THE CANCER LETTER

Vol. 11 No. 37
Sept. 27, 1985

© Copyright 1985 The Cancer Letter Inc
Subscription $150 year North America
$175 year elsewhere

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

PB-8509-018744

CHEMOPREVENTION CONCEPT APPROVED BY DCPC BOARD USES BIOLOGICAL MARKERS TO ASSESS RISK MODULATION

The Div. of Cancer Prevention and Control's Board of Scientific Counselors approved a concept for prevention clinical trials evaluating intermediate endpoints and their modulation by chemopreventive agents last week. The award would provide

(Continued to page 2)

In Brief

THOMAS DAVIS IS NAMED NEW DIRECTOR OF NCCP; SENATE SUBCOMMITTEE GIVES NCI $1.2 BIL. FOR FY '86

THOMAS DAVIS, executive officer of Eastern Cooperative Oncology Group and a faculty member of the Univ. of Wisconsin, is the new director of the Northern California Cancer Program. Davis succeeds Saul Rosenberg of Stanford Univ., who has been filling in as director since Stephen Carter's departure in 1982 . . . **SENATE LABOR-HHS** Appropriations Subcommittee gave NCI $1.217 billion in its markup of the FY 1986 bill, an increase over 1985 of $56.7 million. That does not include money for training or construction, since those programs are authorized in the renewal of the biomedical research authorization act still awaiting final action in Congress. The President's budget had requested $30 million for training and $6.5 million for construction. The House Labor-HHS Appropriations Subcommittee was scheduled to take its bill to the full committee this week; those figures were still being kept under wraps at press time. . . . **MAGNETIC RESONANCE** imaging network contract will be awarded to AMC Cancer Research Center in Denver, as the headquarters, with Marvin Rich as PI. Fox Chase Cancer Center will be the statistical center, with Fox Chase President John Durant as co-PI. Richard Steckle, director of UCLA Johnsson Comprehensive Cancer Center, will be co-PI with the task of organizing and directing the committees which will develop protocols. The award will total $1.173 million for three years. Phil Furmanski of AMC will be deputy PI. Those interested in participating in the project may contact Rich at AMC, 1600 Pierce St., Lakewood, CO, 80214. . . . **MALCOLM BAGSHAW,** radiology chairman at Stanford Univ. Medical School, will receive the American College of Radiology's Gold Medal on Oct. 1. for his work on prostate cancer. . . **ROBERT BOWSER,** program director in the Div. of Cancer Prevention & Control's Cancer Detection Branch, retires Sept. 28 after more than 30 years of federal service. . . . **DCPC's BIOMETRY** Branch is searching for a new section head for its Clinical and Diagnostic Trials Section, branch Chief David Byar told the division's Board of Scientific Counselors. . . . **JOHN MONTGOMERY,** senior VP of Southern Research Institute will receive the American Chemical Society's Alfred Burger Award in Medicinal Chemistry.

CONCEPT WOULD FUND TWO TO SIX AWARDS AT TOTAL ANNUAL COST OF $1.8 MILLION

(Continued from page 1)
approximately $1.8 million a year to support two to six cooperative agreements. While the concept will generate a new RFA, it is a follow up on program intitiatives begun during the past three years, Winfred Malone, chief of the division's Chemoprevention Branch, told the board.

NCI has already funded 26 similar trials in the past, but is seeking to incorporate biological markers in upcoming trials, he said. The cooperative agreement initiatives would support studies that are directed toward examining the role of various biological markers in assessing risk modulation by chemopreventive agents.

The main emphasis of the trials "should be on small, efficient studies aimed at improving future research designs of chemoprevention trials, providing biologic understanding of what is happening in the trials, or providing better, more quantitative and more efficient endpoints for these trials," the concept says.

The document specifies that "one or more tests would be included initially to determine baseline parameters and later serve as a follow up after the administration of the chemopreventive agent." It also notes that the RFA would solicit "applications for pilot studies, which would be expected to last up to three years, full scale intervention studies, or combinations of the two."

Malone emphasized the two part approach to the trials, with small studies to be performed prior to the implementation of a larger study. An example of the two phase approach cited by Malone is a pilot study underway in which an investigator is attempting to reduce thymidine uptake by crypt cells through the administration of 1500 mg/day of calcium carbonate. The second phase will use a reduction in the incidence of adenocarcinoma as an endpoint rather than the first phase's reduction of thymidine uptake alone.

Board members, however, objected to the document's mention of Phase 3 clinical trials, asserting that it was premature and should not be included in the RFA. The concept stated, "After successful completion of the pilot phase and a demonstrated modulation of marker endpoints by the intervention, Phase 3 clinical trials with a defined monitoring test system and a cancer incidence or mortality endpoint could be implemented."

The RFA will specify that such trials are an option available to investigators, but are not required. The award period will be from three to five years, with competing renewals planned.

The "innovative biomedical monitoring tests" being sought by the division are those that "might be useful to determine an intermediate endpoint, serve as a basis to assess risk or assess response to a chemopreventive agent, identify the high risk group or increase the power to detect the risk or the response to chemoprevention."

Relevant tests for risk identification include "adduct excision or DNA repair which are semiquantitative evidence of absorbed dose in high risk populations," it says. "DNA, RNA, protein adducts, SCE and micronucleus tests are related to a biological effective dose of an initiator and/or promoter and would provide quantitative measures of the interaction of carcinogen with cellular targets such as DNA, RNA or protein."

Modulation of effects by the chemopreventive agents on tests that are indicative of neoplastic progression "may be an early indicator of efficacy," it states. Examples of such tests "might include classical cytological techniques, suppression of oncogene encoded protein, etc.," it says.

Effects on tests by the chemopreventive agent might be highly significant in relation to ultimate cancer prevention as well, the concept says. "A series of one or more tests would be included in the chemoprevention intervention clinical trial, initially to determine baseline parameters, and later as a follow up after administration of the chemopreventive agent," it adds. "Biological fluids including urine, blood, sputum, etc. would have to be obtained from participants for analysis." Populations suitable for such interventions could include heavy smokers or groups previously exposed to carcinogens, it says, adding that the groups "may also be appropriate candidates for studies."

Under the cooperative agreement mechanism, NCI staff will assist investigators in obtaining Investigational New Drug permits from FDA, in quality assurance aspects of the clinical laboratory procedures and if necessary, in obtaining the chemopreventive agent to be used in the study. Following approval of a study by the peer review committee, NCI will begin discussions about obtaining the drug with the principal investigator and pharmaceutical industry.

If NCI cannot obtain an agent free of cost, it "may proceed to purchase the agent through normal procurement mechanisms," it says. "Purchase of agents is however, only undertaken after measures to obtain the drug at no cost have been exhausted." Awards will not be made until all arrangements for delivery of the agent are complete, it says, adding that final awards "will also consider not only the cost of the trial but also the cost of the agent and its formulation, encapsulation and packaging if these costs are to be borne by the government."

Other concepts approved by the board are:

Interventions to improve the quality of survival for recovered childhood cancer patients. Two five year awards anticipated, at an estimated annual total cost of $399,000.

The goal of the project is to develop, implement and evaluate approaches to provide optimal care to survivors of childhood cancer and their families.

According to the concept report, it has been estimated that by 1990, one in 1,000 people reaching the age of 20 will be a survivor of childhood cancer and its therapy. By the year 2000, one in 1,000 people between the ages of 20 and 29 will have survived childhood cancer.

Although it is only in the last several years that sufficient numbers of pediatric cancer survivors have existed for potential followup, research has indicated a number of long term effects of childhood cancer and its treatment, the concept notes. Long term effects include: musculoskeletal (growth and development abnormalities); endocrine (including hypothalmic-pituitary and thyroid functioning); genitourinary (temporary or irreversible ovarian and testicular damage, urinary tract problems); nervous system (long term neurotoxicity including neuro-psychological/ intellectual performance) and cardiovascular (effects on organs ranging from the esophagus to the rectum).

Visual, auditory and dental problems may also emerge, as well as possible immunosuppression and surgical effects.

Former pediatric oncology patients also appear to have a greatly elevated risk of developing a second malignant neoplasm, and the birth weight of infants of survivors may be affected by the treatment their mothers received as children.

Several studies have also suggested that survivors experience problems in adjustment ranging from changes in personality to psychiatric symptomatology. There is also some evidence that survivors face barriers in obtaining employment and insurance due to their history of cancer. Other data suggest that childhood cancer survivors may also experience high divorce rates.

The concept report also notes that a number of writers have pointed to the long term financial consequences that pediatric cancer engenders for the family, as well as residual impacts on siblings and the family in general. No firm data has been reported in these areas, however.

Innovative approaches in education and medical-nursing surveillance appear to be emerging, such as a school based intervention to facilitate return to school and an individualized followup care plan for long term survivors directed at community physicians, the document notes.

The purpose of the concept is to "stimulate systematic and scientifically rigorous research focused on interventions to enhance the quality of survival following childhood cancer," it stresses.

The proposed project seeks research studies to develop, implement and evaluate interventions to improve the quality of survival for survivors of pediatric cancer and their families. Some interventions might focus on preventing side effects of treatment, while others may address how to minimize existing sequelae or reduce their effects.

Interventions may be directed toward cancer survivors themselves, their families, the community or health care professionals.

Examples of possible interventions include the following, although the list is by no means exhaustive, and innovative strategies are encouraged.

*Teaching children who receive cranial irradiation how to compensate for possible learning problems

*Improving survivor experiences in obtaining employment and insurance

*Promoting emotional adjustment

*Enhancing awareness or availability of social service or health care resources that address the financial impact on families

*Increasing knowledge of survivor needs among teachers, school nurses, employers or insurance companies

*Teaching community physicians and nurses how to assess and monitor former childhood cancer patients.

*Assessing the long term consequences of new cancer treatments

While a variety of interventions may be appropriate to address the goals of the concept, all studies must be based on the needs of the target population and must feature rigorous evaluation methodology, regardless of approach. The target population must be specifically defined, measurement instruments must be well validated and appropriate to the developmental stage of the participants, and control groups should be selected carefully.

Applicants must also justify and document the number of cases needed to detect findings of interest. Given the relatively small numbers of pediatric oncology survivors, joint ventures between two or more investigators or groups of researchers, e.g., consortia, may be advantageous in many projects. For such studies, applicants must specify procedures for combining and managing data from multiple researchers or agencies.

The concept recognizes that some interventions may be implemented optimally before it is known whether the patient will in fact be a survivor. In this situation, applicants need to specify how they will select participants with a high probability of surviving; it must also be possible to assess impacts on survivors during the course of the study. It is also recognized that some interventions may have occurred prior to the initiation of this research. Studies of the long term impact of such interventions are appropriate, however, the non overlap between the present study and other ongoing efforts must be documented.

The concept defines survival as occurring after three or more disease free years subsequent to last treatment received. Childhood cancer is defined as cancer that is diagnosed during the childhood or

adolescent years. Applicants must specify other definitions used.

"We're so lucky to have this problem," board member Virgil Loeb said. President of the Univ. of Texas Medical Branch at Galveston, Loeb added that he thought it "is a terribly important concept."

Board member Jerome DeCosse, chairman of surgery at Memorial Sloan-Kettering, noted that most of the directions of the examples of interventions in the concept were psychosocial, however. Carolyn Gotay, a program director in DCPC's Community Oncology and Rehabilitation Branch, pointed out that the division intends to make two awards, and that specific interventions will be up to the investigator.

Interactions among micronutrients in the prevention of experimental mammary cancer. DCPC hopes to make three or more three year awards to be reviewed by regular study sections, with costs to be determined by peer review.

The objective is to evaluate the interactions of micronutrients that have been observed to inhibit mammary carcinogenesis. The ultimate aim would be to define a unique set or multiple sets of micronutrients that inhibit mammary carcinogenesis to a greater extent than do the individual nutrients alone. The hypothesis to be tested can be stated as "the preventive effect of low doses of two or more micronutrients in combination is greater than the effect of high doses of a single nutrient."

The project would have the ultimate aim of defining one or more sets of two to five micronutrients which, given together, significantly reduce or block mammary tumorigenesis over an extended period of time (one year or more). Good animal models exist for both viral and chemical mammary tumorgenesis, and any of these are feasible and appropriate test systems for this question, the concept says. NCI anticipates that studies would be carried out in several different laboratories, exploring various combinations of preventive factors in different tumorigenesis models.

Particular program interest in this area addresses such questions as:

1. Which micronutrients are most promising, what range of levels for each different nutrient in the combination achieves maximum preventive effects against specific carcinogenic exposure(s), and, from comparison with the preventive effects of these nutrients administered singly at comparable levels, are the interactions additive, synergistic, or even antagonistic; it cannot be assumed that all interactions will be positive, and negative interactions have also been recorded;

2. For each nutrient, how do the levels that give maximum preventive effect compare with the minimum toxic level, and are there any toxicity potentiations among the nutrients;

3. What regimen of micronutrient administration - timing(s), duration - in relation to exposure to the carcinogenic agent, is needed to maximize the preventive effects; further, is the optimal regimen the same for all micronutrients in the set;

4. Are there any further interactions of micronutrients with hormonal factors in mammary tumorigenesis, and can prevention synergisms be demonstrated among such nutrients and the hormones or antihormones for which mammary tissues and tumors are responsive targets;

5. Do the micronutrients tested exert their preventive effects by similar or by quite different mechanisms of action - effects on carcinogen metabolism, DNA repair, other specific enzymatic processes, hormonal intracellular action, immune response, to name some that have been hypothesized; understanding of the mechanisms of action of the various micronutrients is at present minimal, and although careful, systematic collection of adequate data is the essential first step, studies that go beyond this to probe the mechanisms of action and of interaction will shed greatest light on potential of the nutrients for effective interaction in prevention and for possible extrapolation to human breast cancer.

Evidence from experimental carcinogenesis indicates that a diet supplemented with large doses of single micronutrients, such as specific vitamins, antioxidants, or trace elements, can inhibit both viral and chemical carcinogen induced mammary cancer. The most promising micronutrients for inhibition of breast cancer development appear to be selenium and retinoids. In addition, certain phenolic antioxidants used as food additives have been observed to have favorable chemopreventive effects against mammary carcinogenesis.

However, the use of large doses of such agents is often accompanied by undesirable side effects. Moreover, there is a general reluctance to supplement diets with large doses of factors over a lifetime for fear of cumulative toxicities.

According to the concept, "it is therefore timely to examine the concept that low doses of several such micronutrients used together may be more effective and desirable than high doses of single nutrients." and desirable than high doses of single

Experiments thus far on using two or more factors together have been relatively few, but the results are strongly suggestive. Selenium and retinoids have been shown to have synergistic effects against mammary carcinogenesis. More impressive, vitamin E has been found to be synergistic with selenium at levels of vitamin E which, alone, are not inhibitory.

In a related study, low, subpharmacologic doses of the inhibitors selenium, 13-cis-retinoic acid, and beta-sitosteral, although ineffective alone, in combination provided significant inhibition of azoxymethane induced colon cancer; maximum inhibition was seen when all three factors were used together. Finally, it is worth noting that selenium may also have significant potential for positive interactions with chemotherapeutic drugs; treatment of L1210 leukemia with selenium plus methotrexate was more effective than either administered separately, and selenium has recently been reported to have improved the therapeutic index of cis-diam-minedichloroplatinum (II) against murine fibrosarcoma.

DCPC Director Peter Greenwald told the board that the concept will generate a program announcement to encourage applications.

Board member David Hegsted expressed concern that the concept was too narrowly based, particularly in regard to dietary fat. Hegsted suggested that the concept be expanded to include macronutrients as well, asserting that the interaction of micronutrients with fat "might be as important" as the interaction of micronutrients themselves. The board unanimously approved the concept as amended to include a statement that interactions with other variables such as fat can be considerations.

CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY: RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

HCFA SEEKS APPLICATIONS ON DRGs

The Research and Demonstrations Division of the Health Care Financing Administration has published an RFA for areas of special interest, including the impact of DRG prospective payment on clinical research and blood testing. Applications are due by Nov. 4. To receive an application packet, call Ms. Francis Lariviere at 301-594-7474. To discuss content with program staff, contact Jack Langenbrenner at 301-597-5716, or Joel Broida at 301-594-5104 if interested in the clinical trials aspect. For inquiries relating to blood banking, contact Bill Sebasky at 301-594-8286.

PB-8509-018745

NCI ADVISORY GROUP, OTHER CANCER MEETINGS FOR OCTOBER, NOVEMBER

Limb Salvage in Musculoskeletal Oncology—Oct. 2-6, Hyatt Regency Grand Cypress Hotel, Orland. Second annual Bristol-Myers Zimmer Orthopedic Symposium. Contact Public Communications Inc., 35 E. Wacker Dr., Chicago 60601, phone 312-558-1770.

Div. of Cancer Treatment Board of Scientific Counselors—Oct. 3-4, NIH Bldg 31 Rm 10, 8:30 a.m. both days, all open.

11th Annual Topics in Gastroenterology & Liver Disease--Oct. 3-5, Turner Bldg, Johns Hopkins Medical Institutions, Baltimore. Contact Jeanne Ryan, Program Coordinator, Office of Continuing Education, Johns Hopkins Univ. School of Medicine, 720 Rutland Ave., Baltimore 21205.

Oncology Nursing: Helping You Meet the Challenge --Oct. 3-4, Cleveland. Contact Center for CME, Cleveland Clinic Educational Foundation, 9500 Euclid Ave., Rm TT3-301, Cleveland, OH 44106, phone 216-444-5696.

Humor: Enriching Ourselves, Caring for Others--Oct. 4, Fox Chase Cancer Center, Philadelphia. Contact Dept. of Social Work Services, FCCC, 7701 Burholme Ave., Philadelphia 19111, phone 215-728-2668. e., Philadelphia 19111, phone

Detection & Treatment of Premalignant Lesions & Colorectal Carcinoma--Oct. 4, Roswell Park continuing education in oncology.

New York State Cancer Programs--Oct. 5, Buffalo. Annual meeting. Contact Dr. Curtis Mettlin, Roswell Park Memorial Institute, 666 Elm St., Buffalo 14263.

Fine Needle Aspiration of the Breast & Thyroid Gland—Oct. 5-6, New York. Contact New York Univ. Medical Center Postgraduate School, 555 First Ave., New York 10016, phone 212-340-5295.

Mechanism of Antimutagenesis and Anticarcinogenesis—Oct. 6-10, Lawrence, KS. International conference. Contact Delbert Shankel, Dept. of Microbiology, Univ. of Kansas, Haworth Hall, Lawrence 66045, phone 913-864-3250.

National Cancer Advisory Board Committee on Organ Systems Programs—Oct. 6, NIH Bldg 31 Rm 8, 6:45 p.m.

NCAB Committee on Innovations in Surgical Oncology--Oct. 6, NIH Bldg 31 Rm 7, 8 p.m.

National Cancer Advisory Board—Oct. 7-9, NIH Bldg 31 Rm 6, 8:30 a.m. each day. Closed Oct. 8.

NCAB Committee on Planning & Budget—Oct. 7, NIH Bldg 31 Rm 11A10, 7:30 p.m.

New Solutions to Old Problems in Surgical Pathology--Oct. 7-9, Bethesda. Contact Surgical Pathology, c/o FAES, NIH, Bldg 10 Rm B1-L-101, Bethesda, Md. 20892.

Tutorial & Workshop in the Use of Immunocytochemistry & Electronmycroscopy in Tumor Diagnosis--Oct. 7-11, Detroit. Contact Dr. Jose Russo, Dept. of Pathology, Michigan Cancer Foundation, 110 E. Warren Ave., Detroit 48201, phone 313-833-0710 Ext. 214.

NCAB Committee on Review of Contracts for the Office of Director--Oct. 8, NIH Bldg 31 Rm 7, to follow immediately after the closed session of the full Board.

Occupational and Environmental Significance of Industrial Carcinogens--Oct. 8-10, Bologna. Collegium Ramazzini. Contact Organizing Committee, International Conference on Chemical Carcinogens, c/o Istituto di Oncologia, Viale Ercolani, 4/2, 40138 Bologna, Italy.

American Institute of Ultrasound/Society of Diagnostic Sonographers—Oct. 8-11, Dallas. Annual convention. Contact Convention Dept., AIUM, 4405 East-West Highway, Suite 504, Bethesda, Md. 20814, phone 301-656-6117.

Pathophysiology and Treatment of Leukemia--Oct. 10-12, Omni International Hotel, Baltimore. Fourth regional medical meeting of the Leukemia Society of America. Contact Louise Toglio, LSA, 733 Third Ave., New York 10017, phone 212-573-8484.

Early Breast Cancer: The Psychological Perspective--Oct. 11, New York. Contact Ann Boehme,

Associate Director for Continuing Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042, phone 718-470-8650.

Intraperitoneal Chemotherapy--Oct. 11, Portland, OR. Contact Donna Layman, Oregon Medical Assn. Bldg., 5210 SW Corbett Ave., Portland 97201, phone 503-295-6422.

Hospice Assn. of America--Oct. 12, MGM Grand Hotel, Las Vegas. Inaugural meeting. Contact Deborah Horan, Executive Director, HAA, 210 7th St. SE, Suite 301, Washington D.C. 20003, phone 202-547-5263.

Toward 2000: Directions in Oncology--Oct. 16-18, Fox Chase Cancer Center. Contact Peggy Conners, Conference Coordinator, FCCC, 7701 Burholme Ave., Philadelphia 19111, phone 215-728-3110.

Div. of Cancer Etiology Board of Scientific Counselors--Oct. 17-18, NIH Bldg 31 Rm 6. Closed Oct. 17 9 a.m.-1 p.m.

Community Cancer Care--Oct. 17-20, Hyatt Regency, Indianapolis. Fourth national seminar. Contact Office of Continuing Medical Education, Methodist Hospital of Indiana, 1604 N. Capitol Ave., Indianapolis 46202.

Practical Approaches to Geriatrics, Oncology & Pediatrics--Oct. 17-19, Holiday Inn, Fargo, N.D. Contact Office of Medical Education, St. Luke's Hospitals, 5th St. at Mills Ave., Fargo 58122, phone 701-280-5933.

Chemical Modifiers of Cancer Treatment--Oct. 20-24, Sheraton-Sand Key Hotel, Clearwater, Fla. Contact Suzanne Bohn, American College of Radiology, 925 Chestnut St., Philadelphia 19107, phone 215-574-3150.

Fourth Annual Cancer Symposium and Fifth Annual Cancer Symposium for Nurses--Oct. 21-23, Sheraton Harbor Island Hotel, San Diego. Sponsored by Scripps Memorial Hospital. Contact Nomi Feldman, Conference Coordinator, 3770 Tansy, San Diego 92121, phone 619-453-6222.

Current Concepts in Medical Oncology--Oct. 21-25, Memorial Sloan-Kettering Cancer Center, New York. Contact Continuing Medical Education Planning Office, C180, MSKCC, 1275 York Ave., New York 10021, phone 212-794-6754.

Cancer Clinical Investigation Review Committee --Oct. 21, NIH Bldg 31 Rm 10, open 8:30-9 a.m.

Sixth Annual Meeting of the Cancer Control Consortium of Ohio--Oct. 23, Fawcett Center for Tomorrow, Columbus. Contact Sewall Milliken, 101A Hamilton Hall, 1645 Neil Ave., Columbus 43210, phone 614-422-1382.

Breast Cancer: Recent Progress and Future Prospects--Oct. 25-26, Univ. of Rochester Cancer Center. Contact Barbara Janetakos, Cancer Education Div., Univ. of Rochester Cancer Center, PO Box 704, Rochester, N.Y. 14642, phone 716-275-5537.

International Conference on Anticancer Research--Oct. 26-30, Loutraki, Greece. Contact Dr. J.G. Delinassios, Anticancer Research Editorial Office, 5 Argyropoulou St., Kato Patissia, Athens GR-111-45, Greece.

Div. of Cancer Biology & Diagnosis Board of Scientific Counselors--Oct. 29, NIH Bldg 31 Rm 7, 8:30 a.m. Closed 3 p.m.-adjournment.

Cancer Research Manpower Review Committee--Oct. 31-Nov. 1, Bethesda Holiday Inn, open Oct. 31 8:30-9 a.m.

Nutrition and Aging--Oct. 31-Nov. 1, New York. Contact Ralph Weaver, Bristol-Myers, 345 Park Ave., Rm 43-38, New York 10154, phone 212-546-4310.

Genetics in Clinical Oncology--Oct. 31-Nov. 1, New York. Contact R.S.K. Chaganti PhD, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York 10021, phone 212-794-8121.

Cincinnati Cancer Conference--Nov. 1-2, Cincinnati. Contact Thomas O'Connor, Medical Staff Education, Bethesda Hospitals Inc., 619 Oak St., Cincinnati 45206.

Northern California Oncology Group--Nov. 1-3, Napa Holiday Inn. Fall meeting. Contact Laura Lee, 415-497-7512 or 497-7431.

Immunobiology of Cancer and Allied Immune Dysfunctions--Nov. 4-7, Copenhagen. Contact Scandinavia Hotel, Amager Blvd., 70, DK 2300 Copenhagen S, Denmark.

American Society of Cytology--Nov. 4-9, New York. Annual scientific meeting. Contact Lenore Strigari, American Society of Cytology, 130 S. 9th St., Suite 810, Philadelphia 19107.

Labeled Antibodies--Nov. 5-7, Tokyo. 8th international conference. Contact Dr. K. Kano, Dept. of Immunology, Institute of Medical Science, Univ. of Tokyo, 4-6-1 Shirokanedai, Minatoku, Tokyo 108, Japan.

Detection and Treatment of Minimal Residual Disease in Acute Leukemia--Nov. 6-8, Rotterdam. 2nd international symposium. Contact J.W. van der Velden, MD, c/o Organizing Committee, Leukemia Symposium, Dr. Daniel den Hoed Cancer Center, PO Box 5201, 3008 AE Rotterdam, The Netherlands.

8th Annual Breast Cancer Symposium--Nov. 7-9, San Antonio. Contact Terri Coltman, 4450 Medical Dr., San Antonio TX 78229, phone 512-690-0655.

1st International Congress on Neoadjuvant Chemotherapy--Nov. 7-9, Paris. Contact SOMPS--(Title of Congress), Pavillon Jacquart, Hopital de la Salpetriere, 47 boulevard de l'Hopital, 75651 Paris Cedex 13, France.

Cancer Education Review Committee--Nov. 8, Holiday Inn Crown Plaza, Rockville, Md., open 8:30-10 a.m.

American Assn. for Cancer Education--Nov. 12-15, Hyatt Regency Hotel, San Francisco. Annual meeting. Contact AACE, Stephen Stowe M.D., Secretary, CRTC Bldg Rm A-1020, New Jersey Medical School, 100 Bergen St., Newark 07103, phone 201-456-5365.

Diagnosis and Treatment Strategies for Gynecologic Cancer--Nov. 13-16, Houston. 29th annual clinical conference. Contact Office of Conference Services, Box 131, M.D. Anderson Hospital & Tumor Institute, 6723 Bertner Ave., Houston 77030, phone 713-792-2222.

Management of Cancer Pain--Nov. 14-16, Memorial Sloan-Kettering Cancer Center, New York. Contact CME Planning Office, C180, MSKCC, 1275 York Ave., New York 10021, phone 212-794-6754.

Symposium on Hematological Disorders--Nov. 14, Roswell Park continuing education in oncology. Contact Gayle Bersani.

Ethics in Cancer Care--Nov. 15-16, Cleveland. Contact Center for CME, The Cleveland Clinic Educational Foundation, 9500 Euclid Ave., Rm TT3-301, Cleveland 44106, phone 216-444-5696.
Asbestos Abatement in the Federal Government--Nov. 19-21, Hilton Plaza Hotel, Kansas City, Mo. Contact Hall-Kimbrell Environmental Services, 946 Tennessee, Lawrence KS 66044.
Ella T. Grasso Memorial Conference--Nov. 20, Yale Univ. Latest information on diagnosis and treatment of women's cancer. Contact Peter Schwartz M.D., Dept. of Obstetrics & Gynecology, PO Box 3333, New Haven, CN 06510.
Clinical Cancer Program Project Review Committee--Nov. 21-22, Linden Hill Hotel, Bethesda, - open 8:30-10 a.m.

FUTURE MEETINGS

Ovarian Cancer: Therapeutic Results and Exciting New Leads--Dec. 13-14, NYU Medical Center, New York. Contact Registration Office, NYU Postgraduate Medical School, 550 First Ave., New York 10016, phone 212-340-5295.
Health Implications of Smokeless Tobacco Use--Jan. 13-15, 1986. NIH. Consensus development conference. Contact NIH Office of Medical Applications of Research, NIH Bldg 1 Rm 216, Bethesda, Md. 20892, phone 301-496-1143.
Immunoproliferative and Immunodeficiency Diseases in Children--Feb. 21-22, 1986, Memphis. 20th annual clinical symposium. No registration fees, but attendance will be limited to 200 registrants. Contact Director, St. Jude Children's Research Hospital, PO Box 318, Memphis, TN 38101.
Treatment Planning in the Radiation Therapy of Cancer--Feb. 28-March 1, Sheraton-Palace Hotel, San Francisco. 21st annual San Francisco Cancer Symposium. Contact West Coast Cancer Foundation, 50 Francisco St. Suite 200, San Francisco 94133, phone 415-981-4590.
Monoclonal Antibody Immunoconjugates for Cancer--March 6-8, Hotel Intercontinental, San Diego. Contact Office of CME, UC San Diego School of Medicine, M-017, La Jolla, CA 92093, phone 619-452-3940.
National Conference on Urologic Cancer--April 9-11, Adams Mark Hotel, Philadelphia. American Cancer Society--staging, integrated management of early disease, strategies for treatment of recurrent or advanced disease, psychological and rehabilitation, future development and new research. Contact ACS, (conference name), 90 Park Ave., New York 10016.
Oncology Nursing Society--April 30-May 3, 1986, Los Angeles. 11th annual Congress.
American Society of Clinical Oncology--May 4-6, Los Angeles. 22nd annual meeting.
American Assn. for Cancer Research--May 7-10, Los Angeles. 77th annual meeting. Abstracts are due at AACR offices in Philadelphia by Nov. 27; applications for minority travel grants due March 1; advance registration ends March 24; housing forms due in Los Angeles April 8; employment register forms due in Philadelphia April 25.
National Tumor Registrars Assn.--June 3-6, 1986, Park Plaza Hotel, Boston. Annual meeting. Contact Shirley Foret, Elliot Hospital, 955 Aurburn St., Manchester, NH 03103, phone 603-669-5300 Ext. 2147.
X111 International Pigment Cell Conference--Oct. 5-9, 1986, Holiday Inn Broadway, Tucson. Contact Mary Humphrey, Arizona Cancer Center, Tucson 85724, phone 602-626-6044.
Epstein-Barr Virus--Oct. 17-22, 1986, St. Petersburg, FL. 2nd international symposium. Contact Dharam Ablashi DVM, Laboratory of Cellular & Molecular Biology, NCI, Bldg 37 Rm 1E24, Bethesda, Md. 20892, phone 301-496-9332.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CN-55513-38
Title: Community clinical trial for heavy smokers--intervention centers
Deadline: Approximately Dec. 12

This competitive acquisition is for the establishment of a community clinical trial for heavy smokers which will be a multicenter cooperative intervention research program to test strategies for heavy smokers that (1) are effective in obtaining long term cessation; (2) are practical to implement on a large scale basis; and (3) employ a community intervention approach, working through major organizations and social institutions capable of influencing smoking behavior in large groups of people.

Contracts will be awarded to eight community intervention centers to participate in the design and conduct of a community based clinical trial that will effectively recruit, retain and aid heavy smokers to achieve and maintain long term cessation of cigarette smoking. The study will be conducted in three phases in eight matched pairs of communities over a 75 month period with communities within each pair randomized to either an intervention or control condition.

A preproposal conference will be held in Bethesda, with details to be published in the RFP.

The concept from which this RFP was derived was approved by the Div. of Cancer Prevention & Control Board of Scientific Counselors at its winter meeting and was reported in The Cancer Letter Feb. 1, page 5.

Contracting Officer: Barbara Mercer
RCB Blair Bldg Rm 314
301-427-8745

RFP NCI-CM-57753-22
Title: Development of dosage forms and delivery systems for antitumor agents
Deadline: Approximately Nov. 26

The Developmental Therapeutics Program of the Div. of Cancer Treatment is seeking contractors to carry out innovative studies leading to more effective approaches for the intravenous delivery of compounds that possess limited solubility and/or stability, and to develop parenteral dosage forms of potential antitumor agents that exhibit inadequate solubility and/or stability in vehicles commonly used for intravenous administration. Compounds to be studied are selected by NCI. Resolution of these problems requires approaches more complex than simple solvent approaches or pH adjustment. Frequently, the difference between inherent and desired solubility is 10-3 to 10-4.

These projects will also require considerable pharmaceutical analysis including the development and application of a stability indicating assay. The following analytical instrumentation should be available: ultraviolet, infrared, and proton magnetic resonance spectroscopy; high pressure liquid chromatograph with variable wavelength ultraviolet detection, optical rotation apparatus and thermal analysis equipment.

The goal of the contract effort is a pharmaceutical dosage form suitable for intravenous administration. The government will provide certain target solubility and stability goals. The contractor will prepare a pilot batch (30-100 units) of the finished dosage form as a product of the research effort.

The principal investigator should have a PhD degree in pharmaceutical, physical or medicinal chemistry, physical pharmacy, or pharmaceutics and have at least three years experience in the development of injectable formulations.

The government anticipates multiple contract awards. Offerors must propose at the two and three year staff levels. The PI should devote 475 direct labor hours annually at both levels of effort. Contracts will be awarded on an incrementally funded basis for a three year period beginning on our about July 1, 1986. Each increment will be for a one year period.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors at its spring meeting and reported in The Cancer Letter June 21, page 5.

Contract Specialist: Elizabeth Moore
RCB Blair Bldg Rm 216
301-427-8737

RFP NCI-CM-57752-22
Title: Development and production of pharmaceutical dosage forms
Deadline: Approximately Nov. 26

NCI's Developmental Therapeutics Program is seeking a contractor to provide primarily dosage form development services for sterile freeze dried dosage forms plus the facilities and staff to manufacture small production size batches (about 4,000 units) of these sterile formulations for evaluation in preclinical toxicology studies and in phase 1 clinical trials.

As a minimum requirement, the contractor must be registered as a pharmaceutical manufacturing facility for sterile products with FDA. The contractor will prepare all products in accord with FDA's good manufacturing practice regulations and NCI's product specifications. The government will assign all compounds to be developed and manufactured as pharmaceutical dosage forms.

Annual work load estimates for development and production are, respectively, 3,000 technical staff hours per year and 11 production assignments. Development assignments are estimated to involve five compounds annually. The complexity of the dosage form development work will vary from a simple familiarization work up on an existing formulation to a thorough study of a new chemical entity. Of the work load described above, the government estimates that annually one compound will be developed as an oral dosage form and two production batches of about 50,000 dosage units each will be prepared. The oral dosage form aspects may be subcontracted in part or in total to a manufacturing concern that meets FDA's good manufacturing practice requirements and is acceptable to NCI.

The contractor will be responsible for the quality control testing of all formulation components including the active ingredient, excipients, container closure systems as well as all finished products prepared under the contract.

All products will be labeled and packaged according to the government's specifications. Label preparation may be subcontracted but labeling must be performed at the contractor site.

The principal investigator should have at least an MS degree in pharmacy or chemistry plus three years experience in directing the development and production of parenteral dosage forms.

The government anticipates a single contract award on an incrementally funded basis. Each increment is for one year and the total contract will be awarded for a three year period on or about June 15, 1986.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors at its spring meeting and reported in The Cancer Letter June 21, page 5.

Contract Specialist: Elizabeth Moore
RCB Blair Bldg Rm 216
301-427-8737

The Cancer Letter _Editor Jerry D. Boyd
Associate Editor Patricia Williams
Published forty-eight times a year by The Cancer Letter, Inc., P.O. Box 2370, [illegible]
publisher of The Clinical Cancer
Letter. All rights reserved. None of the content of this publication may be [illegible]
[illegible] retrieval system, or transmitted in any
form or by any means (electronic, mechanical, photocopying, recording or otherwise) [illegible] prior written permission of the publisher.
Violators risk criminal penalties and $50,000 damages.