THE CANCER LETTER

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NCI To Fund Study Of Stomach Cancer In Poles, Polish Americans, In Warsaw And Chicago Areas

NCI plans to fund a case-control study of stomach cancer in Polish Americans in the Chicago area and in Poles living in Warsaw to identify the factors that contribute to the elevated rates of stomach cancer in this ethnic group. Stomach cancer is second only to lung cancer as the leading cause of cancer death in Poland. The rate drops somewhat when Poles migrate to the U.S., but the stomach cancer rate in Polish

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In Brief

Clarke, Einstein Lead ACCC; Changes At CCSG, Cohen Leaves USC For Childhood Foundation

ROBERT CLARKE, chief executive officer of Memorial Medical Center, succeeded **Lloyd Everson**, Indiana Regional Cancer Center, as president of the Assn. of Community Cancer Centers at the organization's annual meeting recently in Washington. ACCC members elected **Albert Einstein Jr.**, director of the Virginia Mason Cancer Center, as president-elect. **Diane Van Ostenberg**, Grand Rapids Clinical Oncology Program, is ACCC secretary, and **Carl Kardinal**, Ochsner Cancer Institute, is treasurer. . . . **CHILDREN'S CANCER** Study Group last week changed its name to the Children's Cancer Group. **Denman Hammond** will end his term as chairman after 25 years; **Archie Bleyer**, M.D. Anderson Cancer Center, will become chairman of the group in November. Hammond has created a new charity, the National Childhood Cancer Foundation, based in Arcadia, CA, and will undertake a national fundraising and public relations program to augment the number of research studies in childhood cancer and enhance data management. **Gordon Cohen**, director of public affairs at the Univ. of Southern California's Kenneth Norris Comprehensive Cancer Center, has left the university to become vice president for development for the NCCF and director of communications for the CCG. . . . **ROGER SMITH**, General Motors Corp. chairman, received the James Ewing Laymen's Award of the Society of Surgical Oncology last month in New York City. SSO President **Charles Balch** said the award recognizes Smith's establishment of the General Motors Cancer Research Awards in 1978, which has given more than $4 million to 48 scientists. Smith was treated for cancer in the early 1960s at Memorial Sloan-Kettering. . . . **RUSSELL LASTER**, head of cancer screening at Southern Research Institute, has retired after 40 years in cancer research. . . . **CLIFTON MOUNTAIN**, prof. of thoracic surgery at M.D. Anderson, has received the first Distinguished Achievement Award given by the International Assn. for the Study of Lung Cancer.

NCI To Study Stomach Cancer Risk Among Poles And Polish Americans

(Continued from page 1)

Americans has been estimated at twice the rate of other white ethnic groups.

NCI's Div. of Cancer Etiology plans to issue a Request for Proposals to select a contractor who would assist in conduct of the study in Chicago and in Poland. DCE's Board of Scientific Counselors recently gave concept approval to the study and committed $800,000 over the next four years to fund it.

The board also unanimously approved concepts for three other new contract projects and recompetition of three contracts.

Following are the concept statements:

A case-control study of stomach cancer in Poland and Polish Americans. Concept for a new contract, $800,000 total over four years.

Stomach cancer remains one of the leading cancers in incidence and mortality worldwide, despite its consistent decline in industrialized countries in recent decades. The stomach cancer rates in Poland are among the highest in Europe, and the decline in mortality rates is smaller than those of other countries in Europe and elsewhere. Stomach cancer still is one of the leading causes of cancer death in Poland, second only to lung cancer. Polish migrants to the U.S. also experience high mortality rates of stomach cancer, although the rates are lower than those of the native country. In Chicago, which has the largest population of Polish immigrants served by a cancer registry in the U.S., it has been estimated that Polish born residents have more than a twofold higher incidence of stomach cancer than other white ethnic groups.

The objectives of this project are to evaluate risk factors for stomach cancer in Poland and Polish migrants to the U.S., and particularly to identify those factors that contribute to the elevated rates of stomach cancer in Poland and among Polish Americans.

Support services are sought to assist in the conduct of parallel case-control studies in Warsaw province in Poland where hospital networks have been established and their cooperation in this study have been assured, and in greater Chicago (Cook County, IL). Cases will be residents of each area newly diagnosed with stomach cancer at ages between 20 and 79. Histologic confirmation for all cases will be sought. About 400 cases from Warsaw province, and 200 each of Polish and non-Polish American cases from greater Chicago will be recruited. In addition to the usual case ascertainment from the local cancer registry in each area, a network will be established for rapid identification and recruitment of cases. It is anticipated that the recruitment of cases in Warsaw will take about 12 months and in Chicago about 36 months.

Equal numbers of controls as cases will be randomly selected from the general population, frequency matched to cases in each geographic area by sex and five-year age groups. In Warsaw, voting lists will be used as a sampling frame. These lists provide over 90% registration of Polish citizens age 18 or older. In Chicago, selection of controls will be conducted using telephone random digit dialing for subjects less than 65 years of age, and the Health Care Financing Administration records for those 65-79. Because about 17% of greater Chicago white residents are of Polish descent, respondents will be screened initially with regard to their ethnic background to ensure recruitment of equal numbers of Polish and non-Polish controls.

The cases and controls will be interviewed in person, using a structured questionnaire to elicit information on potential risk factors. For deceased cases or cases who are too ill to participate, their next of kin will be interviewed. Medical records for the cases will be reviewed, and pathologic slides will be reviewed by a study pathologist to confirm diagnoses and classify cases by histologic type and subsite of the stomach, and search for evidence of precursor lesions such as chronic atrophic gastritis. Blood specimens will be collected from a sample of cases and controls for assay of serum antibodies to H. pylori and storage for future assay for genetic susceptibility, including P450IIE1 genotype. In addition, the specimens from controls will be used for assay for pepsinogens and serum nutrients, including vitamin C, retinol, beta-carotene, other carotenoids, vitamin D, and alpha-tocopherol for inter-country and inter-ethnic comparisons. Paraffin-embedded tissue specimens will be collected for detection of prevalent H. pylori infection, and molecular analyses of cancer associated genes, including p53 mutation and allelic loss on chromosome 5q, 1q, and 7p.

Statistical analyses will employ standard methods for case-control data. Summary odds ratios and corresponding confidence intervals will be calculated, with logistic regression models developed for further analysis of multivariate relationships.

It is anticipated that personnel costs for the study in Poland will be provided by the Polish government. The support services organization awarded the contract proposed herein will subcontract with appropriate institutions in Poland to supplement the funding from Poland, and thus enable the investigation in Poland to parallel that in the U.S.

Cancer following bone marrow transplantation. Concept for a new contract, $650,000 over three years.

As the percentage of transplant patients surviving long term has increased, concern has turned to possible late effects of the total body irradiation and intensive chemotherapy used in conditioning regimens, and to late complications of graft-vs-host disease and its treatment.

The objectives of this study are to evaluate the influence of immunosuppression and therapy with TBI and chemotherapy on the risk of new leukemias and lymphomas among bone marrow transplant patients, and to quantify the change in risk over time. The association of cancer risk will be evaluated in light of the intensity of immunosuppression; degree of HLA match; therapy with TBI or alkylating agents alone and in combination; and the

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effect of fractionated versus single dose TBI. The long term potential of these databases to evaluate the risk of solid tumors will be explored. A small biochemical component will examine the usefulness of the glycoprotein-A assay in identifying increased mutation rates related to radiation dose in the surviving stem cells following high dose TBI and to address issues of stem cell survival.

The cohort of bone marrow transplant patients is expected to include between 15,000 and 20,000 patients. It is anticipated that most subjects will be drawn from the IBMTR. By 1995, the number of 5-year post transplant survivors registered is expected to reach 4,700 patients. Approximately 40-50% of patients reside in the U.S. and 50% of all transplants were performed after 1980.

The cost involved with this contract will be that of updating the followup on all transplant patients, identifying new primary cancers, obtaining verification of all second cancer diagnoses, obtaining detailed treatment data and transplant characteristics on selected patients, and obtaining blood and tissue samples for laboratory analysis. It is expected that many patients will maintain periodic contact with the institution performing the transplant due to their unique medical history, and thus we do not anticipate unusual difficulty in locating study subjects, at least in the U.S. Rosters of U.S. patients will be linked to existing national databases. Pathology reports, records of bone marrow examinations, and other reports documenting the second cancers will be requested from participating transplant groups. Although registry records are expected to include summaries of each patient's treatment, GVHD status, and details of post transplant complications, for some patients it will be necessary to access the available medical records for additional information so that treatment and immune characteristics can be accurately quantified.

A small molecular biology study will be conducted to explore the utility of the GPA assay to identify the number of progeny of mutated stem cells that have survived TBI exposure and to explore clinical issues of stem cell survival over time. The GPA assay measures the frequency of rare variant erythrocytes in human blood, which are believed to be the progeny of mutant erythroid precursor cells. Biochemical studies would be partially funded by this contract and would include collaborations with personnel from the Lawrence Livermore National Laboratory, which developed the GPA assay. Bloods on approximately 25 patients taken prior to treatment with TBI and at intervals after treatment will be evaluated.

Data on patients' primary diagnoses and treatment, transplant characteristics, followup, second cancer occurrence, and biochemical tests will be sent to NCI for review and analysis. For each treatment group and other factors of interest, the observed numbers of second cancers will be compared to the expected numbers based on the person years at risk and cancer incidence rates. Survival analysis techniques will be used to compute the cumulative incidence of second cancers, and time dependent Cox proportional hazards regression models will be employed to identify factors associated with disease while adjusting for other variables of interest. The main focus of the analysis will be identifying factor relating to the risk of secondary lymphoma and leukemia, but other second tumor groups with sufficient numbers will also be evaluated. The separate effects of immunosuppression and radiotherapy will be examined. Comparisons will be made between patients treated with TBI and those with aplastic anemia, 50% of whom did no receive radiotherapy. Allogeneic graph recipients who were heavily treated with immunosuppressive therapy will be contrasted with autologous transplant patients who did not receive those treatments.

Exposure assessment of technicians working with magnetic resonance imaging devices. Concept for a new contract in collaboration with NIOSH, $30,000 for one year.

Since the introduction of MRI in the mid-1980s, the technology has grown rapidly, and about 10,000 technicians are currently working at thousands of facilities in the U.S. Technicians are exposed to high static magnetic fields when positioning patients, and can be exposed to the static and RF fields at the bore mouth when comforting an anxious patient during the procedure. In addition, the technicians are exposed to above average EM fields in the extremely low frequency and very low frequency ranges from the MRI's power supply and control panel.

Objectives of this study are: 1) to develop and assess the methodology for measurement of EM field exposures to MRI technicians at MRI facilities; 2) to assess the feasibility of combining measurements, interviews, and record reviews to make exposure estimates adequate for an epidemiological study of technicians; and 3) to determine the feasibility of identifying a cohort of MRI technicians through formation of a registry using existing resources such as accreditation agencies.

According to current research the MRI fields that may have biologic import are: the static magnetic field; the intensity of the oscillating EM fields; transients from rapidly switched magnetic fields; the frequency and specific absorption rat of the RF field; resonant combinations of the static and RF magnetic fields.

A draft protocol will be developed for measuring technicians' exposure to all these EM field characteristics with existing field meters and personal monitors. This complex measurement protocol will be tested at 2-4 MRI facilities. At these same facilities, technicians will be interviewed on work practices. Relevant records such as instrument specifications, imaging protocols, facility plans, and patient logs will be collected. Information from these data sources will be integrated and evaluated as to their relative usefulness in assessing exposures. As a result of these pilot studies, we will recommend exposure assessment protocols and new measurement methods for assessing MRI exposures to technicians.

Inter and intraspecies identification of cell cultures. Recompetition of a contract held by Children's Hospital of Michigan, $2.225 million over five years.

The study of cultured tumor cells of human and animal origin is fundamental to our understanding of the relationship of viruses to the processes by which tumor formation is initiated or promoted.

In this effort, three basic techniques are used either individually or in combination: isoenzyme analysis, immunofluorescent antibody testing and cytogenetic characterization by chromosome and karyotypic analyses. Since the inception of this service 17 years ago, over 4,600 cultures have been examined. During the first three years of the present contract, over 300 cultures have been analyzed per year, with a composite average of approximately 800 tests per month. Not only is the number of tests increasing, but the level of sophistication and detail of the analysis requested is increasing. To maintain the high technological level and quality of the service, the need for newer types of analyses is continually being reviewed. Among the technologies under consideration for this service are the use of biotinylated probe chromosome analysis using either labeled total human DNA or specific chromosome DNA, and restriction fragment length polymorphism (RFLP) analysis in which DNA from different or transformed cell lines will produce different DNA fragment lengths when treated with the same enzyme.

There is a need to continue this service since it is not physically possible or economically feasible for all laboratories using tissue or cell cultures to have expert in-house capability to identify cell lines in use, and since 11% of the lines submitted for

identification are not what the submitting laboratory presumed them to be.

The successful offeror will provide a laboratory and personnel to analyze up to 400 cell lines per year. Submitted cell lines will be cultured and tested as required based on discussions between the contractor and requestor. Detailed reports will be provided to the requestor and to the government. The contractor will maintain a database of the results of tests conducted, and provide semi-annual reports to the government of observed trends in the number and type of cell cultures which are correctly and incorrectly identified by investigators. This contract operates as part of the branch resources payback system, in which the requestor pays a charge for tests, as set by NCI, to partially offset the cost of the service. During the contract year, the payback receipts totalled approximately $118,000, which represents a 25% recovery. Charges for each test are under review, and will be increased so that recovery will be approximately 30-35% of the costs.

Resource for the xenotransplantation of human tissues and cells into athymic nude mice. Recompetition of a contract held by Hazelton Laboratories of America Inc., $1,510,874 over four years.

The primary objective of this project is to provide an effective bioassay system for human cells experimentally exposed to chemical and biological carcinogens in vitro. This contract is an essential component of the research program of the Laboratory of Human Carcinogenesis.

This contract will provide the continuation of a resource for biological assays of 1) the transplantability of treated and untreated normal, premalignant, and malignant human tissues, 2) the effects of carcinogen, anticarcinogen, or gene transfection pretreatment of human tissues and cells in vitro on their growth patterns and cellular integrity as xenografts, and 3) the relationship between carcinogen-DNA adduct formation, activation of proto-oncogenes, and malignant transformation of human tissue in vitro.

Specifically, employing an AALAC-approved, essentially pyrogen-free facility and a license for use of radiation producing substances and equipment, the contractor will provide 1) an enclosed, self-sustaining facility, requiring sterility of all materials and supplies entering and antibacterial showers for personnel, mice to be bred and maintained on a continuing basis, surviving for at least 24 months; 2) methods for the long term (greater than 20 months) survival of human tissue xenografts in x-irradiated nude mice, established in a variety of sites using prescribed implantation methods, and 3) long term animal holding experiments for periods of up to 2 years, with histopathologic analysis of all tumor bearing and/or found-dead animals, 4) weekly updates at NIH of all colony research data in a prescribed LHC designed IBM dBASE-IV database system. The human xenografts will be monitored frequently; at harvest they will be examined in vitro for viability, integrity of tissue specific characteristics, and pathology characteristics, immunological, enzymatic, and karyological analysis for induced transformation, marker and species identification for human tissues grown in nude mice recipients. Some experimental xenografts will be exposed to carcinogens in vivo. All growing xenografts will be measured periodically, transplanted to new mice, characterized histologically and provided to the LHC for in vitro studies at NIH.

Resource for the collection and evaluation of human tissues and cells from donors with an epidemiologic profile. Recompetition of a contract held by Univ. of Maryland (Baltimore), $2,392,916 over four years.

This procurement is the major resource for both collection of human tissues and studies of molecular epidemiology serving the LHC research program. It is required for the collection of normal appearing and neoplastic lung, bronchial, intestinal, colonic, pancreatic and hepatic tissues and cells at the time of surgery for cancer or non-cancer conditions, and at immediate autopsy of non-cancer donors from organ transplant units and shock-trauma sources, or routine autopsy from medical examiner cases. These tissues will contribute to ongoing case-control studies in molecular epidemiology.

The successful offeror will obtain a) approval for the project from the local institutional review board monitoring the protection of human subjects in research, b) the cooperation of the surgery department, the pathology department, the shock-trauma unit, the organ transplant department, and the pulmonary diagnostics services, and the medical examiner's office for permission to contact patients, other area wide volunteers and/or the next of kin for informed consent to collect preoperative diagnostic materials or residual, diagnosed tissues and body fluids, to review the medical charts and to administer a questionnaire for medical, personal, and occupational histories.

The design includes 1) collection of preoperative medical histories and subsequently, nontumorous and tumorous target organ tissues and pleural mesothelium at the time of surgery or autopsy, 2) venous puncture for peripheral blood lymphocytes, red blood cells and sera from smoking and nonsmoking patient volunteers, 3) administering an LHC and EEB designed and OMB approved questionnaire to provide a personal profile for each donor, 4) proven methods for collecting and transporting viable specimens to NIH, and 5) characterization and pathological diagnosis of the tissues by histochemical and immunological methods, light and electron microscopy. For all tissues delivered, tumor marker analysis should include: a) staining (AB/PAS, + or - glycogen) for mucus and adenomatous differentiation, b) immunostaining for keratin and epithelial origin of tumors and differentiation, c) cytoskeletal proteins (i.e., actin, tubulin, calmodulin), growth factors (EFG, EGF receptors, and alpha TGF), hormones (alpha HCG, beta HCG) and oncogene products (ras, raf, myc and erbB-2 protein) and tumor suppressor gene products p53 and Rb. Donors found HIV or HBV positive will be rejected.

The contractor will also recruit and interview volunteer participants to provide biological specimens (blood, urine and tissue) and epidemiological profiles from cases and controls for case-control and prospective studies of the molecular epidemiology of various cancers, especially cancer of the lung.

Synthesis of large amounts of retinoids for experimental chemoprevention of prostate cancer. Concept for a new contract, $1.5 million over five years.

The Laboratory of Chemoprevention has received approval to initiate long term animal studies on the mechanism of prostate carcinogenesis and its prevention by certain pharmacological agents. The laboratory will use an effective rat model, the Lobund/Wistar strain, which is initiated by the carcinogen methylnitrosourea (MNU) and promoted by testosterone propionate (TP). This rodent model provides a good experimental system to: 1) investigate the molecular biology and biochemistry of normal prostatic epithelia and mesenchymal cells as well as preneoplastic and prostatic adenocarcinoma, 2) investigate the biologic changes and identify biomarkers as intermediate end points of prostate cancer for diagnostic and prognostic purposes and 3) identify chemical, biochemical and pharmacological agents such as retinoids and steroid analogs that prevent and suppress the progression of prostate cancer.

The success of these long term animal studies depends on the availability of kilogram amounts of retinoids. The laboratory is

interested in testing certain retinoids in which pharmaceutical companies may have no proprietary interest. This contract will support the synthesis of drugs the laboratory wishes to test for their chemopreventive qualities. The specific retinoids to be synthesized will be determined as the animal project progresses. However, the following is a list of agents being considered:

--N-(4-hydroxyphenyl) all-trans-retinamide
--N-(3-hydroxyphenyl) all-trans-retinamide
--N-(2-hydroxyphenyl) all-trans-retinamide
--N-(4-carboxyphenyl) all-trans-retinamide
--N-(3-carboxyphenyl) all-trans-retinamide
--N-(2-carboxyphenyl) all-trans-retinamide
--13-cis-retinoic acid, and its amide derivatives
--9-cis-retinoic acid
--9-cis-retinoic acid ethyl amide
--9-cis-retinoic acid 4-hydroxyphenylamide
--selected esters of all-trans, 13-cis, and 9-cis retinoic acid

The laboratory plans to conduct 13 experiments per year; 10 with single pharmacological agents and three with a combination of agents. Each experiment will involve 225 rats. Each experiment will require two groups receiving high doses (2 mmoles/kg of diet) of the retinoid and one group receiving a low dose (1mmole/kg of diet).

The DCE board also gave unanimous concept approval to contract for followup of DES-exposed cohorts, which the division has already issued as an RFP (**The Cancer Letter,** April 3).

The board also gave unanimous concept approval to a noncompetitive, interagency agreement that will provide $900,000 over three years to the U.S. Dept. of Energy's Oak Ridge National Laboratory for analytic support for the collection, separation and elucidation of environmental carcinogens including combustion and smoking related exposures.

ACS Adopts 'Measures Of Success' To Mark Progress By Year 2000

The American Cancer Society, having adopted last year a set of "Priorities for the Decade of the 90s," has followed that up with development of "Measures of Success" as a benchmark for measuring progress in addressing the priorities.

The ACS Planning Advisory Council and national board of directors approved at their recent meeting the "Measures of Success" drafted by an ad hoc committee chaired by former President Harmon Eyre. The committee worked for a year, aided by national and division staff and volunteers, ultimately involving 50 of the 57 divisions and 130 separate focus group meetings.

The approved measures cover four ACS core programmatic areas. Eyre's committee decided to delay completion of measures of two other areas--volunteer involvement and Crusade and income development--until a later time. It was determined that the rationale and scientific data for making sound growth estimates in those two areas was insufficient.

The "Measures of Success by the Year 2000," for the four programmatic areas:

Resources, Information, and Guidance (RIG)

Primary Goals:

Increase the proportion of cancer patients (including patients and family members) diagnosed with a new cancer who use American Cancer Society information and referral services to 50 percent from an estimated 20 percent.

Increase the proportion of all other cancer survivors diagnosed with cancer one to five years ago (not including in the past year) who annually use ACS information and referral services to 40 percent from an estimated 10 percent. It is estimated that 50 percent of the 2.9 million current survivors in this category are in need of ACS services.

Enabling Goals:

Increase the proportion of the public that is aware of ACS information and referral services to 50 percent from an estimated 20 percent.

Increase the proportion of the public that is aware of the ACS 800 number to 30 percent from an estimated 14 percent.

Increase the proportion of newly diagnosed cancer patients who are referred to ACS information and referral services by health care providers (initial focus on physicians, social workers and nurses) to 50 percent from an estimated 20 percent.

Increase patient/family member satisfaction with ACS information and referral services to 90 percent from an estimated 75 percent.

Comprehensive School Health Education

Primary Goals:

Reduce the proportion of 9th and 12th grade students who have tried cigarette smoking to 42 percent and 48 percent respectively from 75 percent and 75 percent.

Reduce the proportion of 9th and 12th grade students who smoked cigarettes on 20 or more of the last 30 days (defined as at least one cigarette a day) to 4 percent and 8 percent respectively from 8 percent and 16 percent.

Reduce the proportion of male high school students who use chewing tobacco or snuff to 12 percent from 19 percent.

Increase the proportion of high school students who daily eat no more than two services of selected foods that typically are high in fat content to 80 percent from 65 percent. These foods are defined as hamburger, hot dogs, sausage, french fries, potato

chips, cookies, doughnuts, pie, and cake.

Increase the proportion of high school students who daily consume five or more servings of fruits and vegetables to 35 percent from 13 percent. These are defined as fruit, fruit juice, green salad, and cooked vegetables.

Enabling Goals:

Increase the proportion of states that require schools to implement comprehensive school health education to 75 percent from 56 percent. This is defined as planned and sequential education, at each grade K-12, designed to reduce risk factors, including inadequate diet and tobacco use which substantially contribute to leading causes of morbidity and mortality.

Increase the average proportion of the nation's school districts that require comprehensive school health education to be implemented across each grade range K-6, 7-9, and 10-12 to 90 percent, 75 percent, and 50 percent respectively from 79 percent, 65 percent, and 26 percent.

Increase by 20 percent the average proportion of the nation's schools that implement comprehensive school health education across each grade range K-6, 7-9, and 10-12.

Tobacco Control

--Comprehensive year around campaign driven by concerted fall initiative tied to the Great American Smokeout as its centerpiece.

Primary Goals:

Reduce overall smoking prevalence among adults age 20 or older to 15 percent from 29 percent.

Reduce cigarette smoking prevalence among specific adult high risk target groups:

--To 20 percent from 36 percent for blue collar workers.

--To 18 percent from 34 percent for Blacks.

--To 15 percent from 24 percent for Hispanics.

--To 12 percent from 29 percent for women of reproductive age.

--To 20 percent from 34 percent for people with a high school education or less.

Enabling Goals:

Increase the proportion of cigarette smokers (emphasis on above target groups) who participate in the Great American Smokeout to 50 percent from 33 percent.

Increase the proportion of Smokeout participants who stay off cigarettes for 24 hours to 30 percent from 15 percent.

Increase to 10-15 percent from an estimated 5-10 percent the proportion of Smokeout participants successfully staying off cigarettes for 24 hours who maintain abstinence for at least three months.

Increase the proportion of worksites with 50 or more employees that have a formal policy which prohibits or severely restricts cigarette smoking at the workplace to 75 percent from 27 percent.

Increase the proportion of adult smokers seeing a primary care physician or oral health care provider in the past 12 months who received smoking cessation assistance to 75 percent from an estimated 50 percent.

Breast Cancer Detection

Primary Goal:

Increase the proportion of breast cancers diagnosed stage 1 or earlier to 65 percent from 48 percent.

Enabling Goals:

Increase the proportion of women aged 40 and older who have ever had a mammogram to 75 percent from 40 percent.

Increase the proportion of women aged 40 to 49 who have had a mammogram within the past two years to 50 percent from 20 percent.

Increase the proportion of women aged 50 and older who had a mammogram in the past year to 50 percent from 15 percent.

Increase the proportion of women aged 65 and older who had a mammogram in the past year to 35 percent from 10 percent.

Increase the proportion of primary care physicians who follow ACS mammography guidelines for their patients to 70 percent from 37 percent.

Note: Although ACS recommends mammography for asymptomatic women, the above percentages reflect total mammography use. While indirect estimates of mammography use in asymptomatic women are possible, total mammography provides the best direct basis for surveillance.

ACS Approves New Workplace Intervention Cancer Control Program

The American Cancer Society is sending requests for applications to its divisions this month for development of workplace intervention demonstration projects. The program, which received concept approval at the ACS national board meeting last month, will award planning grants to up to five divisions, to be followed by full scale intervention grants to three divisions, all after competitive peer review.

Planning grants will be for no more than $10,000 each for seven months; intervention grants for up to $100,000 each per year for three years.

Project requirements and restrictions:

A. The projects must reflect a partnership between

an American Cancer Society unit or division, a workplace health promotion program, the employees' insurer, and a community health care provider.

B. The projects must significantly increase the access to and utilization of ACS recommended early detection services, particularly for breast, colorectal, skin, and cervical cancer.

C. Projects must demonstrate improved use of workplace, insurer, and community health care resources to provide detection services. ACS funds are not intended to reimburse for these services.

D. The demonstration project must be carried out in a work setting having sufficient numbers of employees to yield results that are statistically valid and generalizable to other working populations.

E. The project must incorporate an evaluation plan that will provide information on the costs and effectiveness of the intervention. One goal of the evaluation will be to determine whether employer and insurer contributions to the program are cost effective.

F. The projects should be multifaceted and demonstrate innovative and effective use of ACS volunteers in the workplace. The primary roles of the volunteer may be to provide cancer education and as a source of information concerning ACS resources and services.

The successful planning grant application will include:

A. Identification of employer, insurer, and community healthcare collaborators likely to commit to project development and implementation. The number of employees, their demographic characteristics, the extent of collaborator commitment will be significant factors.

B. An orderly planning process that will provide thorough assessment of needs, resources, and opportunities. The planning process must reflect the volunteer driven nature of ACS.

C. Volunteer expertise in cancer control program evaluation and adequate volunteer and division staff to guide program planning and development. Dedicated program staff can be supported in the ensuing project budget, but the planning budgets are intended to support travel, meeting, pilot data collection, and consultant expenses, not staff salary.

The program will be a cancer control demonstration project conducted through the Cancer Control Dept. Program development and direction will be overseen by a workgroup of ACS volunteers who will report to the Medical and Scientific Committee through the Prevention and Detection Committee. Review of proposals will be conducted by the Cancer Control Technical Review Committee.

Waldmann, Columbia, Netherlands Awarded Bristol-Myers Grants

Thomas Waldmann, chief of the Metabolism Branch in NCI's Div. of Cancer Biology, Diagnosis & Centers, last week received the Bristol-Myers Squibb Award for Distinguished Achievement in Cancer Research. The annual prize, which consists of $50,000 and a silver medallion, was presented at a luncheon in New York.

The award recognizes Waldmann for his pioneering studies of the immune system that have led to promising new ways to use monoclonal antibodies to treat leukemias, lymphomas, and autoimmune diseases, and to prevent organ and bone marrow transplant rejection. Waldmann was selected for the award by a panel of cancer researchers chaired by Alan Sartorelli of Yale Univ. He was nominated by NCI Director Samuel Broder.

Broder praised Waldmann for "bridging the gap between molecular biology and the patient." One of Waldmann's "most crucial contributions has been his recognition that the receptor for the IL-2 growth factor that controls the differentiation of immune system T-cells can be used for treatment of a variety of immune diseases," Broder said.

That insight has led to a new treatment currently in clinical trials, for adult T-cell leukemia, which is associated with HTLV-1. Waldmann has been able to extend the survival of patients with the disease. In some instances, patients with a life expectancy of 20 weeks have been able to survive more than two years.

Waldmann used genetic engineering techniques to substitute human components for mouse components in the anti-Tac monoclonal antibody to counter immune response to the antibody. He then added a modified toxin to kill cancer cells.

More recently, he has armed the Mabs with radioactive isotopes to kill leukemia cells. He has received permission to use these latest Mabs in clinical trials.

Waldmann joined NIH in 1956 and became chief of NCI's Metabolism Branch in 1971.

Columbia Univ. Comprehensive Cancer Center was awarded a $500,000 cancer research grant by the Bristol-Myers Unrestricted Cancer Research Grants Program.

Bernard Weinstein, director of the center, plans to use the grant as seed money to fund the work of talented young scientists. The center is a leader in research on the environmental causes of cancer. Weinstein said he believes that nearly 80 percent of all cancers are caused by environmental factors such

as cigarette smoke, diet, chemical pollutants, radiation and certain viruses.

Netherlands Cancer Institute in Amsterdam was awarded a $500,000 grant through the BMS research grants program. The institute is a leader in drug resistance research. Bob Pinedo, director of the institute, said the grant will enable him to start a new program in the clinical applications of molecular biology. One area of Pinedo's interest is how to make tumor cells more sensitive to anticancer drugs.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD.

RFP NCI-CB-21001-32

Title: Master agreement for tumor tissue resources for evaluation of promising diagnostic and prognostic approaches

Deadline: Approximately May 4

NCI is seeking experienced organizations that are able to access and provide large numbers of paraffin embedded tumor tissues (or whenever available, frozen tumor specimens) with associated patient follow-up data to be used for the validation of promising new diagnostic and prognostic assays. The tumor tissue required and the assays to be performed will be defined by Master Agreement Orders issued during the period of performance. The MAOs will be awarded based upon competition among members of the Master Agreement pool. MA holders selected for award shall provide a minimum number of paraffin blocks (and/or frozen tissue whenever available) of breast, colorectal, and/or bladder tumor tissue of specific tumor stages with a minimum number of years of clinical follow-up. MA holders shall perform evaluations of promising new diagnostic and prognostic techniques as defined by individual MAOs. Offerors may qualify to perform one, all, or any combination, of the following methodologies: Flow cytometry studies of cell proliferation, molecular biology studies, and/or immunohistochemical assays. MAs will be awarded to all organizations whose technical proposal is considered acceptable. Multiple MAOs may be issued in each year.

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Program Announcement

PA-92-66

Title: **Exploratory/developmental grants in cancer therapy**

NCI encourages the submission of exploratory/developmental grant applications for new pilot, phase I or phase II, therapeutic clinical trials that take advantage of recent laboratory developments. New and experienced investigators may submit an application to test or develop new treatment strategies or to conduct pilot studies relevant to the following areas of clinical research: (1) treatment of breast, prostate, lung, ovarian, and cervical cancer; (2) therapies to overcome resistance to cytotoxic and biological anti-cancer agents.

This PA supersedes the PA, "Small Grants for Lung, Breast, and Ovarian Cancer Clinical Trials (PA-92-06)."

Applications may be submitted by foreign and domestic, for-profit and non-profit organizations, public and private. Applications may be from a single institution or may include arrangements with one or more institutions.

Support of the program will be through the NIH exploratory/developmental grant (R21) mechanism. The direct costs of an award may not exceed $48,000 per year. The total project period may not exceed two years. These grants are non-renewable and continuation of projects developed under this program will be through the traditional unsolicited grant program.

The purpose of this PA is to encourage applications from individuals who are interested in conducting clinical trials in patients with cancer using new agents or therapeutic approaches. These clinical studies would not be developed fully enough for a standard R01 and would therefore be considered high risk. It is expected that these R21 grants will serve as a basis for planning future clinical research grant applications (R01) or NCI cooperative clinical trial group studies.

Two areas of special interest to NCI have been identified for the solicitation of R21 grant applications. The first area involves solid tumors including breast, prostate, ovarian, and cervical cancer. In addition to these tumor sites, lung cancer has also been included in this PA.

The second area of research targeted in this PA is that involving clinical studies designed to identify and overcome resistance to cancer therapy. A formidable challenge to cancer therapeutics continues to be the emergence and growth of treatment-resistant tumor cells after the initial response to therapy. Recent research efforts concerning this phenomenon have resulted in the identification of a number of genotypic and phenotypic alterations that appear to correlate with the development of resistance to cytotoxic and biological anti-cancer agents. Preclinical efforts have also resulted in the development of new clinical strategies to overcome this resistance. Research directed at correlating the results of laboratory assays of drug resistance with results of clinical trials is an essential step in the development of effective regimens of cancer therapeutics.

The aim of this initiative is to stimulate pilot, phase I, or phase II therapeutic clinical trials to move new treatment strategies more rapidly from the laboratory into the clinic. Clinical studies must involve human subjects and be designed to ultimately improve cancer treatment. The clinical studies must be based on a strong rationale and preclinical data should support the underlying hypothesis. The research plan should be focused on the clinical trial proposed. Laboratory studies to address the mechanism of action of agents utilized in the clinical studies or pharmacology studies may be included, but are not necessary.

Applications must be focused on one of two research areas for this Program Announcement:

1. Pilot, phase I, or phase II clinical trials for the treatment of breast, lung, prostate, ovarian, or cervical cancer. New therapeutic studies utilizing drugs, biologics, radiation, or surgery, whether used as a single agent/modality or in combination are appropriate.

2. Pilot, phase I, or phase II clinical trials directed at investigating specific strategies for overcoming or reversing clinical resistance to cytotoxic and biological anti-cancer agents. Inclusion of assays to measure phenotypic or genotypic alterations correlated to resistance are appropriate. The clinical trials can be focused on any type(s) of carcinoma.

Written and telephone inquiries are encouraged and may be directed to Diane Bronzert, Program Director, Cancer Therapy Evaluation Program, Div. of Cancer Treatment, National Cancer Institute, Executive Plaza North, Room 734, Bethesda, MD 20892; phone 301/496-8866, fax 301/480-4663.