and preparation of the agent, and solubility in tissue culture media, standardized tests for assay of the agents, criteria for quality control of the tissue culture procedure. The investigator will develop and submit monthly a final report on the results of each study.

Evaluation of chemopreventive agents by in vivo screening assays. Recompetition of an RFP; master agreement orders. Five to six task orders to be issued annually, estimated award $1.2 million per year, five years; total $6 million.

The primary objective of this study is the in vivo screening for efficacy of various selected chemopreventive agents in animal models. The animal models are chosen for their relevance to the human cancer problem including an emphasis on lung, colon, and breast cancer. The emphasis of the activity will be to take the initial leads from the published literature, and the results from chemoprevention's in vitro screening program and focus on the most promising chemopreventive agents. The efficacy data obtained in the in vivo screening assays on the selected agents will be expanded by an extended efficacy evaluation of the dose response, bioavailability, spectrum of target sites, and potential toxicity as well as studies of combinations of promising chemopreventive agents.

Presently, 107 agents or regimens are being studied; testing on an additional 20 new compounds will begin in vivo screening for efficacy this year.

Master agreement contracts will be issued to all investigators or institutions who are deemed to be qualified to carry out the proposed tasks. Awards will be for five years. As agents become available, applications will be requested and reviewed, and the best proposal will be selected for funding and implementation. Up to 25 new agents will be studied per year; the number of studies and target organs will be determined as necessary for each compound evaluated. All master agreement contract holders will be asked to submit a master protocol for in vivo efficacy screening studies in at least one target organ including lung, colon, mammary, bladder or model they feel is relevant, in their technical proposals.

Preclinical toxicology of chemopreventive agents. Recompetition of an RFP, master agreement orders; five to six task orders will be issued annually. Estimated award $1.2 million a year, five years; total $6 million.

The primary objective of this study is the preclinical toxicology evaluation of various selected chemopreventive agents in order to qualify agents for human clinical trials. The studies will include acute, subacute/subchronic and chronic toxicity evaluation on selected chemopreventive agents. The studies will be conducted on two species of animals (rodents and dogs) and may include, in addition to conventional short term studies, lifetime studies in rodents, pharmacokinetic studies, multigeneration teratogenicity studies, as well as carcinogenicity assays.

The chemopreventive agents that are selected for preclinical toxicology evaluation are those agents having the highest priority for clinical relevance and potential after having been evaluated by a rigorous selection process which is as follows:

Each potential agent undergoes a systematic review to evaluate clinical, laboratory, and epidemiologic research data. If the data provides evidence of tumor inhibition and a reasonable prospect of safety, it is further evaluated by several criteria. These include the dose at which it is efficacious, the number of organ model systems in which activity is demonstrated, the number of laboratories in which its activity has been confirmed, the evidence that it has an inverse association with human cancer risks, the data supporting in vitro inhibitory activity, and the reasonable prospect of the agent's availability.

If the agent has a high priority based on the published literature, it is entered into the chemoprevention preclinical laboratory program to obtain information necessary to further characterize the agent and to potentially qualify it for clinical studies. This includes carrying out in vitro screening in selected transformation assays and in vivo screening for efficacy in a battery of animal model systems, determining the efficacy and safety of single and combination agents in dose response studies in animal systems relevant to potential human application, acquiring and/or producing the agent in sufficient quantity to accomplish this work, and determining its purity and stability. If the agent remains of high priority based on this efficacy evaluation and the other selection criteria, it is entered into preclinical toxicology evaluation as required by FDA as the last step before phase 1 human evaluation.

Twenty agents or combinations are undergoing extended animal efficacy testing at present, with more to be added this year.

Master agreement contracts will be issued to all investigators or institutions deemed via peer review to be qualified for carrying out the proposed tasks. As agents become available, applications will be requested and reviewed. Up to five new agents will be studied per year; the number of studies will be determined as necessary for each compound.

Preclinical evaluation of intermediate endpoints and their modulation by chemopreventive agents. Concept for a new RFP, master agreements; five to six awards. Approximately $160,000 per award, total $950,000 per year, over five years; total $4.75 million.

The application of biological markers to clinical cancer prevention trials carried great promise in relation to ultimate cancer prevention. When neoplasia itself is used as an end point in studies of this type, a very large number of subjects tested for long durations are often required. The major objective of this concept is to conduct animal cancer model studies of biomarkers and intermediate endpoints that might be used in human clinical trials in order to examine in detail the biomarker modulating effects of selected chemopreventive compounds. In addition, the studies will improve biomarker sensitivity, specificity, assay methodology, and sample handling. The emphasis will be on efficient studies aimed at providing more quantitative, and more validated, intermediate endpoints for future human clinical trials. Intermediate endpoints or biomarkers that are directly associated with the evolution of neoplasia, and that develop with much higher frequency in abnormal cells of susceptible individuals than do the actual tumors, will make it possible in the future to carry out many studies on fewer subjects for shorter durations. If such biomarkers were found to be modified by a particular intervention regimen in preclinical studies, a rationale would be provided for carrying out clinical studies.

A number of compounds and/or dietary components have been shown to inhibit carcinogenesis in animal models, in vitro systems, and to be associated with cancer reduction in epidemiological studies. Results from animal studies suggest that a number of compounds and/or dietary components may affect several stages of carcinogenesis. A variety of excellent biomarkers have become available. Examples include reversal of abnormal cytology, ornithine decarboxylase and/or prostaglandin synthetase inhibition, DNA ploidy alterations, changes in colonic mucosal proliferation, and oncogene suppression tests. The development and verification of sensitive and accurate intermediate endpoints should enhance the ability to design effective human clinical trials.

Master agreement contracts will be issued to all investigators or institutions who are deemed by peer review to be qualified for carrying out the proposed studies. Studies will be directed toward examining the dose of a given chemopreventive agent that exhibits a pharmacodynamic effect on an intermediate endpoint and then to do a dose response study to determine the minimum dose at which this biological effect is observed and to confirm the

maximum nontoxic dose. Initial studies will have the goal of evaluating and validating a number of intermediate endpoints in several appropriate organ based animal systems correlating their modulation with the cancer incidence endpoint. These endpoints or biomarkers will require determination of normal levels or baseline studies in appropriate species and organ systems. The use of animal models will permit studies to optimize sampling methodologies, sample preparation and extraction methods, and analytical techniques.

In some cases new sampling methodologies, sample preparation and extraction methods, and analytical techniques may need to be developed. Practicality and feasibility of these techniques for human intervention trials will be of prime importance. In cases where no validation of an intermediate endpoint exists, serial sampling or sacrifice to evaluate biomarkers will be performed until carcinoma or tumor incidence can be verified.

Experimental animal model systems also will be used to explore and evaluate new intermediate endpoints for future human intervention trials. These studies will also be able to determine the appropriate statistical analyses and sample sizes necessary for a given biomarker.

Phase 2 clinical trials of new chemopreventive agents. Concept for a new RFP, master agreement orders, four awards. Estimated $500,000 per award, $2 million per year, five years; total $10 million.

The major objective of this concept is to encourage cancer chemoprevention clinical trials that use biochemical and biological markers as intermediate endpoints. The emphasis in phase 2 clinical trials will be on small, short term, efficient studies that will determine the dose of a given chemopreventive agent that exhibits a pharmacodynamic effect on an intermediate endpoint and then to do a dose response study to determine the minimum dose at which this biological effect is observed and to confirm the maximum safe dose.

The second stage of the phase 2 study will involve a randomized blinded trial in a small group of subjects whose endpoint will be a measurable biological effect of the agent versus the placebo. These studies will improve future research designs and will also provide a better biologic understanding of the agent and provide more quantitative endpoints. Intermediate endpoints or biomarkers that are directly associated with the evolution of neoplasia, and that develop with much higher frequency in abnormal cells of susceptible individuals than do the actual tumors, make it possible to carry out many studies on fewer subjects for shorter durations. If such biomarkers are found to be modified by a particular intervention regimen in short term studies, the rationale may be strengthened for carrying out long term studies.

Master agreement contracts will be issued to all investigators or institutions who are deemed by peer review to be qualified for carrying out the proposed studies. One or more intermediate endpoints might be evaluated initially in a give study and organ system to determine baseline levels and feasibility.

If it is determined that an intervention has successfully fulfilled the biological, biochemical, and statistical criteria established in these studies, then a full scale phase 3 intervention trial may be justified. Biological fluids or tissues including urine, blood, sputum, and feces would be obtained from participants for analysis. Examples of populations suitable for such interventions may include subjects with premalignant lesions, subjects previously exposed to an identified carcinogen, or those curatively treated for a malignancy who are at high risk for the development of a second malignancy.

Black, Hispanic Cancer Initiatives To Establish Regional U.S. Programs

NCI advisors have approved plans for the expansion of a national effort to establish cancer control, education, early detection and prevention outreach programs in black American communities, and approved a similar effort for Hispanics.

The Div. of Cancer Prevention & Control Board of Scientific Counselors approved two new RFA concepts: one for continuation of the National Black Leadership Initiative on Cancer and one for establishment of the National Hispanic Leadership Initiative on Cancer. The board committed a total of $10 million over five years for the RFAs.

The concepts call for one cooperative agreement award per initiative to institutions that would organize and support national outreach and mobilization of black and Hispanic leaders to address the cancer problem. Six regional offices for each initiative would be run by a national office.

The NBLIC was established in 1987 at the behest of Louis Sullivan, then a member of the National Cancer Advisory Board, now HHS secretary. The concept approved recently would fund the initiative for the next five years. NCI staff and executives, in consultation with advisors, decided to establish a similar initiative for the Hispanic population.

Following are the concept statements:

National Black Leadership Initiative on Cancer. Concept for a new RFA, cooperative agreement, one award; $1 million per year, five years; total $5 million.

This concept seeks to continue the development of a national structure which will facilitate outreach and mobilization of black Americans to address the cancer problem through NBLIC community outreach programs. Moreover, this concept will measure the effectiveness and impact of NBLIC efforts to reduce cancer incidence and mortality rates, risk behaviors and improve screening use and early detection rates. Objectives are:

a. To continue to mobilize black leaders in order to address the cancer control needs of the black community.

b. To increase the number of NBLIC community cancer coalitions by 100 percent.

c. To collect, summarize and disseminate effective cancer control intervention outreach programs in the black community.

d. To evaluate the effectiveness of the national initiative.

Blacks experience the highest overall age adjusted cancer incidence and mortality rates than any other group in the U.S. At a 1986 meeting of the National Cancer Advisory Board, the NCI director and Louis Sullivan, then an NCAB member, discussed the elevated tobacco related cancer rates in the black population. In response to this discussion, Sullivan chaired a national working group whose responsibility was to devise a strategy to mobilize the leadership of the black community in order to address these cancer control needs.

The committee held six regional meetings in 1987-88. In 1989, NCI funded a three year followup phase of the NBLIC. Currently,

the NBLIC has created a network of concerned and active black leaders throughout the country to help organize, implement and support cancer prevention programs at the national and local level. The followup phase is in its 24th month.

The Philadelphia NBLIC was instrumental in deterring R.J. Reynolds Co. from marketing "Uptown" cigarettes to blacks.

The NBLIC will address cancer control barriers including risk factors and cancer control service utilization aspects of black communities and will directly or indirectly impact 24 million blacks which represent 80 percent of the U.S. black population. This initiative will mobilize leaders in the black community to increase the number and utilization of cancer prevention and control programs which are culturally appropriate. It is anticipated that the leaders will marshall various community resources in order to implement effective primary and secondary prevention as well as policy related activities.

The awarded institution will organize and initially support, administratively and financially, six regional offices. Each regional office will be staffed by a full time regional coordinator and relevant support staff. Additionally, in each region a prominent leader in the black community will serve as the regional chairperson. This person may be a health provider or community leader.

A full time national coordinator will be hired to interface daily with the regional coordinators and regularly with the regional chairpersons. This coordinator will provide technical advice and support to all regions, facilitate the establishment of regional coalitions, and monitor all regional subcontracts.

Community cancer control coalitions will be organized to establish a formal structure to conduct cancer control programs with regions. A few examples of community cancer coalition activities are: conducting outreach programs aimed at increasing awareness, increasing participation in screening and early detection programs, initiating support groups for cancer survivors, and initiating media campaigns targeted against tobacco advertisement in black communities. The number of coalitions during the funding period would be increased by 100 percent.

NCI program staff will provide overall technical oversight as program directors to the initiative. In addition to scientific input, NCI staff will routinely facilitate "technology transfer" to the NBLIC as results of prevention, early detection, and treatment trials occur. This function will ensure the rapid translation and transfer of research results to the black community. NCI program staff will have direct input on the implementation of the evaluation plan for this activity.

National Hispanic Leadership Initiative on Cancer. Concept for a new RFA, cooperative agreement, one award; $1 million per year, five years; total $5 million.

This program will establish a national structure for the delivery of cancer control outreach programs to Hispanic communities through the establishment of six regional offices. Objectives are:

a. To develop and support cancer control intervention outreach activities in Hispanic communities.

b. To stimulate participation of Hispanic community leaders as members of community cancer control coalitions.

c. To collect, summarize and disseminate effective cancer control intervention outreach programs in the Hispanic community.

d. To evaluate the effectiveness of this national initiative.

Hispanics are a heterogeneous population comprised of four major subgroups: Mexican Americans, Puerto Ricans, Cubans, and others. Existing data, though limited, strongly suggest that Hispanics experience an overall lower cancer incidence rate than other ethnic/racial groups; however, the data also show increasing rates for certain cancers in Hispanics when compared to Anglos. Other data show that in the future, smoking may be a problem with Hispanic populations; that knowledge of cancer and of cancer warning signs is not as high as among Anglos; and that certain cancer survival rates are lower for Hispanics.

Cross sectional access to major Hispanic subpopulations within the U.S. and improved geographic representation in a variety of NCI programs will result from this initiative.

The NHLIC will address cancer control barriers including risk factors and cancer control service utilization aspects of Hispanic communities and will directly or indirectly impact 16 million Hispanics, which represents 80 percent of the U.S. Hispanic population during the first five years.

[The remainder of the concept statement discusses the organization of the NHLIC and NCI oversight identical to the National Black Leadership Initiative above.]

BSC members expressed enthusiasm for the two initiatives. "NCI has gotten a lot of mileage out of the NBLIC," said board member Alfred Haynes. "It has reached a lot of people. I'm very enthusiastic about it."

"The NCI Executive Committee, [NCI Director] Dr. [Samuel] Broder and myself see this as the centerpiece of our strategy to reach the black and Hispanic populations," said DCPC Director Peter Greenwald. The initiatives will be overseen by DCPC's Cancer Control Science Program, headed by Claudia Baquet.

Board members also said that, while cancer rates in Hispanics currently are lower than those in whites and blacks, outreach should be done in the community to try to keep the rates lower and improve knowledge of cancer risk factors, screening, and early treatment.

Board member Rumaldo Juarez said increasing smoking rates, poverty, and other factors indicate that "the worst is yet to come."

Greenwald agreed that low-cancer risk Hispanic diets have been shown to change rapidly to typical American diets after immigration. "We should be in a position to tell this population that there are some parts of your culture that you might not want to give up."

"Fifty years ago, cancer rates in blacks were reported to be much lower that whites," said Haynes. "As I look at Hispanics, I say, 'I hope what happened to blacks doesn't happen to you.'"

Juarez suggested that the proposed funding for the initiatives, originally set at $800,000 per year, be increased.

Board member Maryann Roper agreed, noting that the current budget for the NBLIC followup phase is $780,000 in total cost, while the RFA concepts "are asking them to do more and pay people."

The board approved the concepts unanimously, modifying the budgets to $1 million a year each.

RFPs Available

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

RFP NCI-CP-15688-18

Title: Record linkage studies utilizing resources in population based tumor registries

Deadline: Approximately Sept. 7

NCI's Div. of Cancer Etiology wishes to contract with population based tumor registries in the U.S. and in other countries in order to collaborate in the conduct of record linkage and subsequent analytical investigations.

The duties required in support of the record linkage studies include: develop a study plan which includes the evaluation of existing records that are potentially valuable for record linkage; develop or apply the appropriate record linkage procedures to link a population file with the cancer registry files; and provide results of the record linkage study to the project officer either on computer tape or in tabulated form as requested. After the record linkage study has been completed, it may be desirable to consider additional analytical investigations that require data beyond that found on computer tapes.

Offerors should have cancer incidence data for all patients diagnosed within a defined geographic locale for at least five years during the previous decade, 1980-89, and have the ability to ascertain all cancer cases within the registries catchment area of women of all age groups and U.S. minority populations. The offerors must have experience in the collection of cancer data from a variety of medical sources and multiple institutions, and must have legal authority to collect medical data within the given geographic area or be able to demonstrate the willingness of all medical facilities within that area to participate in data collection and patient followup activities.

Master agreements will be awarded. The initial award is nonmonetary, to establish a pool of contractors qualified to perform services. Each master agreement holder will be eligible to compete for awards of master agreement orders to carry out specific record linkage and subsequent analytical studies. This is a recompetition of existing master agreements. Master agreements will be awarded for a four year period.

Contract specialist: Catherine Baker
RCB Executive Plaza South Rm 620
301/496-8611

RFP NCI-CP-21000-21

Title: Laboratory support for processing and storage of biological specimens from persons at high risk from cancer

Deadline: Approximately June 10

The Epidemiology and Biostatistics Program of NCI is seeking a contractor to provide for the maintenance of the existing EBP inventory of biologic specimens and to receive, process and store new samples as they are collected. This is a 100 percent small business set aside. The contractor shall provide the services described below, in accordance with contractor developed, government approved protocols:

1) separation and viable cryopreservation of blood mononuclear lymphocytes, 2) separation, aliquotting and storage of serum, plasma and/or urine as needed, 3) cryopreservation of bone marrow samples, 4) storage of tumor extracts, 5) cryopreservation of whole tumor tissue, 6) cryopreservation of intact red blood cells, 7) viable cryopreservation of previously established lymphoblastoid cell lines, 8) storage of DNA and other biological materials as specified by the project officer, 9) extraction of DNA from biologic materials, 10) logging in, labeling and tracking of each vial of each sample employing an NCI developed computerized specimen tracking system, including all laboratory safeguards to ensure the fidelity and purity of each sample, maintenance of the previously established repository currently containing 300,000 biological specimens and allowance for an estimated increase of up to 25 percent of freezer storage space.

The contractor shall, for example, provide messenger service for pick up of specimens or interlaboratory communication from medical care facilities in the Washington, D.C., area or at area transportation centers (i.e., Dulles, National, and BWI Airports); be responsible for recording and monitoring shipping and receiving of specimens to minimize delay or loss; maintain a repository of biologic specimens which shall include frozen serum, plasma, urine, tumor tissue, tumor tissue extracts, whole red blood cells, separated and frozen white blood cells or fractions of white blood cell populations, bone marrow cells, body fluids, lymphoblastoid cell lines, DNA, stool specimens or smears on slides and other types of specimens as specified by NCI; provide and train primary and backup staff in the operation of a computerized record system for specimens which have been developed and furnished by NCI; prepare a variety of specimens for storage; utilize freezers equipped with a stylus recording system indicating consistency of temperature; maintain a central alarm system monitored 24 hours a day, 365 days a year; keep clear records of all manipulations on all specimens and carefully document specimen type, volume, cell concentration, source, "crisis event," etc. for each sample; prepare specimens for shipment; supply shipping containers and make arrangements to send biologic specimens to collaborating investigators in an expeditious fashion; inventory, store and maintain a large repository of sera and cells used for immunogenetic tissue typing; be prepared to process up to 1,100 mls. of blood per day, four days per week, from lymphocyte harvesting (coded from as many as 60 donors per day); handle international shipments of biological specimens (blood components, urine, gastric juice and biopsy specimen) and clearance of these specimens through U.S. and foreign customs; and submit monthly computerized and written reports, annual reports and a final report.

Contract will be a cost reimbursement type for a 48 month period. The total estimated level of effort to be provided is 89,740 direct labor hours. Award is anticipated by April 30, 1992.

Evaluation criteria, in descending order of importance shall be 1) technical approach (demonstration of specific technical competence in processing all specimen types as reflected in the quality and detail of submitted protocols, 2) organizational experience, 3) personnel and 4) facilities. The contractor is expected to provide the facilities and all major equipment necessary to perform the proposed work including but not limited to the following equipment: laminar flow hoods; CO2 incubators; tissue culture facilities; refrigerated centrifuges; microscopes; liquid nitrogen storage tanks; mechanical freezers; and refrigerators. Additional government furnished equipment, currently in use under the existing contract, will be provided.

Contract specialist: Barbara Shadrick
RCB Executive Plaza South Rm 620
301/496-8611