THE CANCER LETTER

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Senate Committee Adds $200 Mil. To NCI Request For FY92; Centers, Women's Health, Targeted

Sen. Ernest Hollings (D-SC) pushed an amendment to the NIH budget through the Senate Appropriations Committee last week that would give NCI the largest increase it has received in a decade and raise NCI's FY 1992 budget to a record $2 billion. The committee approved a Labor, HHS, Education appropriations bill that included $1.825 billion for NCI, a $15 million increase over the President's request of $1.81 billion. The Hollings amendment added another $185 million, which, together with

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In Brief

New San Antonio Center Wins Core Grant; ASCO Forming A Technology Assessment Committee

NEW CANCER CENTER: The Institute for Cancer Research and Care in San Antonio, TX, has been funded for the first time as an NCI clinical cancer center, making it the newest of 57 NCI designated cancer centers. ICRC was created in May 1990 as a cooperative effort between the Cancer Therapy and Research Foundation of South Texas and the Univ. of Texas Health Science Center at San Antonio. Charles Coltman is the director of ICRC. The new center will receive $951,032 for the first year of a three year cancer center support grant. Five major programs make up the center, representing coordinated efforts in breast cancer research, clinical investigations, drug development, growth factor research, and molecular genetics. . . . **TECHNOLOGY ASSESSMENT COMMITTEE** is being formed by the American Society of Clinical Oncology to examine new technologies. Rodger Winn, M.D. Anderson Cancer Center, is chairman of an ad hoc committee formed to establish policies and procedures for a formal committee. Other committee members are Jane Henney, Univ. of Kansas; Jerome Yates, Roswell Park; Carl Kardinale, Ochsner Clinic; Robert Bast, Duke Univ.; and Gregory Burke, FDA. . . . **ALFRED HAYNES** was selected chairman of NCI's Div. of Cancer Prevention & Control Board of Scientific Counselors. He replaces Edward Bresnick, whose term recently expired. . . . **CHARLES SMART** has retired as chief of NCI's Early Detection Branch. Smart came to NCI in 1985 from the Latter Day Saints Hospital in Salt Lake City, where he was chief of surgery. He was instrumental in the creation of the NCI working guidelines for the early detection of cancer and in getting NCI to agree with American Cancer Society guidelines so that the two spoke with one voice to the public with regard to screening. He returned to Salt Lake City where he will be working at the Utah Cancer Registry. **Barnett Kramer** was named acting chief of the branch.

Hollings Amendment Boosts NCI Budget $200 Mil. Above Request

(Continued from page 1)

the committee's bill, would give the Institute an FY92 budget of $2.01 billion. That is an increase of $296 million over NCI's FY91 operating level of $1.714 billion.

The figure of $200 million above the President's request was targeted by cancer program advocates in budget hearings this spring as the amount necessary to restore the Institute's budget to its 1980 level as measured in constant dollars. The effort was organized and led by the National Coalition for Cancer Research.

In its report on the budget, the committee urged NCI to put part of the increase toward cancer center core grants, and basic and clinical research in breast, ovarian, and cervical cancer, among other areas.

"It is critical to the people of South Carolina as well as the nation that America maintain its leadership in cancer research," said Hollings in a statement issued last week.

"My amendment to restore American leadership in cancer research is especially important to South Carolina, which leads the nation or is in the top three states in mortality from cancer of the prostate, cervix, esophagus, pancreas, head and neck, and multiple myeloma. This funding is a crucial investment in the health of our citizens."

Since passage of the National Cancer Act of 1971, the cancer survival rate has gone from 39 percent to 52 percent, Hollings said. "Over 7 million people are alive today because of this research. However, we have a long way to go and Cancer Institute funding has been slipping," he said. Budget increases for NCI over the past decade have fallen behind increases to the other institutes, and funding for cancer centers has fallen more than 30 percent in real terms. "We will lose in the long run both financially and in the lives of our citizens without this investment."

Last month the House Appropriations Committee added $20 million above the President's request to NCI's FY92 budget (**The Cancer Letter,** June 28). The final figure will be determined in conference between the House and Senate in a few months. In the meantime, Hollings will have to win over the powerful chairman of the House Labor, HHS, Education Appropriations Subcommittee, Rep. William Natcher (D-KY).

The additional funds in the Hollings amendment cannot be made available to NCI until the last day of FY92, that is, Sept. 30, 1992. According to Senate sources and cancer program advocates, this was done because the committee had extra budget authority available, but had used up its available funds, or outlay authority.

The Senate bill allocated $8.959 billion for NIH overall, the same amount requested by the Administration. That amount does not include the nearly $185 million added to NCI.

In its report, the committee noted that this year is the 20th anniversary of the National Cancer Act, "legislation which committed the nation to a public/private partnership of research, education, and prevention."

The committee said it expects the $185 million in additional funds "will be used to maintain a balanced program in our cancer research efforts and address the increasing incidence and death due to cancers which commonly afflict men and women, especially older Americans and minorities."

Following are topics the committee highlighted:

▶Program project (P01) grants--"Emphasis on the number of new and competing awards must not jeopardize funding mechanisms that advance scientific progress," the committee said. "The committee is distressed that NCI is considering eliminating program project grants in an effort to demonstrate an overall greater number of awards [Ed. note: NCI executives have not publicly said P01s would be "eliminated," but have pointed out that grant funding targets set by Congress make funding the large P01s difficult. In FY91, NCI has been able to fund nearly the same number of P01s as the previous year by using "exception" funding. See **The Cancer Letter,** June 21]. The P01 mechanism has played an essential role in the transfer of basic research findings to bedside practice. The committee recognizes that funding

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limitations make it difficult to both support P01s and reach the target levels set for new and competing awards, and, therefore, feels that numerical goals for grants should not force the elimination of useful mechanisms of research."

▶Research project grants--The committee said it "supports the use of traditional investigator initiated grants, particularly research project grants, to facilitate the rapid translation of state of the art prevention and treatment research conducted through clinical trials into widespread clinical practice. NCI should also seek alternative means to disseminate important research results from clinical trials to reduce the delays associated with publication of clinical data in major peer reviewed journals."

▶Cancer centers--"A strong cancer centers program is essential to NCI. NCI will continue to support excellent centers and will seek to achieve greater geographic diversity. The committee urges that, within available funds, there be no reduction in the number of centers and that centers be provided with appropriate inflation adjustments.

"The committee learned that funding for NCI supported cancer center core grants has decreased by 14 percent between 1980-91, measured in 1980 constant dollars. And yet, it is the administration's position that the diversity and strengths of the cancer centers represent the most reliable and most productive research and outreach element of the National Cancer Program, and furthermore, that 50 percent of all the laboratory and clinical trials supported by NCI take place in institutions with cancer centers.

"Several years ago this committee requested a study of the NCI cancer centers program by the Institute of Medicine, which recommended that the National Cancer Institute strengthen its core support of cancer centers in order to exploit fully the application of these advances in the prevention and treatment of cancer and its consequences. The committee expresses its serious concern about this matter and urges NCI to take appropriate budgetary actions to remedy this situation. Appropriate portions of the increases for NCI should be used for this purpose."

▶Women's health--The committee included a $40 million increase for expanded research on breast, ovarian, and cervical cancer. "The committee urges that this priority be reflected throughout NCI's basic research efforts, education and information dissemination activities, cancer centers, and the proportional representation of women in all NCI supported clinical trials."

A total of no less than $132 million is to be made available for breast cancer research, $30 million more than requested. Of that, $20 million should be made available for basic breast cancer research and $10 million is to be used to establish up to six specialized breast cancer research centers, through the P50 grant. The committee also asked NCI to conduct longitudinal studies on the potential adverse side effects associated with silicone breast implants, particularly those used for breast reconstruction after mastectomy or injury.

At least $31 million is to be made available for cervical cancer research, $5 million more than requested. At least $17.5 million is to be spent on ovarian cancer research, $5 million more than requested. The committee asked that these amounts be increased with additional funds from the NIH Office of the Director for Women's Health.

▶Synthetic estrogen DES, which was prescribed to 5 million pregnant women from 1941-71, and is linked to reproductive tract anomalies in children and clear cell adenocarcinoma in daughters. The committee said it was concerned that DES research had declined and asked for longitudinal studies of those exposed to DES.

▶Cancer prevention and control--The committee singled out the Community Clinical Oncology Program for its "critical role in NCI's clinical trials network by bringing together community cancer specialists, primary care physicians, and other health care professionals. These efforts are strengthened by the minority based CCOPs which provide minority populations with increased access to state of the art therapy through clinical trials and cancer prevention and control research. The Committee is concerned that CCOP be funded at $16.5 million and funds not be diverted for other purposes, such as the tamoxifen trial."

▶Prostate cancer--The committee included an additional $3 million for prostate research, but gave the funds to the National Institute on Diabetes, Digestive & Kidney Diseases, and directed the two institutes to work together.

▶Cancer vaccines--The committee urged NCI to "explore and develop innovative approaches" to cancer vaccines for primary and secondary prevention. "The Institute is encouraged to use the full breadth of molecular biology, immunology, tumor biology, and its clinical trials apparatus to bring about testable vaccines as rapidly as possible." NCI is directed to use funds from the budget increase for this effort.

▶Retrovirus research--Retroviral infections in large domestic animals are "excellent models for retroviral induced diseases such as leukemia lymphosarcoma and AIDS in humans," the committee said, noting that Iowa State Univ. would be a possible location of a

retrovirus research center. [Senate Labor, HHS, Education Appropriations Subcommittee is chaired by Sen. Tom Harkin (D-IA).] Up to $1 million should be made available for such a center, the committee said.

▶International collaboration--"To maximize our current international efforts and capitalize on new opportunities, the committee urges the Institute to more aggressively pursue international collaboration in cancer prevention, with special emphasis on training and information dissemination." The committee expects a plan in six months for such programs.

▶Cancer in Native Americans--The committee said it was pleased by NCI's effort to address the cancer control needs of Native Americans in organizing a conference on the subject in October 1989. Data indicate that American Indians experience excessive cancer incidence for stomach, cervix, primary liver and gallbladder. Survival rates also are low for colon, breast, cervix, and prostate cancers.

However, the committee said that none of the funding it provided last year, $9 million, for an initiative for Native Americans, has been awarded, possibly due to the absence of quality research proposals. The committee urged NCI to organize four research training events "which emphasize development of technical skills, training in research methodology and education, and proposal development in fiscal year 1992."

▶Behavioral research--The committee encouraged NCI to "expand its portfolio of health and behavior research in the areas of smoking cessation, especially of women and minorities, the impact of dietary fat modification on breast and colorectal cancers, interventions on moderating exposure to ultraviolet radiation, and screening and detection of breast and cervical cancers." The committee also urged NCI to continue to explore the impact on survival and quality of life from psychosocial counseling for cancer patients.

▶Pediatric AIDS--The committee provided an additional $4 million for pediatric AIDS research.

▶Neurofibromatosis--The committee included an additional $3 million in the budget of the National Institute of Neurological Diseases & Stroke for NF research, and directed NCI to work with NINDS.

Other topics the committee discussed: The need for NCI to continue outreach efforts to reach disadvantaged populations on the importance of prevention, early diagnosis and treatment; the need for highly trained cancer researchers and expansion of NCI's Science Enrichment Program for minority high school students; NCI development of taxol in cooperation with Bristol-Myers Squibb; and continued expansion of gene therapy research.

DCE Advisors OK $10.8 Million Worth Of Competitive Research Contracts

Advisors to NCI's Div. of Cancer Etiology gave concept approval recently to the recompetition of nearly $10.8 million worth of research and supply contracts. Among the largest are two contracts worth more than $3 million each for provision of materials needed by the DCE's Laboratory of Tumor Cell Biology.

DCE's Board of Scientific Counselors unanimously approved all of the concepts, presented at its recent meeting. Following are the concept statements:

Provision of Hematopoietic Cell Cultures, Growth Factors and Retroviral Proteins. Recompetition of contract held by Advanced BioScience Laboratories Inc. Total $3,062,730 million over four years.

The Laboratory of Tumor Cell Biology has a commitment to research on human immunodeficiency virus and AIDS. Recently, these studies have moved toward the study of the role of HIV in AIDS-associated Kaposi's sarcoma (KS), the development of diagnostic and therapeutic reagents for AIDS and a program to develop an effective vaccine against HIV infection and against progression to AIDS in HIV infected persons. The Laboratory is also conducting research on HTLV-I, focusing on its possible involvement as a co-factor for progression to AIDS in HIV-1/HTLV-I doubly infected people and on its involvement in neurological diseases such as tropical spastic paraparesis. There are also ongoing studies into the possible involvement of HIV and/or HTLV regulatory gene products in disease development.

There has been particular emphasis on the study of AIDS-related KS. Efforts have been directed at defining the malignant cell type, the role of HIV-1 in the disease, the role of viral or cellular factors in KS cell proliferation, factors produced by the KS cells which may contribute to growth of the KS lesion (which is composed of multiple cell types), development of a small animal model for in vivo KS studies and identification of drugs which are effective in blocking KS cell growth.

This contract was established in 1987 for three major purposes: (1) to provide purified and partially purified growth, differentiation or possible immunoregulatory factors from conditioned media (CM) produced by culture of a variety of cell types, (2) to provide cultured cells from cord blood, adult peripheral blood or other hematopoietic tissue, including long term cultures of lymphocytes and monocyte/macrophages, and (3) to purify retroviral proteins and cellular proteins to homogeneity and produce monoclonal antibodies to them.

Objectives: (1) To provide the capability to purify the KS cell growth factor currently under study, and other factors which may be found by the LTCB to be capable of promoting the growth, differentiation or regulation of human hematopoietic cells, bone marrow progenitor cells, endothelial cells or other normal or malignant target cells. The contractor shall also conduct functional assays for the factors, produce polyclonal and monoclonal antibodies to the factors and provide primary structural analysis, especially amino acid sequence analysis preliminary to the cloning of the gene(s) for the factor(s) by LTCB staff.

(2) To provide the capability to produce the KS growth factor (and, during the course of the contract, perhaps other cellular growth/regulatory factors or proteins and/or viral proteins) in a

bacterial or mammalian expression system.

(3) To purify, to chemical homogeneity, proteins from viruses, growth factors and other proteins from cells, and proteins produced in recombinant expression vector systems. Polyclonal and/or monoclonal antibodies to the purified proteins will also be produced.

(4) To provide cultured cells for use in various virus isolation and analysis studies and studies involving cellular growth factors and regulatory factors.

(5) To provide the capability to screen recombinant immunoglobulin gene libraries (produced by LTCB) for expression of specific molecularly cloned human antibodies and to produce the cloned immunoglobulins. This will provide the capability, for example, to produce sizeable quantities of neutralizing antibodies to HIV-1 and HIV-2 and to produce antibodies against HIV and HTLV-I regulatory gene products for studies of the in vivo role of these proteins in virus expression and disease progression.

Detection and Characterization of Virus, Viral Antibodies, Viral Proteins and Cellular Proteins. Recompetition of contract held by Advanced BioScience Laboratories Inc. Total $3,425,523 over four years.

This contract provides a variety of services, tests and assays to detect and/or characterize viruses, antibodies, cells, growth factors, cytokines and other regulatory factors in support of several Laboratory of Tumor Cell Biology programs.

Assays, tests and services provided include: ELISA, Western bolt, Radioimmunoprecipitation (RIP), Radioimmunoassays (RIA), Immunofluorescent assays (IFA), Cell phenotyping, Virus neutralization assays, Syncytium inhibition assays, Reverse transcriptase assays, Antigen capture assays, Growth factor and cytokine activity assays, Assays of cell growth in response to factors, Production and concentration of viruses

This contract will provide immunological testing for detection and characterization of viral antibodies from infected humans and animals. It will provide assays (such as antigen capture assays, reverse transcriptase assays, neutralization assays, RIP, RIA, IFA and PCR assays) for detection and characterization of biologically active virus, viral proteins or viral nucleic acids in cell cultures and tissues.

This contract will provide assays for characterizing viral proteins, including the processing of viral proteins and analysis of the carbohydrate portions of envelope glycoproteins. It will provide assays in support of studies on viral receptors and characterization of viruses and host cells.

Assays for growth factor activity and for detection of various growth factors and cytokines will be available to LTCB under this contract. This contract will produce moderate amounts of virus to be used in vaccine studies and to provide reagents for many of the assays for virus and antibody detection.

Preparation and Supply of Fresh and Cultured Mammalian Cells. Recompetition of contract held by Biotech Research Laboratories Inc. (now called Cambridge Biotech). Total $405,150 over four years.

This contract was established in 1987 to provide support for several LTCB research programs. The contract provides the capability to supply cultures of normal cells, neoplastic cells and mammalian tissue culture cell lines, both uninfected and infected with retroviruses. It also provides for the supply of human peripheral blood and bone marrow samples, either fresh or after short term culture and for the performance of reverse transcriptase assays on cultures. This contract provides for the receipt, processing, distribution and storage of fresh human cells and tissues as well as for the storage and maintenance of tissue culture cell line stocks and hybridoma stocks.

This contract will provide tissue culture support for research conducted at the LTCB. It will provide fresh and/or cultured human peripheral blood, bone marrow and cord blood cells as needed. It will provide cultured cell lines, including providing gram quantities of a variety of tissue culture cells as required. It will provide the capability of culturing viral-infected cells, including cells infected with human retroviruses.

The contract will provide liquid nitrogen storage of fresh cells and tissue culture cell line stocks.

Production of Purified Recombinant Human Viral Proteins in E. coli. Recompetition of contract held by Pan-Data Systems Inc. Total $378,000 over three years.

One of the expanding areas of research in the LTCB involves the study of human retroviral (HIV and HTLV) regulatory gene products and their role in pathogenesis. Studies have shown that Tat protein can be released by HIV-1 infected cells and stimulate the growth of Kaposi's sarcoma (KS) derived spindle cell lines in tissue culture. This stimulation can be blocked by monoclonal antibodies to Tat. These in vitro findings indicate Tat may play a role in vivo in AIDS associated KS development.

In light of these findings, it was decided to examine the effects of HTLV-I regulatory proteins Tax and Rex. This contract was established in 1989 to produce milligram quantities of purified HTLV-I Tax and Rex as well as antibodies to these proteins.

Objectives of this contract are:

(1) To obtain milligram quantities of purified, biologically active HIV-1 Tat protein produced in a recombinant vector in an E. coli expression system.

(2) To obtain monoclonal antibody to HIV-1 Tat which will block Tat biological function.

(3) To obtain milligram quantities of purified, biologically active HTLV-I Tax protein and Rex protein produced in recombinant vectors in an E. coli expression system.

(4) To produce monoclonal antibodies to HTLV-I Tax and Rex which will block the activity of these proteins.

Genetic Factors in Patients at High Risk of Cancer: DNA Polymorphisms for Linkage Analysis. Recompetition of contract held by Integrated Genetics Inc. Total $1.832 million over four years.

In June 1986, the Board approved a concept which funded two five-year contracts for gene mapping studies: one with Integrated Genetics Inc. for the assay of DNA polymorphisms, and one with UCLA for protein polymorphisms. The funds obligated to UCLA totaled $213,234; those for the two contracts combined totaled $2,010,167. Over the last four years the number of available DNA polymorphisms has increased dramatically; consequently, we have utilized the contract for DNA studies much more heavily than that for protein studies. When the UCLA contract terminates in Sept. 1992, we do not plan to recompete it. Rather, we will use a new contract for DNA polymorphisms as our main gene mapping resource.

The purpose of this contract is to map genes causing cancer to specific chromosome regions through the analysis of familial segregation patterns of cancer or preneoplastic syndromes in conjunction with those of DNA restriction fragment length polymorphisms (RFLPs) with known chromosome locations. Analysis of DNA polymorphisms will also be used to verify that fibroblast or tumor cell lines obtained by NCI for a variety of laboratory investigations have not been mislabelled or cross contaminated. Occasionally, analyses of polymorphic markers may also be needed to determine zygosity in cases of multiple births and to assess paternity in studies other than linkage

analyses in which verification of biologic parents is essential.

We shall submit to the laboratory specimens on approximately 150 persons per year from families in which a known or suspected Mendelian trait is segregating which causes or is associated with cancer. Ideally, the families should have multiple living affected members and specimens should be obtained from both affected and unaffected individuals. DNA from each individual will be assayed for RFLPs by hybridization with a large series of probes whose distribution covers every autosomal chromosome arm. The accuracy of the assay results can be verified by inspection of the data from parents and offspring for internal (genetic) consistency. Cases suggestive of non-paternity will be excluded from analysis. The assay results will be tabulated and sent to NCI for linkage analysis by our staff in conjunction with the pedigree data. There are several persons with expertise and experience within the Program in using the analytic methods for linkage analysis as implemented in the computer programs LIPED, LINKAGE, SERIATE, MAPMAKER, etc.

Efforts over the last year of the current contract and the first year of the new contract will focus on studies of CMM/DN and NBCC. For each of these projects the families for study have already been identified and many of the DNAs have been prepared and are ready for RFLP analysis. Once these two disorders are in the final phases of analysis, we will start studies of four families with chronic lymphocytic leukemia (CLL) and ten with Hodgkin's disease (HD). Our efforts in CLL will focus on chromosome 12, as trisomy 12 is the most common cytogenetic finding in CLL cells. Our work in Hodgkin's disease will address RFLPs in the HLA region on chromosome 6, since there is evidence of involvement of this locus in HD etiology. Other future plans include collection and analysis of 16 already-identified ovarian cancer families in an effort to locate and map cancer susceptibility genes in these pedigrees.

Operation and Coordination of a Nationwide, Multiple-study, High-volume Death Certificate Acquisition and Management System. Recompetition of contract held by Westat Inc. Total $775,000 over five years.

Staff members in the Epidemiology and Biostatistics Program formulate hypotheses concerning the environmental and host determinants of cancer. Using various data sources, the hypotheses are tested by analytical studies such as cohort (follow-up) and case-control studies. Data for "exposed" subjects are obtained from hospitals, clinics, unions, professional organizations, cancer registries, governmental agencies, and other organizations. The quality of many studies depends on knowledge of the vital status of study subjects.

The exact number and nature of studies that will require support cannot be accurately projected at this time. It should be noted, however, that many studies are currently ongoing within the Epidemiology and Biostatistics Program. In the area of occupational epidemiology, cohort studies are under way to investigate a wide range of exposures, including acrylonitrile, formaldehyde, pesticides, organic and inorganic dusts, metal fumes, and organic solvents (e.g., trichloroethylene, perchloroethylene, methylene chloride, benzene, benzidine). Some of the activities in the area of radiation epidemiology include: a survey of breast cancer among women treated for scoliosis; an evaluation of the use of low-dose radiotherapy to treat uterine bleeding; long-term follow-up of patients who received multiple chest fluoroscopies during lung collapse therapy for tuberculosis; a study of patients treated for hyperthyroidism with radioactive iodine; and others.

This concept provides for the recompetition of a contract under which an experienced firm will independently furnish all the services, qualified personnel, material, equipment and facilities necessary to acquire and process death certificates, as described below.

The NCI Project Officer provides the contractor with lists containing all pertinent information available for each deceased subject, such as date of death, town or city and/or state of death, as well as other known personal identifiers (social security number, sex, date of birth, race, last known address, occupation, etc.). The contractor will acquire large numbers of death certificates from Vital Statistics Offices of all 50 states, using an automated acquisition system to maintain detailed information on the status of all searches in progress. The contractor will request an average of 12,000 death certificates per year from multiple Vital Statistics Offices. This will be accomplished by making three to four annual submissions of roughly equal size.

Over the past 5 years, a total of approximately 60,000 death certificates have been requested through this contract mechanism. Attachment 3 provides a partial list of publications for which death certificates were acquired under the current contract.

Continuation of Follow-up on Participants in the Breast Cancer Detection Demonstration Project. Recompetition of contract held by Westat Inc. Total $900,000 over three years.

The proposed study is a continuation of a follow-up study on a sample of 64,185 of the 280,000 women who participated in a five-year multicenter breast screening program, the Breast Cancer Detection Demonstration Project, conducted during 1973-1980. This sample was chosen to include all women who had a breast cancer diagnosed while they were in the screening project (4,275), all who had a biopsy or aspiration that was determined to be benign (25,115), all who had a surgical evaluation recommended by the project but did not undergo biopsy (9,629), and a sample of those who had neither surgery nor a recommendation for further evaluation (25,166).

The follow-up study to date has been done in two phases. The first phase, initiated at the end of the screening program, involved yearly telephone interviews to obtain information on the known or suspected breast cancer risk factors. In addition, information on physical, mammographic, and thermographic breast examinations and reports of any breast procedures since the end of the screening program or since the last interview were obtained. Baseline interviews for the first phase were completed by 61,437 of the 64,185 study subjects. A total of 60,079 of these subjects were traced as alive as of 1987 and were eligible for the second phase of the follow-up study, which involved a mailed questionnaire sent in 1988-1989.

Continued follow-up of this cohort would be valuable both with respect to issues of prevention (e.g., survival of screening-identified cases, persistence of use of screening, identification of very high-risk groups for screening) and etiology. For this reason the study will be a collaborative effort between DCE and the Div. of Cancer Prevention & Control, with each division contributing one-half of the study costs.

Proposed is an additional follow-up in 1993-1994 of the 58,371 women thought to be alive based on phase II of the follow-up study. The purpose is to determine the occurrence of a number of endpoints since the last questionnaire and to update exposure information. Information on the following endpoints will be sought: breast procedures (including both benign and malignant outcomes), other cancers, gallbladder disease, diabetes, heart disease, colon polyps, osteoporosis, fractures after age 45, hospitalizations for other conditions, and mortality. Exposure and outcome information will be obtained by a mail questionnaire. After several attempts have been made to obtain the information by mail, telephone interviews will be pursued among non-

responders. For any cancers or breast operations reported, surgeons and hospitals will be contacted to obtain copies of the hospital discharge summaries and pathology reports. For any subjects found to be deceased, copies of death certificates will be requested.

Completed questionnaires were obtained for 51,696 (86 percent) of the participants eligible for the second phase of the follow-up study. Questionnaires were not obtained for 1,708 participants (3 percent) who were deceased, 505 (1 percent) who were too ill to be interviewed, 1,459 (2 percent) who refused, and an additional 4,711 participants (8 percent) who could not be contacted by the end of the follow-up period.

At present 1,795 cases of breast cancer have been reported during the follow-up; 997 were reported during phase I and 798 during phase II. Combined with the 1,226 cases expected in the proposed continuation of the follow-up, this study would yield a total of 3,021 breast cancers. Approximately 293 colorectal cancers, 286 endometrial cancers, and 104 ovarian cancers were also reported since the start of the follow-up study in 1979. Together with the cases expected to develop in the proposed continuation of the study, there would be a total of 807 cases of colorectal cancer, 551 cases of endometrial cancer, and 245 cases of ovarian cancer. Approximately 14 percent of the cohort (7,043 women) who responded to the phase II interview reported ever having been diagnosed with gallbladder disease, 6 percent (2,900) with diabetes, 9 percent (4,838) with heart disease, 6 percent (3,177) with colon polyps, 8 percent (3,989) with osteoporosis, and 13 percent (6,844) with fractures after the age of 45. Hospitalizations since the last interview for other conditions were reported by 18 percent of the cohort (9,256 women).

Information collected during the second phase of the study demonstrates sufficient exposure among women in the cohort to factors of interest to allow for their adequate evaluation. For example, 42 percent of the cohort ever smoked, 10 percent reported having a mother and 13 percent a sister with breast cancer, and 20 percent reported use of menopausal hormone pills since their last interview, with 15 percent reporting ever taking estrogen and progestin pills in the same month. Fifty-one percent of the cohort also reported engaging in vigorous physical activity at least once a week.

A number of analyses using data from the follow-up study are underway or have been completed. Analyses are in progress to assess survival in screening-detected vs. interval-detected cases during the screening program. A variety of factors in the etiology of breast cancer are also being investigated. For example, follow-up of the women with various types of benign breast disease diagnosed during the screening program showed relative risks for subsequent breast cancer of 1.5, 1.9, and 3.0 associated with non-proliferative disease, proliferative disease without atypia, and atypical hyperplasia, respectively.

Using mammograms available from the screening program, analyses are also underway to assess the interactive effects of mammographic parenchymal patterns and family history of breast cancer on subsequent risk of breast cancer. The effects of exogenous menopausal estrogen use and reproductive factors on risk of breast and colorectal cancers are also being evaluated. Based on ten years of follow-up, preliminary results on the effect of menopausal estrogens on all-cause mortality indicate that women reporting ever having used menopausal estrogens at the start of follow-up have a relative risk of 0.77 (95 percent CI, 0.6-0.9) compared to non-users. The reduction in risk appears limited to recent users (RR=0.64), with no additional protection conferred with increasing years of use, even among women taking estrogens for more than 12 years. The decreased risk associated with estrogen use is also restricted to women with low family incomes, suggesting that social class differences between estrogen users and non-users may account for part of the observed protection.

Advertising Orders Still Accepted For Special 20th Anniversary Issue

Orders for advertising space in the special publication, "The National Cancer Act of 1971: 20 Years of Progress as Reported in **The Cancer Letter**," are still being accepted. The deadline for advertising copy is Aug. 15, but commitments for space should be made as soon as possible before then.

To reserve space and for further information, phone **The Cancer Letter** at 202/543-7665; fax, 202/543-6879; or write to PO Box 15189, Washington DC 20003.

The publication will include a year by year summary of **The Cancer Letter's** coverage of the National Cancer Program since passage of the National Cancer Act of 1971, plus an index of each issue. It will be printed in full color on coated paper, and will be distributed to all subscribers and to others involved in cancer research and treatment, with a guaranteed distribution of at least 10,000.

Copyright Violation Of Cancer Letter Results In "Substantial" Payment

A substantial cash payment has been made to The Cancer Letter Inc. by an organization which admitted it had photocopied complete issues of **The Cancer Letter** over a period of more than three years. The payment was a negotiated settlement of the copyright violation.

Amount of the settlement and identity of the organization were not revealed, under terms of the agreement.

"We intend to vigorously defend our rights under the copyright laws," Cancer Letter Editor Kirsten Goldberg said. "We always give permission for copying single articles from our newsletters as long as appropriate credit is given. But we absolutely refuse to permit copying or reproducing entire issues. Most of our subscribers understand our reasons for this policy and comply with it and the law. The few who do not are not fair to the rest. Our subscription price is modest compared with the industry average for a weekly newsletter. Any dilution of our subscription base eventually will be reflected in a higher price."

Companies, centers, clinics, and other organizations where several persons read **The Cancer Letter** meet that need by passing it around with a "buck slip." If that is not convenient, or if there are too many

individuals for that to be feasible, "additional subscriptions are not much more costly than photocopying when staff time is considered, they are legal, and they certainly are cheaper than defending against copyright infringement," Goldberg said.

Each issue of the newsletter contains a statement on page 2 prohibiting reproduction, plus the notice that violators are subject to statutory damages of up to $100,000 for each work violated, and that criminal penalties may apply in certain circumstances.

"We have also publicized each instance of violations we have discovered, so our policy and the consequences of violating it should be clear to everyone," Goldberg said. "We were disappointed to learn that some still do not consider such violations serious."

RFPs Available

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

RFP NCI-CP-21000-21

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

Deadline: Aug. 29

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

1) Separation and viable cryopreservation of blood mononuclear lymphocytes, 2) separation, aliquotting and storage of serum, plasma and/or urine as needed, 3) cryopreservation of bone marrow samples, 4) storage of tumor extracts, 5) cryopreservation of whole tumor tissue, 6) cryopreservation of intact red blood cells, 7) viable cryopreservation of previously established lymphoblastoid cell lines, 8) storage of DNA and other biological materials as specified by the project officer, 9) extraction of DNA from biologic materials, 10) logging in, labeling and tracking of each vial of each sample employing an NCI developed computerized specimen tracking system, including all laboratory safeguards to ensure the fidelity and purity of each sample, 11) maintenance of the repository containing 300,000 biological specimens and 12) allowance for an estimated increase of up to 25 percent of freezer storage space.

The contractor shall, for example, provide messenger service for pick up of specimens for interlaboratory communication from medical care facilities in the Washington DC area, be responsible for recording and monitoring shipping and receiving of specimens to minimize delay or loss, maintain a repository of biologic specimens which shall include frozen serum, plasma, urine, tumor tissue, tumor tissue extracts, whole red blood cells, separated and frozen white blood cells or fractions of white blood cell populations, bone marrow cells, body fluids, lymphoblastoid cells lines, DNA, stool specimens or smears on slides and other types of specimens as specified by NCI, provide and train primary and backup staff in the operation of a computerized record system for specimens which has been developed and furnished by NCI, prepare a variety of specimens for storage, utilize freezers equipped with a stylus recording system indicating consistency of temperature, maintain a central alarm system monitored 24 hours a day, 365 days a year, keep clear records of all manipulations on all specimens and carefully document specimen type, volume, cell concentration, source, crisis event, etc., for each sample, prepare specimens for shipment, supply shipping containers and make arrangements to send biologic specimens to collaborating investigators in an expeditious fashion, inventory, store and maintain a large repository of sera and cells used for immunogenetic tissue typing, be prepared to process up to 1100 mls of blood per day, four days per week, from lymphocyte harvesting (coded from as many as 60 donors per day), handle international shipments of biological specimens and clearance of these specimens through US and foreign customs, and submit monthly computerized and written reports, annual reports and a final report.

Contract will be a cost reimbursement type for a 48 month period. The total estimated level of effort to be provided is 89,740 direct labor hours. Award is anticipated by April 30, 1992. The contractor is expected to provide the facilities and all major equipment. Additional government furnished equipment will be provided.

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

RFP NIH-ES-92-11

Title: Studies to evaluate the toxic and carcinogenic potential of 60 Hz magnetic fields in laboratory animals

Deadline: Sept. 13

The National Institute of Environmental Health Sciences is soliciting proposals for studies designed to characterize the toxicity and carcinogenicity of 60 Hz sinusoidal magnetic fields in Fischer 344 rats and B6C3F1 mice, to determine if such fields alter pineal function, and to determine if such fields cause developmental or reproductive toxicity.

This project will be separated into two phases. Phase 1 will be a six month period comprised only of those work activities associated with procurement of equipment and materials needed to construct the exposure and monitoring systems, ant the developmental effort needed to determine that the systems function appropriately and will meet the National Toxicology Program specifications. The government will evaluate the results of phase 1 and may exercise an option for phase 2 requirements. Phase 2 will be a four year, six month period involving the conduct of eight week and 104 week studies in which animals will be exposed to magnetic fields of specified intensities using the exposure system developed in phase 1. Phase 1 will require approximately .67 professional person years of effort and .48 technical person years of effort. Phase 2 will require approximately 5.8 professional person years and 20.1 technical person years.

For copies of the complete RFP contact NIEHS Contracts & Procurement Management Branch, OM, ATTN: Mary Armstead, Contracting Officer, 79 TW Alexander Dr., 4401 Research Commons Bldg., PO Box 12874, Research Triangle Park, NC 27709, phone 919/541-7893.