THE CANCER LETTER

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

Vol. 19 No. 38
Oct. 1, 1993

Price $225 Per Year US, Canada
$250 Per Year Elsewhere

ODAC Prefers Three-Hour Taxol Infusion, Says Data On Dosage Still Uncertain

A three-hour infusion of Taxol is preferable to the currently approved 24-hour infusion for most patients with refractory ovarian cancer, FDA's Oncologic Drugs Advisory Committee said last week.

The committee voted 10-0 to recommend the shorter infusion, based on data from a Canadian and European study. Patient and physician convenience, safety of administration, and comparable efficacy were the primary considerations in the decision, the committee said.

The committee was acting on a supplemental New Drug Application

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In Brief

Lasker Awards: Blobel, Metcalf, Wexler, Rogers; Borch Named Center Director

ALBERT LASKER Medical Research Awards were presented this week to three scientists and one former Congressman. **Gunter Blobel**, Rockefeller Univ. and Howard Hughes Medical Institute, received the Lasker award for basic medical research for his work in protein trafficking. **Donald Metcalf**, Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia, received the Lasker award for clinical medical research, for his work on the cellular basis of blood cell formation. Winners of the Lasker public service award were **Nancy Wexler**, Columbia Univ., and **Paul Rogers**, of the Washington law firm Hogan & Hartson, and former House member from Florida. Wexler, a clinical psychologist, was honored for organizing an international research effort to find the gene for Huntington's disease. Rogers was instrumental in "virtually every piece of health legislation in the U.S. in the past 25 years," according to the Lasker citation--including the National Cancer Act of 1971. Each award winner receives or shares a $25,000 honorarium. . . . **SAN ANTONIO** Cancer Institute will expand its community education, outreach and research efforts with help from a $500,000, five-year grant awarded by Bristol-Myers Squibb Co. through its unrestricted cancer research grants program. . . . **RICHARD BORCH** has been appointed director of the Univ. of Rochester Cancer Center following a national search. Borch served as interim director following the death of center director Robert A. Cooper Jr. in March 1992. Borch joined the university from Univ. of Minnesota in 1982. . . . **SENATE CANCER** Coalition, a new group, will hold its first hearing Oct. 4. The coalition, chaired by Sens. Connie Mack (R-FL) and Dianne Feinstein (D-CA), will mark National Breast Cancer Awareness Month. NCI, ACS, the Susan G. Komen Foundation, National Breast Cancer Coalition and ational Coalition for Cancer Reseach will be represented.

ODAC: 3-Hour Taxol Preferred; Leaves Dosage Up To Doctors

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submitted by Bristol-Myers Squibb Co. to change the recommended Taxol dose and schedule from 135 mg/m² administered intravenously over 24 hours every three weeks to 175 mg/m² iv over three hours every three weeks.

However, the committee said data were not conclusive to recommend the higher dose over the lower dose.

The supplemental NDA was based on data from BMS 15, a randomized trial of Taxol (paclitaxel) in platinum pretreated ovarian cancer: high versus low dose; long versus short infusion. The trial was coordinated by the National Cancer Institute of Canada; 34 centers in Canada and Europe accrued patients to the trial from July 1991 to March 1992.

When the committee could not reach consensus on the drug dose, ODAC member Paul Bunn, Univ. of Colorado Cancer Center, suggested the package insert list response data for all four arms of the study. Clinical response by arm was as follows:

	175/24	175/3	135/24	135/3
patients	n=84	n=63	n=83	n=74
CR (n)	1	2	1	—
PR (n)	21	10	8	10
CR+PR %	26%	19%	11%	14%

"Let's let the physician choose," Bunn said. "I don't think there is sufficient evidence to say 175 is preferred" based on the data BMS submitted on the first 300 patients enrolled. Data on the full 400 patients in the trial provide "some indication the higher dose is better," Bunn said.

BMS analyzed the data on 300 patients in order to submit the supplemental NDA as quickly as possible, said Renzo Canetta, vice president for clinical cancer research, BMS Pharmaceutical Research Institute. The data on the full 400 patients could be submitted to FDA in the next three to six months, he said.

Already, committee members said, physicians are using the three-hour infusion more often, based on a presentation of the NCIC data on more than 300 patients at the American Society of Clinical Oncology annual meeting last May (Abstract 810).

"One senses the presentation at ASCO has had major consequences for practice," ODAC Chairman Charles Schiffer, Univ. of Maryland Cancer Center, said. "The patient population has shifted from in-patient to out-patient."

The committee's recommendation to FDA "suggests a label that would compel physicians to think," Schiffer said.

FDA reviewer Grant Williams noted that the response rate was higher with the highest dose and the longest infusion. "I feel it is almost withholding data from the physician" not to provide that information on the drug label, he said.

Study results would be displayed in one section of the label, while the section on dosage and administration could recommend the three-hour infusion at "135 to 175 mg/m²," FDA Oncology & Pulmonary Drug Products Div. Director Gregory Burke suggested.

However, the committee split 5-5 on a vote whether the dosage recommendation use the wording 135 "to" 175 mg/m², implying a range of doses, rather than 135 "or" 175 mg/m².

In his own practice, Bunn said, he would use the lower dose and shorter infusion for most refractory ovarian cancer patients. However, he said he would use the higher dose and longer infusion "if I had a 35-year-old movie star with outstanding hematology."

ODAC Approves First "Paper NDA"

In a separate action, the committee last week recommended approval of bleomycin sulfate (Blenoxane) as a sclerosing agent for the treatment of malignant pleural effusions and for the prevention of recurrent pleural effusions.

Bristol-Myers sought approval of a supplemen-

THE CANCER LETTER

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Tel. (202) 543-7665 Fax: (202) 543-6879

Subscription $225 per year North America, $250 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter.

tal NDA for the agent, which has been widely used for the indication but never approved for that purpose by FDA.

The submission was the first for an oncology drug based on a review of the literature, under FDA's initiative last year to provide more expedient review for supplemental indications.

From a literature search, the company found 18 studies conducted over 21 years, providing efficacy data on 442 patients, and safety data for 601 patients. Four trials of bleomycin versus tetracycline with 200 patients found malignant pleural effusions were well controlled 70 percent of the time, said John Ruckdeschell, director and chief executive officer, H. Lee Moffitt Cancer Center.

ODAC voted 6-2, with two abstentions that there is substantial evidence that chest tube drainage plus intrapleural Blenoxane was more effective than chest tube drainage alone. The committee voted 8-0, with two abstentions to recommend approval of the supplemental NDA.

The labeling should emphasize that the agent should be used only for patients whose lungs have re-expanded, the committee said.

ASCO Sees Efforts On Reform Pay Off In First Clinton Draft

Early this year, when a White House panel went to work on overhauling the U.S. health care system, the American Society of Clinical Oncology stood poised to present its case for across-the-board reimbursement for clinical trials.

Now, it appears that ASCO and the coalition it put together got what they asked for: the plan the Clinton Adminstration is expected to present to Congress is almost certain to include a provision on reimbursement of patient care in clinical trials (**Cancer Economics**, September 1993).

The Adminstration is yet to submit its formal proposal. However, a leaked draft report of the health care plan contains a provision that was taken almost verbatim from the document drafted by ASCO last February (**Cancer Letter**, March 26, 1993)

After drafting a language that could be supported by patients and other advocacy groups, ASCO met with the "benefits group" of the health care reform panel.

From the start, ASCO realized that health care reform presented an opportunity for making a fundamental change in the way clinical trials are reimbursed, said Stacey Beckhardt, the association's director of government relations.

"ASCO recognized from the start that it was going to take a broader effort to resolve this issue," Beckhardt said. "We had to look at the big picture: not just Medicare and Medicaid, but people insured through private payors."

"The initial reaction [from White House panel members] was, `we never really thought about it,' " Beckhardt said to **The Cancer Letter**.

While the panel was interested in assessment of outcomes, its original focus was on assessment of existing technologies, not on technologies under development, Bechhardt said.

"Our goal was to ensure open access to clinical trials, but that needed to be countered against those trials being high quality peer reviewed trials," Beckhardt said. "There was some concern that we would not automatically extend coverage to community trials reviewed on ad hoc basis, where there is no real attempt made to analyze the data."

At the first meeting with the White House panel last spring, ASCO was respresented by Beckhardt, the association's counsel Samuel Turner, an attorney with Fox, Bennett & Turner, a Washington law firm and Joseph Bailes, chairman of ASCO's Clinical Practice Committee.

The patients were represented by Ellen Stovall, executive director of the National Coalition for Cancer Survivorship, who spoke both for her group and a broader coalition, the Cancer Leadership Council.

The latter group includes NCCS, Cancer Care Inc., Candlelighters Childhood Cancer Foundation, The Susan G. Komen Foundation, National Alliance of Breast Cancer Organizations, US TOO and Y-ME.

Subsequently, the leadership council issued its own statement on health care reform, one that included ASCO's language on reimbursement of clinical trials (**The Cancer Letter**, March 12, 1993).

"The Leadership Council drew on several documents, one of which was ASCO's," Stovall said to **The Cancer Letter**. "Reading the draft document [of the President's plan], the language is very much akin to our request."

Beckhardt said ASCO made certain that other groups would not say, "We have a better way." "There was a consistent message from the cancer community, regardless of who was speaking," Beckhardt said.

Similarly, ASCO made certain that the AIDS Action Council as well as advocacy groups that repre-

sent other diseases would not object to the statement.

According to the draft of the Administration's plans, clinical trials would be reimbursed under patient care rather than research. Now, Beckhardt said, ASCO will be lobbying to keep the patient care costs associated with clinical research funded in this manner rather than through a separate medical research trust fund similar to the one proposed by Sens. Tom Harkin (D-IA) and Mark Hatfield (R-OR) (**The Cancer Letter**, May 28, 1993).

"We can't lose signt of the fact that clinical research is actually patient care, and therefore it must be covered as a patient care expenditure," Beckhardt said.

Army Releases Broad Agency Announcement; Names Panel

The U.S. Army Medical Research & Development Command has released a Broad Agency Announcement for the Army's FY1993-94 breast cancer research program.

The announcement was mailed to investigators who had submitted letters of intent last month, and others interested in the program. The first deadline for applications is Nov. 1. Copies of the announcement may be obtained by contacting Col. Patricia Troumbley, acting director of the breast cancer research program, phone 301/619-7071.

The Army has formed a Program Integration Panel to provide oversight to the breast cancer program, similar to the role of an NIH advisory council.

Members of the Program Integration Panel are:

Anna Barker, International BioClinical Inc; **Nancy Brinker**, Susan G. Komen Breast Cancer Foundation; **Robert Day**, Fred Hutchinson Cancer Research Center; **Kay Dickersin**, Univ. of Maryland; **Laurie Lee Fajardo**, Univ. of Arizona; **Harold Freeman**, Columbia Univ., Harlem Hospital; **Emil Frei**, Dana-Farber Cancer Institute; **Elizabeth Hart**, Susan Komen Breast Cancer Foundation; **Jean Johnson**, Univ. of Rochester Cancer Center; **Peter Jones**, Kenneth Norris Jr. Comprehensive Cancer Center; **Mary Mahowald**, Univ. of Chicago; **Marsha McNeese**, M.D. Anderson Cancer Center; **James Potchen**, Michigan State Univ.; **Jean Richardson**, Univ. of Southern California School of Medicine; **Susan Sieber**, deputy director, Div. of Cancer Etiology, NCI; **Helene Smith**, Geraldine Brush Cancer Research Institute; **Frances Visco**, president, National Breast Cancer Coalition; **Stephen Wyatt**, Centers for Disease Control & Prevention.

NCI FY95 Bypass Budget Seeks $3.6 Billion, 63% Raise

The NCI Bypass budget submitted to President Clinton recently asks for $3.6 billion in fiscal 1995, a 63 percent increase from the President's budget proposal for the upcoming fiscal year.

The budget, submitted by the Institute under a unique authority, reflects the funding level NCI says it needs to pursue all scientific opportunities in cancer research. Following is a summary of the program levels included in the FY95 Bypass budget:

Basic research: $1.6 billion

--Increased support to untargeted areas of research to promote basic studies which provide the underpinnings for future advances in cancer research.

--Support 50 percent of approved competing Research Project Grant applications.

Women's health: $657.7 million

--Expand the number of SPORES that address cancer sites specific to women.

--Increase breast, ovarian and cervical cancer research, including new methodology for early detection of ovarian cancer.

--Expand accessibility and delivery of state-of-the-art health care to medically underserved women.

--Promote the design, construction and clinical development of breast or ovarian cancer vaccines.

Breast cancer: $497.7 million

--Support breast cancer at a level of $497.7 million, a $234.8 million increase over the 1994 comparable President's Budget, of which a portion would be available as two year obligation authority. The Trans-NIH Breast Cancer Initiative of $70 million is subsumed within this figure and includes $5 million for a Clinical Genetics Screening Center.

--Direct efforts to basic research, clinical applications, screening, diagnosis, prevention, psychosocial factors, rehabilitation research, training, and epidemiology activities.

--Increase the number of breast cancer SPORES.

Cancer prevention and control: $325.5 million

--The Bypass budget fulfills the requirement in the NIH Reauthorization passed last year which requires that not less than 9% of the budget be available for carrying out cancer control in FY 1995.

Prostate cancer: $145 million

--Further identify those factors that influence the onset, detection, progression and management of prostate cancer. Include within the Prostate, Lung,

Cervical, and Ovarian Trial aspects to facilitate the development of genetic and biochemical markers.

--Implement and expand developmental prevention clinical trials such as Proscar.

--Intensify research on PSA and other biomarkers as a screen for prostate cancer.

Environmental/occupational carcinogenesis: $400 million. Develop and expand molecular epidemiologic and geographic studies.

Cancer prevention and bionutrition research center: $100 million. Provide support for a dedicated facility to conduct cancer prevention and bionutrition research.

Vaccine research: $140 million

--Expand fundamental molecular biology and immunology research. Solicit investigator-initiated approaches for the development of vaccines with cancer applications.

--Develop guidelines and implement clinical trials of vaccine-based primary and secondary prevention and treatment in diverse malignancies.

Gene therapy: $40 million. Expand preclinical and clinical initiatives in gene therapy.

AIDS: $253.9 million

--A $254 million level of support would be provided, an increase of nearly $41 million over the 1994 President's budget.

--Expand the identification of new active compounds, both natural and synthetic.

--Increase resources to discover and develop antiretroviral drugs that suppress the AIDS virus.

--Expand studies of cervical cancer in HIV-infected women.

--Increase support for AIDS vaccine studies, including the development of synthetic peptide vaccines and genetically-engineered vaccines.

--Augment basic and clinical research targeting AIDS-related malignancies, with special focus on a multi-state AIDS/Cancer match registry, tissue procurement and tissue and fluids repositories.

Natural products: $56 million. Aquisition of new natural products.

Clinical trials: $550 million

--Increase number of patients accrued onto clinical trials in lung, breast, colon and prostate cancers, women's health, and underserved populations.

--Accelerate, expand high priority clinical trials.

--Increase support for prevention clinical trials, with an emphasis on breast and prostate cancers.

Oncologic imaging: $120 million. Support diagnostic imaging initiatives expanding novel research in the diagnosis, staging, and management of cancer.

Proton beam/heavy particle therapy: $50 million

--Support three proton beam therapy and heavy particle therapy initiatives.

--Expand novel research in neutrons and alpha particles and other therapeutic radiation fields.

Rehabilitation and pain research: $50 million

--Expand activities to improve the quality of life, including organ and limb-sparing treatments.

--Increase emphasis on the behavioral and psychosocial aspects of cancer rehabilitation and on the special needs of cancer survivors.

--Support new research into pain management, including the pharmacology of pain control.

Minority and underserved: $250 million

--Emphasize prevention initiatives targeted to African Americans, Hispanics, Native Americans, Native Hawaiians, American Samoans, Native Alaskans and Asian Americans. Improve technology transfer to rural and impoverished populations.

Over 65 population: $50 million

--Expand efforts to determine survival/mortality differentials in the over 65 populations.

Information dissemination: $230 million

--Increase information dissemination activities directed toward underserved populations, including low literacy populations and the rural poor. Other groups would include Hispanics, African Americans, Asian Americans, Native Americans, and older Americans.

--Accelerate novel information dissemination activities with an emphasis on Eastern Europe and developing countries.

International activities: $40 million

--Extend bilateral agreements, conferences and training exchanges with Eastern Europe, South America, and Africa.

Cancer centers: $191.2 million

--Expand support for activities related to regional research needs.

--Supplement ongoing centers for pilot and feasibility studies in high priority research areas, particularly those that focus on cancers found to be disproportionate among women and minorities.

--Expand outreach initiatives, prevention and control initiatives, quality of life issues.

--Initiate Regional Enhancement Cancer Centers in geographically underrepresented areas.

--Award several planning (P20) grants to assist in the development of additional cancer centers.

--Promote development of formal Cancer Center programs targeting AIDS-related malignancies under

joint auspices of cancer investigators and AIDS investigators.

Specialized Programs of Research Excellence: $72.4 million. Expand the number of SPOREs which address breast, ovarian, prostate, lung, brain, melanoma and gastrointestinal cancers.

Special program project initiatives: $30 million

--Provisions have been included to accommodate the initiation of several large scale cross cutting program project grants to include research into environmental carcinogenesis, prevention initiatives, gene therapy, and computational analysis research.

Multi-year funds availability: $215 million

--$215 million of the Bypass budget is proposed for two year availability. This would allow NCI additional time, if needed, for the completion of large, complex awards, such as construction grants and large scale clinical trials.

Human resource professional development: $116.7 million

--Expand support for predoctoral and postdoctoral trainees. Maintain the Science Enrichment Program.

--Expand innovative education programs on pain research, rehabilitation, psychosocial issues and community outreach education.

--Accelerate research training for the Research Career Programs.

--Support career development training opportunities for researchers in specific disease-oriented disciplines through the SPOREs.

--Expand efforts to increase minority participation in cancer research.

--Intensify intramural research training programs.

Construction: $282.7 million

--Initiate renovation, modernization and construction of extramural cancer research facilities throughout the nation using two year obligational authority.

--Provide support to upgrade facilities appropriate for breast cancer, vaccine development, prevention research and high technology clinical research.

Cancer Meetings Listed For October, November

American Society for Therapeutic Radiology and Oncology—Oct. 11-15, New Orleans, LA. Contact ASTRO, Tel. 703/648-8910.

Great Lakes Cancer Nursing Conference—Oct. 19-20, Novi, MI. Contact Victoria Rakowski, phone 517/371-2920.

Cancer-Related Anemia—Oct. 28, Philadelphia, PA. Contact Kathy Smith, Fox Chase Cancer Center, phone 215/728-5358.

Cancer Therapy: Current Controversies—Oct. 29, Philadelphia, PA. Contact Univ. of Pennsylvania Cancer Center, Tel. 215/662-6480.

Women's Health: Occupation and Cancer—Nov. 1-2, Baltimore, MD. Contact Carmen Warren, Tel. 301/907-3844.

American Cancer Society National Conference on Clinical Trials—Nov. 3-5, Atlanta, GA. Contact Andy Cannon, ACS, 1599 Clifton Rd NE, Atlanta, GA 30329-4251, phone 404/329-7604.

Immunocytochemistry Pathology Review Workshop—Nov. 3-5, Philadelphia, PA. Contact Kathy Smith, Fox Chase Cancer Center, phone 215/728-5358.

Growth Control, Signal Transduction and Oncogenesis: Bristol-Myers Squibb Cancer Research Symposium—Nov. 4-5, Beverly Hills, CA. Contact UCLA Extension, Tel. 310/206-8983, Fax 310/206-3223.

Pittsburgh Cancer Conference: Breast Cancer—Nov. 4-5, Pittsburgh, PA. Contact Univ. of Pittsburgh Conference Management, Diane Applegate, phone 412/647-8263.

Colorectal Cancer—Nov. 4-7, Houston, TX. Contact Conference Services, M.D. Anderson Cancer Center, phone 713/792-2222.

San Antonio Breast Cancer Symposium—Nov. 5-6, San Antonio, TX. Contact Cancer Therapy & Research Center, Lois Dunnington, 8122 Datapoint Dr. Suite 600, San Antonio, TX 78229.

Chemotherapy Foundation Symposium XI: Innovative Cancer Chemotherapy for Tomorrow—Nov. 10-12, New York City. Contact Jaclyn Silverman, Mount Sinai School of Medicine, phone 212/241-6772, fax 212/996-5787.

National Coalition for Cancer Survivorship Annual Assembly—Nov. 11-14, Seattle, WA. Contact NCCS, Tel. 301/650-8868.

European Conference on Clinical Oncology & Cancer Nursing—Nov. 14-18, 1993, Jerusalem, Israel. Contact Secretariat, Dept. of Radiotherapy, University Hospital St. Rafael, Capucijnenvoer 33, 3000 Leuven, Belgium.

American Geriatrics Society/American Federation for Aging Research Annual Meeting—Nov. 15-19, New Orleans, LA. Contact AGS, phone 212/308-1414.

Pediatric Hematology/Oncology Care—Nov. 18-20, Orlando, FL. Contact Nancy Cowen Pollock, Florida Assn. of Pediatric Tumor Programs, PO Box 13372, Gainesville, FL 32604, phone 904/375-6848.

American Assn. for Cancer Education—Nov. 18-21, Houston, TX. Contact Robert Chamberlain, M.D. Anderson Cancer Center, 1515 Holcombe Blvd. Box 189, Houston, TX, phone 713/792-3020.

Sources Sought: NCI

Sources Sought: **NCI-CP-40521-02**
Title: Support services for viral epidemiology
Deadline: Approximately Oct. 4

The AIDS and Cancer Section of the Viral Epidemiology Branch, in NCI's Div. of Cancer Etiology is soliciting tailored capability statements from qualified small business firms under SIC Code 8731 with a size standard of 500 employees. Based upon the responses received from this sources sought announcement the proposed acquisition may be solicited as a 100% small business set-aside. This is not an RFP and does not commit NCI to award a contract now or in the future. No RFP package is available at this time.

Objectives of this contract are to collect, process and analyze data for the VEB through the use of technical managerial and clerical support. Specific objectives include providing various levels of support (except for retrovirus and immunologic testing of specimens) for a number of epidemiologic studies involving case-control cohort or observational designs, as well as analysis of large public access databases. Specific objectives also include a number of support activities that cut across individual projects including counseling of study subjects and providing educational materials to clinicians, assuring the adequate protection of human subjects, establishing liaison with and obtaining clearances from all necessary parties and organizations, management and tracking of specimen shipments and laboratory data statistical analysis of data under the guidnnce of NCI staff, and providing financial management and advice to the project officers for optimal use of available funds based on sound budget projections.

The types of activities needed in the conduct of the studies can be divided into nine tasks: 1) initiation, liaison and administrative management, 2) word processlng and computing, 3) development of study materials and procedures, 4) identifying and tracing study subjects, data collection and monitoring, 5) laboratory aspects involving biologic specimens, tests and laboratory data, 6) data preparation 7) data processing 8) data analysis and 9) documentation, monitoring quality control and priority actions. Single award for a period of five years based on total level of effort of 170 person-years.

Contract specialist: Michael Loewe, RCB Executive Plaza South Rm 634, Bethesda MD 20892, Tel. 301/496-8611.

RFAs Available

RFA CA-93-032
Title: **Development and evaluation of minimal access surgery in cancer**
Letter of Intent Receipt Date: Oct. 20
Application Receipt Date: Dec. 22

The Cancer Therapy Evaluation Program of NCI's Div. of Cancer Treatment invites applications for cooperative agreements from institutions or consortia, including the DCT Clinical Trials Cooperative Groups, capable of and interested in performing phase II and phase III evaluations of minimal access surgery.

Phase III studies should be designed to evaluate minimal access surgery versus standard surgery. Phase II studies should evaluate the practicality and safety of minimal access surgery for specific tumor sites. Solid tumors relevant to this RFA include cancers of the brain, lung, stomach, pancreas, colon, ovary, endometrium, and cervix.

Applications may be submitted by domestic organizations. An applicant institution may consist of a single institution or a consortium of institutions. Foreign institutions are ineligible to apply or be a collaborating institution within an applicant institution. All accrued patients must be treated in the U.S.

The funding instrument will be a cooperative agreement (U01). Total project period may not exceed three years. Anticipated award date is July 1, 1994. Approximately $750,000 in total costs per year for three years will be committed to fund applications. Funds will support two phase III awards, four phase II awards, or some combination thereof.

This RFA is not intended to duplicate or supplement support for any phase II or phase III trials supported by any other mechanism. Phase III studies will evaluate minimal access surgery versus standard surgical technique, including cancers of the brain, lung, stomach, pancreas, colon, ovary, endometrium and cervix. Developmental phase II studies will be aimed at broadening the applicability of minimal access surgery for specific tumor sites by evaluating the practicality and safety of this approach.

Each application is expected to focus on a specific solid tumor. An applicant institution may submit more than one application. In addition, an individual scientist, individual institution, or consortium of institutions may be included on more than one application (or tumor site).

All institutions accruing patients must be able to

document adequate surgical experience with minimal access surgery as well as adequate patient accrual to complete a phase II or III trial in a timely manner. For phase III trials, outcomes of interest include morbidity (acute and chronic), mortality, efficacy of treatment, length of hospital stay, time to return to normal activities, quality of life, and cost. Applications should include an analysis of what outcomes are expected to vary importantly between minimal access surgery and conventional surgery. It is recommended that costs be measured in terms of health-related resource utilization, such as hospital days, operating room time, office visits, days until resumption of normal activities, etc. Applications should include documentation of a cost-related data source that is comprehensive and available to the researcher. Applications must include a statistical section describing plans for analysis of data designed to test the hypotheses, as well as a power/sample size analysis for cost and clinical endpoints.

Inquiries: For scientific issues, Dr. Edward Trimble, DCT, NCI, Executive Plaza North Suite 741, Bethesda, MD 20892, Tel. 301/496-2522, FAX 301/402-0557; for programmatic issues and letter of intent, Dr. Roy Wu, Grants Program Director, DCT, NCI, Executive Plaza North Rm 734, Bethesda, MD 20892, Tel. 301/496-8866, FAX 301/480-4663.

RFA CA-93-040

Title: **Immunobiology of AIDS lymphoma**

Letter of Intent Receipt Date: Nov. 15

Application Receipt Date: Jan. 7

The intent of this initiative is to stimulate basic research on biologic and immunologic mechanisms involved in the development of lymphomas in AIDS patients.

Applications for NIH R01 grants may be submitted by domestic and foreign for-profit and non-profit organizations. Approximately $1,500,000 in total costs per year for four years will be committed. At least six to eight R01 grant awards will be made.

This RFA is intended to encourage and promote research into the basic immunologic mechanisms that underlie lymphomagenesis in AIDS patients. Since there are many factors that affect B-cell lymphomagenesis it is important to elucidate the inter-relationships between cellular and molecular mechanisms in AIDS-associated lymphomagenesis. While the use of patient-derived material may be the most direct approach to this problem, the use of animal models of AIDS lymphoma or other human immunodeficiencies may be appropriate and is encouraged. The proposed studies should include cellular and molecular approaches and may include collaborations between basic and clinical scientists. Applicants who propose to use tissues or cells from AIDS patients must document that they have adequate access to these resources. Applicants who do not demonstrate this access will have their applications returned without review.

Inquiries: Dr. John Finerty, Div. of Cancer Biology, Diagnosis, and Centers, NCI, Executive Plaza North Rm 501, 6130 Executive Blvd., Bethesda, MD 20892-9904, Tel. 301/496-7815, FAX 301/496-8656.

Program Announcement

PA-93-112

Title: **Breast Cancer: Etiology and Prevention**

The Chemical and Physical Carcinogenesis Branch of NCI's Div. of Cancer Etiology invites investigator-initiated grant applications for multidisciplinary research on the etiology and prevention of breast cancer. Support will be through the NIH R01 or the FIRST award (R29).

The following research questions are relevant to this initiative: 1) What is the target cell in the breast that ultimately becomes the cancer cell and what are the characteristics that could make it identifiable? 2) What molecular events initiate breast cancer and what factors (diet, hormones, etc.) stimulate proliferation of the initiated cell? 3) What is the natural history of breast cancer and what new markers, among the probes now available or under investigation, might be most promising for characterizing normal breast tissue at its various stages of development, distinguishing normal from abnormal, following the natural history longitudinally, and assessing the efficacy of chemopreventive agents? 4) What is the mechanism that conveys a protective effect of first birth on breast cancer risk in humans? 5) What are the critical hormonal interactions with genetic constituents that can lead to breast cancer and how can chemopreventive agents modulate the outcome?

A discussion of specific topic areas encouraged by this PAis contained in the full text, available from the program director.

Inquiries: Dr. David Longfellow, DCE, NCI, Executive Plaza North Suite 700, Bethesda, MD 20892, Tel. 301/496-5471, FAX 301/496-1040.