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## GAO Study Claiming No Benefit Seen In Adjuvant Breast Cancer Treatment Flawed, NCI Responds

The General Accounting Office has missed the mark once again in a study involving NCI, this time in an attempt to determine whether there has been any improvement in survival for breast cancer patients as a result of adjuvant chemotherapy. GAO concluded that survival has not increased and

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*In Brief*

## Curt Appointment Now Official; Bipartisan Effort Seeks $150 Million FDA Budget Increase

**APPOINTMENT** of Gregory Curt as associate director of the Div. of Cancer Treatment and director of the Clinical Oncology Program has been made official. He will return to NCI July 1, a year after giving up the position of DCT deputy director to become chief of pharmacology and director of medical education at Roger Williams General Hospital in Rhode Island. Curt will also assume the title of NCI clinical director, last held by none other than Vincent DeVita. NCI Director Samuel Broder, who as COP director served as deputy clinical director, determined that the head of NCI's intramural clinical research program (the COP director) should be the clinical director, whose role crosses division lines. DCT Director Bruce Chabner has been serving as interim clinical director since DeVita's departure. . . . **CORRECTION:** Barbara Blumberg's position and employer in Dallas (**The Cancer Letter**, March 31) is director of education, Komen Alliance Clinical Breast Center, Sammons Cancer Center, Baylor Univ. Medical Center. . . . . **ROSE KUSHNER**, author and breast cancer program advocate, has received an award as the Oustanding Volunteer for Women's Health from Maryland Gov. Donald Schaeffer. . . **BIPARTISAN EFFORT** to "revitalize" FDA is being made by Senators Edward Kennedy, Orrin Hatch, Quentin Burdick and Dale Bumpers, who have asked the Budget Committee to increase the allocation for the agency by $150 million. Of that amount, $100 million would replace the proposed users fees in the President's budget request, and $50 million would be used for additional space, facilities, personnel, training and equipment. An alliance of industry and professional groups, the FDA Council, is spearheading a drive to "meet urgent infrastructure needs of FDA". . . . **ERIC ROSENTHAL**, formerly manager of the American College of Physicians news bureau, has been named director of public affairs at Fox Chase Cancer Center.

## GAO Misses Mark In Adjuvant Breast Cancer Therapy Report, NCI Contends

(Continued from page 1)
recommended that HHS conduct a more detailed study to find out why. NCI officials criticized the report's methods, saying the patient sample used was too small to detect any difference in survival.

"The study doesn't prove much," Div. of Cancer Treatment Director Bruce Chabner told **The Cancer Letter** last week. "What is really needed is a careful patterns of care study."

This is not the first time that a GAO report has gotten such a reaction at NCI. A study released in January 1988 on treatment advances for seven types of cancer also was criticized for its methods. Over the years, other GAO studies of NCI and NCI supported programs produced conclusions refuted by NCI for the most part.

GAO is the so called "watchdog" agency of Congress, and submits its reports to Congress.

The recent report, "Breast Cancer: Patients' Survival," is, in effect, a follow up to the 1988 study. GAO said the report was in response to a request from the House Subcommittee on Health and the Environment to examine the issue of cancer patient care.

The report used data from NCI's Surveillance, Epidemiology and End Results program, which receives information on incidence and follow up from cancer registries in the U.S. and Puerto Rico. The registries cover about 12 percent of the population. The study looked at data from node positive breast cancer patients under age 50 who were diagnosed between 1975 and 1985.

The objective, the report said, was "to determine, for one specific medical advance, whether its potential to extend patient survival has been realized."

Adjuvant therapy for breast cancer was picked because it fit six criteria:

1. It had been proven to increase patients' survival in a large randomized clinical trial.
2. The results of the trial had been published by 1982.
3. The treatment was relevant for an identifiable group of cancer patients.
4. The therapy was relevant for a large number of patients.
5. There was no known change in prognosis of patients that was unrelated to the treatment.
6. There was a considerable increase in the frequency with which the treatment advance was given to patients.

The first trial of adjuvant therapy was concluded in 1975, and the percentage of premenopausal, node positive patients receiving chemotherapy nearly doubled in 1976, according to the report.

An NIH consensus conference in 1985 declared that, "adjuvant chemotherapy has demonstrated a highly significant increase in disease free survival and a significant reduction in mortality in premenopausal women with histologically positive axillary lymph nodes. Adjuvant chemotherapy can now be considered standard care for these patients."

The GAO report included SEER data on breast cancer patients 50 years old or younger at time of diagnosis who were node positive and who did not have metastases to distant sites. Their tumors could not exceed 5 cm in size.

The study used three statistical procedures to measure overall survival of the patients. The first method was to compare the observed survival rates of each cohort of patients.

The second method, called the lifetable method, compares the actual length of survival of all cases across groups and provides statistical tests that indicate whether survival is different between the groups. The third method was a Cox regression that controlled for the age, race and size of tumor of the patients.

No matter which method of analysis was used, the report found, "there has been no detectable change in patients' survival since 1975, the year in which adjuvant chemotherapy was proven effective in prolonging the lives of cancer patients."

There was one exception, however. Women diagnosed in 1980 did significantly better than women diagnosed the previous year and the year after. GAO had no explanation for that finding.

**THE CANCER LETTER**

**Editor: Jerry D. Boyd**

**Associate Editors:**
**Patricia Williams, Kirsten Boyd Goldberg**

**P.O. Box 2370, Reston VA 22090**
**Telephone (703) 620-4646**

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In its conclusions, GAO ruled out the explanation that the chemotherapy was not beneficial. "Based on the trials conducted, it has been stated conclusively that chemotherapy should have efficacy in the treatment of this group of patients," the report said.

GAO said this lack of improvement may be the result of "one or a combination of the following:

--Many patients still do not receive adjuvant chemotherapy.

--The benefits of chemotherapy are small and therefore difficult to detect.

--There are problems with how well the treatments are implemented.

GAO contended that the explanation that the benefits of chemotherapy are difficult to detect "does not appear to lend itself to any immediate policy resolution."

However, in a footnote to that remark, the report notes: "One potential resolution would be to expand the number of cases available for analysis. This option, however, would require a considerable expansion of the SEER program.

GAO concluded, "We cannot now recommend a policy to adopt because we cannot say which of the three explanations or what combination of them more accurately reflects reality."

GAO recommends that HHS conduct a study "to determine why there has been no visible improvement in the survival of premenopausal, node positive breast cancer patients despite the advent of adjuvant chemotherapy."

**Chabner criticized the report as "an attempt to use SEER survival data in an effort to determine treatment practices."**

He said the data sample in the report was too small to draw any conclusions, especially considering that not all breast cancer patients who should receive adjuvant therapy get it.

"This study does not tell us much about how breast cancer is treated today," Chabner said. NCI does not intend to comply with GAO's recommendation for a study to determine why there has been "no visible improvement" in survival, but a "careful patterns of care study is needed," Chabner said.

The Div. of Cancer Prevention & Control has considered undertaking a patterns of care study, Deputy Director Joseph Cullen said.

HHS responded to the draft of the report, and its comments are included in the back of the final document. The comments reflect NCI's view of the report, Chabner said.

Judging from those comments, GAO's draft report was much more troublesome than the final copy.

First, the report's original title: "Breast Cancer: Patients Have Yet To Realize The Benefits Of Adjuvant Chemotherapy."

HHS complained that the title "is uninformative and possibly misleading. If this conclusion means that the breast cancer patients who actually received adjuvant chemotherapy showed no survival benefit, we disagree: GAO did not provide evidence to support this assertion. If it means that there has been no discernible impact on the whole stage 2, premenopausal population, we also disagree."

The department suggested an alternative title, "Adjuvant Chemotherapy for Breast Cancer: Is A Survival Benefit Detectable in the National Statistics?"

Instead, GAO opted for the shorter and less precise, "Breast Cancer: Patients' Survival."

HHS also objected to the report's opening statement:

"The report opens with the assertion that the nation spends billions of dollars on new medical technologies. Since the passage of the National Cancer Act in 1971, the National Cancer Institute has spent a total of $4.55 billion on all forms of cancer treatment research out of its total appropriation of $14.3 billion during this time period. The largest expenditures have been for basic research."

HHS objected to another GAO comment:

"GAO expresses a concern that the department may be promoting therapies which, though effective in clinical trials, do not change patient outcomes when used in clinical practice," HHS said. "There is no inherent reason why adjuvant breast cancer therapies which are effective in clinical trials cannot be delivered correctly in clinical practice. The critical concern is that practicing physicians may modify effective therapies, thereby rendering them less than optimally effective."

GAO deleted that paragraph on promoting therapies in its final draft.

Following are more excerpts of the HHS response:

"The department shares GAO's concern that the survival advantage may not be reaching stage 2, premenopausal breast cancer patients nationally. Our concerns are two fold: first, that not all eligible patients are receiving adjuvant chemotherapy, a concern borne out by the GAO analysis which shows that 31 percent of eligible patients did not receive chemotherapy as late as 1983; and second, that

patients who are being treated may not be receiving chemotherapy with the intensity (dosage and timing of treatment) needed to achieve the potential survival advantage.

"The department believes, however, that the statistical power of the GAO analysis is not sufficiently strong to allow the sweeping conclusion that no increase in survival benefit can be detected.

"The major reason for this is that the SEER database contains too few stage 2 premenopausal patients who meet the GAO selection criteria (approximately 400 to 650 per year), to be able to draw a definitive conclusion given the magnitude of the survival advantage expected base on clinical trials data (7 to 10 percentage points at 5 years post diagnosis) and given the statistical approach used by GAO.

"NCI is supporting extensive research to develop therapies which will confer greater survival advantages. However, while this 7 to 10 percent survival improvement represents a significant accomplishment of adjuvant chemotherapy, detecting this difference using the methods employed by GAO would require two to three times as many patients as are available in the SEER database.

"The department's analysis indicates that the GAO approach had less than a 50 percent chance of demonstrating an improvement in 5 year survival using the SEER database. This means that there was at least a 50 percent chance that the GAO analysis would miss finding a survival advantage even if one existed.

"The department believes that an incomplete transfer of the adjuvant chemotherapy treatment advance to the community also contributed to GAO not detecting a survival advantage. The fact that only 69 percent of eligible patients received adjuvant chemotherapy in 1983 speaks to this point.

"On a recent analysis of the SEER database, (NCI) also found that there were proportionately more patients with four or more positive lymph nodes in the treatment group than in the overall SEER population of stage 2 premenopausal breast cancer patients.

"This would result in a smaller than expected survival benefit for the treatment group since patients with four or more positive lymph nodes receive a lesser benefit from adjuvant chemotherapy than does the general population of premenopausal stage 2 breast cancer patients.

"The department believes that this incomplete transfer of adjuvant chemotherapy to the community may have been a major contributing factor to a lower than expected national survival benefit.

"Although the SEER database is the best currently existing resource to have used for the GAO study, it does not contain enough information about patient treatment to definitively answer questions about the impact of particular treatments on survival and about patterns of care.

"The SEER database does not capture information about the nature of treatment, the dosages given, or the length of treatment. It is, therefore, not possible to determine whether adjuvant therapy is being given using the same methods which improve survival in clinical trials."

HHS said it had three major concerns with the report:

--"The conclusion gives the erroneous impression that no progress against stage 2 premenopausal breast cancer has been made since the advent of adjuvant chemotherapy.

--"GAO interprets its analysis to show that no increase in survival is detectable by any means. However, the GAO analysis does not have sufficient statistical power to be able to justify this definitive statement.

--"The department agrees with GAO that a closer examination of the actual chemotherapy delivered to breast cancer patients would be useful."

Since the sample size was too small, HHS said, "it is not appropriate for GAO to recommend a study to determine why there has been no apparent survival improvement, but whether adjuvant therapy for breast cancer has been successfully transferred from clinical trials to clinical practice."

HHS noted that a patterns of care study would depend upon the availability and adequacy of patient records, with detailed information about the chemotherapy used, the dosage, frequency and length of treatment.

"Access to records of patients not participating in a clinical trial would be essential and would require an unprecedented level of cooperation and openness on the part of physicians and their patients.

"Should an advisory committee determine that a patterns of care study is feasible, it would be advisable to conduct a pilot study.

"Additionally, a patterns of care study would require a significant commitment of personnel, equipment and financial resources over several years."

## Wisconsin Group Takes Lead In Effort To Change Perception Of Cancer Pain

A Wisconsin organization that has been working to change the public and physician perception of cancer pain management is developing model programs that physicians in other states could use.

The Wisconsin Cancer Pain Initiative was started in 1986 by June Dahl, former chairman of the state Controlled Substances Board and a professor of pharmacology at the Univ. of Wisconsin Medical School, and David Joranson, a former staff member of the board.

The initiative group has been designated a demonstration project by the World Health Organization.

"Our overall goal is to make cancer pain relief as high a priority as possible in the state health system," Joranson said.

That involves public education, to change the prevailing attitude that cancer pain cannot be treated.

"The only thing you ever hear about is the heroin issue," Joranson said. "That really is a disservice to patients."

According to Joranson, calls to NCI's Cancer Information Service in Wisconsin specifically on questions about cancer pain have gone up by about 120 percent in the past year.

"Cancer pain is one of those areas that falls through the cracks, because symptom relief is not as high a priority as treatment of the disease," Joranson said.

Dahl and Joranson had worked together for 13 years on the state controlled substances board to develop some solutions to the problem of the illegal use of prescription drugs.

"In working with doctors and pharmacists, we got dramatic and lasting decreases in the abuse of prescription drugs," Joranson said.

"We also became aware that some prescription drugs were underprescribed. In the need to control availability, you also have to assure availability," he said.

The board had gotten involved in the issue of cancer pain because of bills that had been introduced in Congress on legalizing heroin for terminal cancer patients.

Dahl and Joranson decided to oppose the legislation. "The science and literature say that those patients who do not respond to morphine will not respond to heroin, since heroin immediately converts to morphine in the body," Joranson said.

The better use of existing analgesics is the solution to the cancer pain issue, Joranson said.

But health professionals and the public have a wary attitude about the use of narcotics to control pain.

"We felt that as a controlled substances board we had duty to explain that addiction is not a problem for most patients."

Less than one in 1,000 people treated with narcotics who had no prior history of drug abuse develop psychological dependence to the narcotic, Joranson said.

The Wisconsin Pain Initiative was started in 1986 when the substances board brought together a group of physicians and health professionals.

The group has "several hundred" members, Joranson said, though he could not provide an exact figure.

The group's major source of financial support has been a grant from the Public Health Service's Interagency Committee on Pain and Analgesia.

"The visibility of WHO and the support from PHS has really gotten this going," Joranson said.

Dahl since left the controlled substances board to become chairman of the initiative. Joranson also left to become a staff member of the group and associate director for policy studies at the Univ. of Wisconsin Medical School.

The initiative has conducted an analysis of federal and Wisconsin law for impediments to pain treatment.

One impediment in the state law is a limitation in the pharmacy regulations that allows the prescription of only 120 dosage units, or a 34 day supply, of opiates to be dispensed per patient. The main problem, Joranson said, was confusion over what constitutes a "dosage unit."

Another limitation is that the state medical regulations adopted in 1978 set forth indications for which amphetamines could be prescribed. The indications did not include sedation as a result of aggressive pain treatment. Since there was no intention to ban the use for sedation, Joranson said, the initiative group is trying to get the state to rewrite the regulation.

"We're fortunate in Wisconsin that we only have those two barriers," Joranson said. "Some states define the term 'addict' or 'drug dependent' as one who is habituated or depends on use on narcotic drugs.

"That is such a broad definition it could apply to cancer patients. They may well be physically dependent but not addicted."

In addition, some state laws require physicians to report those "habituated" patients to state authorities, which is a deterrent to the prescription of narcotics.

"There have been reports that cancer patents have been treated like addicts," Joranson said. "A patient who is undertreated is going to ask for pain medications."

Dahl recently traveled to India to encourage the country to allow the prescription of oral morphine for pain treatment. Some Indian physicians visited Dahl in Wisconsin.

The group is sponsoring a national meeting of professionals interested in pain treatment and issues, July 6-8. The event is by invitation only, but Joranson said, "If people contact us, we can invite them."

The initiative group is trying to interest physicians in other states to start similar groups. Stratton Hill, a pain specialist at M.D. Anderson Cancer Center, has started a Texas Cancer Pain Initiative modeled after the Wisconsin group (**The Cancer Letter,** April 14).

The group also has sponsored several professional education programs, including a study of the attitudes of physicians and new medical school students about pain management.

As a result of the work, the group has convinced the state medical schools to include more information on treatment of pain in the curriculum. The group is now doing follow up studies to determine if attitudes have changed.

Several physicians involved in the group have written a handbook on cancer pain management that Joranson called state of the art.

The handbooks are available, for $3 a copy, by writing to the Wisconsin Pain Initiative, 3675 Medical Sciences Center, Univ. of Wisconsin Medical School, 1300 University Ave., Madison, WI 53706. Other correspondence to the group may be sent to that address.

## Insurance Payment For Mammography Screening Mandated In Colorado

Colorado Gov. Roy Romer this week signed legislation mandating insurance reimbursement for screening mammography for women aged 35 to 65 in the state.

The bill passed handily in the Colorado General Assembly earlier this year, with votes of 56 to 7 in the House and 35 to 4 in the Senate.

Under the new law, all group insurance policies will have to cover one baseline mammogram for women aged 35 to 40. Women aged 41 to 50 will be covered for one mammogram every other year. Women aged 51 to 65 will get a mammogram annually.

Women over age 65 will be covered in 1990 by Medicare. The law sets a $60 cap for screening mammography.

The legislation was a victory for a campaign started by the AMC Cancer Research Center, in Denver. AMC started an organization, called High Priority, to promote breast cancer research and education.

The group has attracted celebrities such as Cher and Lynda Carter, as well as other prominent women volunteers, some of whom have survived breast cancer.

The group's first goal was the passage of mammography screening reimbursement legislation.

Bette Iacino, national program director of High Priority, said the Colorado legislation is a model that other states should follow. "This should challenge the rest of the states that haven't passed legislation to do this," she told **The Cancer Letter.**

The legislation was introduced in the state Senate by Sen. Dave Wattenburg of Walden, whose wife died of breast cancer, and in the House by Rep. Carol Taylor-Little.

"The bill requires no state appropriation or tax money, yet has the potential to save many lives," Taylor-Little told the "Rocky Mountain News."

AMC began a low cost screening mammography program in 1985 that cost $37.50. The cost has since gone up to $49.50.

High Priority organized a statewide chapter in Colorado, composed of women who are viewed as leaders in their local communities. The women attended a two day training workshop earlier this year, which taught breast self exam and the benefits of screening mammography.

The event received substantial coverage in state and local newspapers, generating interest in the reimbursement legislation.

Proponents of the legislation said mammography screening could cut dramatically the death rate by catching breast cancer early.

In hearings before the state House Business Affairs and Labor Committee, small business

and insurance industry lobbyists testified that the legislation might prompt some small businesses to stop providing health insurance for their employees.

The Health Insurance Assn. of American also testified that health insurance premiums could jump by $70 million in Colorado because of the bill. Proponents of the legislation said that was an overstatement of the cost.

AMC officials testified that 97 percent of patients live at least 10 years when breast cancer is detected early. The chance of surviving that long is about 16 percent when breast cancer is detected later.

The new law requires coverage of mammograms when no symptoms are present and without need for referral by a physician. The law goes into effect with insurance policies issued after Jan. 1, 1990.

According to AMC, breast cancer cases have increased by 50 percent since 1982 in Colorado.

Persons interested in mounting campaigns in other states for legislation requiring reimbursement for mammography screens may contact Iacino for advice and assistance at AMC Cancer Research Center, 1600 Pierce St., Denver 80214, phone 303/233-6501.

## Rich Left AMC For "Personal Reasons," Is Looking At "Several Options"

Marvin Rich resigned as director of AMC Cancer Research Center in Denver "for personal reasons," interim Director Donald Iverson told **The Cancer Letter.**

Iverson was contacted last week, after **The Cancer Letter** had gone to press with the story on Rich's replacement by Joseph Cullen, deputy director of NCI's Div. of Cancer Prevention & Control. Iverson said AMC has offered no further explanation for Rich's departure.

Rich, also contacted last week, said that he also agreed, in the legal settlement with the center, "not to discuss my reasons for leaving."

Rich said he has "several options, with the opportunity to do interesting things" and will "spend some time looking around." He has just been reelected for a four year term as secretary general of the International Breast Cancer Assn. and intends to continue that activity.

Jean Hager, Rich's scientist wife, also resigned from her position at the center.

Iverson, former director of the Prevention Research Program at DCPC, is professor of family medicine at the Univ. of Colorado. He had been working part time at AMC as director of cancer control research. When Rich resigned, Iverson was asked by the AMC Board of Directors to serve as interim director.

The Board restructured the center's administration, creating the position of president and chief executive officer. That position has been filled by Bob Baker, who has extensive experience with financial institutions.

Cullen will fill the new position of director of programs.

Iverson said he had been considering a career change himself, after being offered an attractive position with a California company. However, "I'm reconsidering that now, with Joe coming here. I'm excited about the prospects for cancer control research, and the leadership Joe Cullen can provide."

## Black Physicians, Community Group To Work With NCI On Minority Health

NCI Director Samuel Broder and HHS Secretary Louis Sullivan met recently with members of two national minority organizations to discuss the problem of the disproportionate cancer mortality rate of minority populations.

The meeting earlier this month at the Smithsonian in Washington was held to kick off "National Minority Cancer Awareness Week."

At the meeting, the National Medical Assn., predominantly black physicians group, and LINKS Inc., a black women's organization, signed agreements to work with NCI to disseminate information on nutrition and diet to their local chapters.

NCI gave community service awards to NMA and to the spouses' auxilliary of NMA, and certificates of appreciation to 13 chapters of LINKS representing Maryland, Virginia and District of Columbia.

"It was a good opportunity to come out in the local community to interact with the local chapters of the groups we have worked with," said Linda Bass, director of minority health education programs.

NMA has said it will work to increase involvement of black physicians in community education about cancer and nutrition.

LINKS, which has about 200 chapters around the country, has adopted NCI's Cancer Prevention Awareness Program as its major initiative this year. NCI is providing the group

with information packets, slide shows and other materials.

NCI also unveiled a public service radio advertisement it developed on the cancer problem in blacks that will be released in early May. Titled "Eat Your Way to Good Health," the ad contains general statistics on black cancer rates and advice on nutrition.

## Reimbursement By Philadelphia BC Requires More Than NCI Approval

Eleanor Nelson, medical director of Independence Blue Cross of Greater Philadelphia, has asked that her statement quoted in **The Cancer Letter**, March 24, dealing with reimbursement for patient care costs in clinical trials be explained in further detail.

Nelson appeared at the March 15 meeting of the National Committee to Review Current Procedures for Approval of New Drugs for Cancer & AIDS (the Lasagna Committee), representing Independence Blue Cross. She made it clear she was speaking only for Independence Blue Cross and not for any other Blue Cross or Blue Shield plan or for the Blue Cross and Blue Shield Assn.

**The Cancer Letter** summarized Nelson's statement on Independence reimbursement policies as stating that it "does pay for patient care costs for patients in NCI approved protocols, and has reimbursed for costs associated with interleukin-2/LAK trials at two Philadelphia institutions."

Nelson pointed out in a letter to **The Cancer Letter** that she had qualified that statement, as follows:

"Independence Blue Cross has long recognized that in some instances a drug which is technically experimental/investigative may be medically appropriate and has made individual exceptions. In keeping with this policy and with the need for more flexibility in management of benefits, a formal procedure for covering investigational treatments of cancer was developed and implemented about two years ago. The procedure would be applicable to treatments for AIDS or other life threatening disease.

"The protocol, which must be NCI approved with an NCI licensed investigator, must be submitted with supporting documentation and references for review by an internal committee and an advisory panel of oncologists familiar with research protocols. Approval is based on evidence of therapeutic efficacy, which is often represented by phase 3 clinical trials.

"To date, the interleuken-2/LAK protocol has been approved at two Philadelphia institutions. Other protocols submitted have been phase 1 trials which do not meet our criteria. There have not been any requests for doverage of formal clinical trials for agents used to treat AIDS. However, in response to individual requests, Independence Blue Cross has covered alpha interferon for Kaposi's sarcoma."

## 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, NIH, Bethesda, MD 20892. Proposals may be hand delivered to the Executive Plaza South, 6130 Executive Blvd., Rockville, MD. RFP announcements from other agencies will include the complete mailing address at the end of each.

**RFP NCI-CP-95646-56**
Title: Induction, biological markers and therapy of tumors in primates
Deadline: May 31

NCI is soliciting proposals to provide a broad data base on the carcinogenic risk to humans of a variety of chemicals and drugs. The results obtained from this project will serve to identify agents with high carcinogenic potential, and will provide the basis for removal of such agents from the environment or from clinical use, thereby reducing the incidence of cancer in humans.

Specific objectives are:

1. Obtain comparative data on the response of nonhuman primates to known rodent carcinogens and to materials suspected to be carcinogenic in humans.
2. Evaluate the long term effects of antineoplastic agents which are being used clinically for long term remission, in adjuvant therapy, and in treatment of diffuse collagen disorders.
3. Obtain model tumor systems in nonhuman primates in order to ascertain the potential usefulness of various anticancer agents in man.
4. Attempt to develop models for chemoprevention therapy.
5. Develop biological markers and diagnostic tests for detecting preneoplastic changes as well as frank neoplasia and for monitoring nonhuman primates during and following therapy.
6. Make available material from normal and tumor bearing animals for pharmacologic, toxicologic, biochemical and immunological studies.
7. Maintain a breeding colony of various species of primates so that offspring may be readily available for use.

This is a recompetition. It is expected that a cost reimbursement type contract will be awarded for a period of five years. It is mandatory that the contractor's facility be within close proximity of the NIH campus in Bethesda, MD, so that daily consultation and visits may be made by the government project officer.

Contract Specialist: Donna Winters
RCB Executive Plaza South Rm 620
301/496-8611