THE CANCER LETTER

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Republican Congress To Shift Priorities, But Cancer May Get New Opportunities

The priorities of cancer-related issues may have shifted as a result of the Republican sweep of Congress last week, but overall, NCI and cancer researchers and care providers are unlikely to be worse off as a result on the changes.

In many areas, including appropriations, NCI may even encounter new opportunities.

In other areas, including issues related to health care reform, drug

(Continued to page 2)

In Brief

Ortho Biotech Gives $1 Million To Fund Fatigue Initiative; Lippman, Pike Honored

ONCOLOGY NURSING Society and the Oncology Nursing Foundation have received a $1 million grant from Ortho Biotech Inc. to support a new project, the Fatigue Initiative through Research and Education. The project will fund education programs and research grants on fatigue, one of the most frequently reported symptoms of cancer and cancer treatment. Three developmental grants and a multi-institutional grant will be supported from 1997 to 2000, a professional education course will be offered, and ONS will support a Fatigue Clinical Research Scholar. Project directors are Mel Haberman, ONS director of research, and Bridget Culhane, ONS director of education. For an application for the clinical research scholar, contact ONS, Tel: 412/921-7373. . . . **SUSAN G. KOMEN** Breast Cancer Foundation presented its 1994 Basic Research Award to **Marc Lippman**, director of the Vincent T. Lombardi Cancer Research Center at Georgeown Univ. The foundation's Clinical Research Award was given to **Malcolm Pike**, professor and chairman of preventive medicine, Univ. of Southern California School of Medicine. . . . **MARK KOCHEVAR**, administrative officer, NCI Div. of Cancer Etiology, has resigned to become executive director of the Univ. of Maryland Cancer Center in Baltimore. **Ginny Kiesewetter** is acting administrative officer. . . . **STEVE TRONICK**, acting chief of the DCE Laboratory of Cellular and Molecular Biology, resigned Nov. 1 to take a position at Santa Cruz Biotechnology. **Jacalyn Pierce** was named acting chief. . . . **VICTOR FUNG**, National Toxicology Program liaison, was named DCE special assistant for environmental carcinogenesis. . . . **ELIZABETH ANDERSON** has retired after 38 years with NCI, 19 as a laboratory scientist and 19 as a scientist administrator, all related to breast cancer research. She also has been adjunct professor of entomology at George Washington Univ.

Challenge: Protect Position Amid Impending Budget Cuts

(Continued from page 1)

pricing, alternative medicine, research on possible links between cancer and occupational exposure, it is almost certain that political challenges to the Institute will abate or come to an end.

While NCI may be fine politically, retaining its funding level will be a challenge, considering that the Republican Contract With America program calls for a $20 billion cut in government funding for science over the next five years.

"We are vulnerable," said one lobbyist who represents cancer interests. "The challenge is how do we protect ourselves."

Likely Republican Chairmen

One plan under consideration on the Hill is to consolidate authorization and appropriations into a single process. Whatever action is ultimately taken, several of the Republicans most likely to take over committees relevant to cancer research and cancer care have considerable familiarity with the field.

Rep. John Porter (R-IL), the likely chairman of the Labor, HHS & Education Subcommittee, was the only House member to try to increase NCI funding this year. Porter would replace Neal Smith (D-IA), who was defeated in last week's election.

Last summer, during markup of the committee bill, Porter introduced an amendment to boost NCI funding by $105 million, but withdrew the amendment after it became clear that it had no chance of passing.

Over the years, Porter's remarks at appropriations hearings showed a real understanding of the Institute and its problems. In several hearings, Porter expressed support for funding NCI at the level of the Bypass Budget.

The chairmanship of the full committee is expected to go Rep. John Myers (R-IN), who has been interested in mammography standards and breast cancer research since his wife was diagnosed with breast cancer several years ago. The committee's ranking Republican member, Joe McDade (R-PA) is under indictment, and his future is uncertain.

In the Senate, Arlen Specter (R-PA) is in line to replace Tom Harkin (D-IA) as chairman of the Labor, HHS & Education subcommittee.

It is unclear how much time Specter, a likely Presidential candidate, would be willing to devote to the subcommittee.

In recent years, Specter was among supporters of funding for breast cancer research conducted by the Dept. of Defense. Earlier this year, Specter made an attempt to mediate the controversy over the National Surgical Adjuvant Breast & Bowel Project.

The changeover at the subcommittee will mean that Harkin will be in a weaker position to influence the work of the NIH Office of Alternative Medicine.

The full committee is likely to be taken over by Mark Hatfield (R-OR), who, along with Harkin, proposed a plan to create a trust fund for supporting biomedical research. The fund was to be financed through a surcharge on health insurance premiums.

Nancy Kassebaum (R-KS) is expected to replace Edward Kennedy (D-MA) as chairman of the Senate Labor & Human Resources Committee. Kassebaum, a moderate with an interest in health issues, is expected share her predecessor's sympathy to the cancer program.

It is unclear whether Republicans would take control of the scientific misconduct issues once John Dingell relinquishes chairmanship of Energy & Commerce and its subcommittee on Oversight & Investigations.

Even if Oversight and Investigations survives the expected reforms, it is uncertain whether the subcommittee's likely new chairman, Dan Schaefer (R-CO), would be have the funding—and the staff—to conduct investigations.

A Casualty: Tobacco Control

Tobacco control is the most likely casualty of the election, as the Health and the Environment subcommittee of the House Committee on Energy & Commerce switches over from Henry Waxman (D-CA) to Thomas Bliley (R-VA).

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Bliley, who is also a contender for chairmanship of Energy & Commerce, has said that he planned to end that committee's attack on tobacco companies.

In other changes:

●While a wide ranging health care reform is now unlikely, Republican leadership has said in the past that it may tackle the problems of the uninsured, including denial of coverage as a result of preexisting conditions and the lack of portability of coverage.

●It is unclear whether Rep. Larry Combest (R-TX), the likely new chairman of the Regulation, Business Opportunities and Technology Subcommittee of the Small Business Committee, would continue the systematic examination of the NIH technology transfer policies.

In recent years, the subcommittee, headed by Rep. Ron Wyden (D-OR), has challenged the agreement that led to development of the drug Taxol as well as the proposed agreement between Sandoz Pharmaceutical Co. and Scripps Research Institute.

Recently, Wyden and Combest asked NIH to account for its role in the discovery of the BRCA1 hereditary breast cancer gene. Wyden won his re-election campaign.

●Both Sens. Connie Mack (R-FL) and Diane Feinstein (D-CA) survived the elections, returning to their co-chaired Senate Cancer Coalition.

● Olympia Snowe (R-ME), co-chair of Congressional Caucus for Women's Issues, a critic of NCI's decision to change the mammography screening guidelines for younger women, has won a Senate seat. Rep. Patricia Schroeder (D-CO), the other co-chair of the caucus, was re-elected to her House seat.

NCI Won't Approve Wolmark While NSABP Is A Plaintiff

NCI had declined to approve Norman Wolmark as chairman of the National Surgical Breast & Bowel Project for as long as the cooperative group's Executive Committee remains among plaintiffs in a suit against the Univ. of Pittsburgh.

The suit, which is still pending after nearly two months of court-ordered negotiations, seeks reinstatement of Bernard Fisher to the position of chairman of the group.

While NSABP Executive Committee officials have repeatedly assured NCI that they meant business when they appointed Wolmark to lead the group, Institute officials are yet to accept their assurances.

"Before NCI can approve you as new NSABP Chair, we need reasonable assurances regarding your, and the Executive Committee's commitment to the appointment," Bruce Chabner, director of the NCI Div. of Cancer Treatment, wrote in a recent letter to Wolmark.

A copy of the letter was obtained by **The Cancer Letter**.

"We are particularly concerned with the pending lawsuit in which the NSABP... is seeking to reinstate the former Chair. We recognize that NSABP does not necessarily control this suit because it is not the only plaintiff, but it seems incongruent, and likely to subject the NSABP to further criticism, to have the Executive Committee endorse a new candidate for Chair when NSABP is seeking to reinstate the former Chair," Chabner wrote in a letter dated Oct. 26.

"We do not believe it would be acceptable for you to relinquish your position in favor of Dr. Bernard Fisher. Thus, we seek your and the Executive Committee's assurance that this will not occur," he wrote.

Deckers: Wolmark Is Chairman

Responding to Chabner's letter, NSABP search committee chairman Peter Deckers wrote that when the Executive Committee elected Wolmark to the position of chairman, it meant to do just that.

"The concept that the NSABP Executive Committee 'is seeking to reinstate the former Chair' is naive and unfounded in fact," Deckers, executive vice president of the Univ. of Connecticut Health System, responded in a letter dated Oct. 27. "This was never my intent or the intent of the Executive Committee. Quite frankly, I don't know how this opinion was ever developed. It truly makes no sense."

Subsequently, the Executive Committee, at a meeting Nov. 14, adopted a resolution in support of Wolmark as chairman and principal investigator. "There needs to be immediate completion and actuation of new protocols, which can only be accomplished by NCI cooperating in establishing the Chairman as Principal Investigator with control of scientific operations for both treatment and prevention programs," the resolution said.

Sources said to **The Cancer Letter** that in the past three weeks there has been no movement in the negotiations between Fisher and Pitt.

While the Institute is withholding final approval for Wolmark, it is insistent that the chairman-elect,

who is based at Allegheny General Hospital in Pittsburgh, engage in negotiations with Interim Chairman Ronald Herberman, an official of the Univ. of Pittsburgh, where NSABP offices are based.

To make certain that negotiations take place, NCI has dispatched Susan Hubbard, director of the International Cancer Information Center, to Pittsburgh. Hubbard has been stationed in Pittsburgh for a week and is expected to remain there for another two weeks, sources said.

According to documents obtained by **The Cancer Letter**, NCI's original goal was to work out an agreement between Wolmark and Pitt by Nov. 15.

Though the deadline has not been met, negotiations continue. Herberman and Wolmark acknowledged that they have met several times, but declined to discuss the details. Also, Wolmark was said to have met with NCI Director Samuel Broder on the NCI campus.

NCI's plan is to break up the NSABP cooperative agreement into two separate awards, one of which would support the operations office, while the other would support the Biostatistical Center.

Applications for renewal of those awards are due Aug. 25, 1995, and the award would be made on March 1, 1996. Another application, for a Community Clinical Oncology Program research base grant which supports the tamoxifen chemoprevention trial, is due on Aug. 25, 1995, but the award would be made on June 1, 1996.

Under the NCI plan, the grants would remain at the Univ. of Pittsburgh until recompetition. In the interim, Wolmark would in effect serve as a scientific director reimbursed by Pitt.

Responsibilities Of Chairman

In a letter to Wolmark, Chabner wrote that the cooperative group chairman's office would be responsible for "general scientific leadership, assuring development of scientific plans and protocols and continuation of current scientific activities."

According to the letter, the chairman's other responsibilities would include:

- "Periodic review of accrual, performance, credentials and membership status of each performance site, based on data provided by the Biostatistical Center;
- "Ethics and related educational activities, particularly to safeguard against scientific misconduct;
- "Logistical support to scientific and disease committees, including travel to scientific planning meetings;
- "Preparation for publication (in consultation with the Biostatistical Center) of scientific reports based on NSABP research; and
- "Preparation and coordination of competing renewal applications in prevention and therapy."

According to the letter, the operations office would provide logistical support for protocol development, logistical support for preparation of meetings, preparation of agendas and progress reports and disbursement of payments to participating institutions.

NSABP Resumes Prevention Trial

The Univ. of Pittsburgh Medical Center has begun accrual of subjects for the Breast Cancer Prevention Trial administered by NSABP.

The trial, which tests the potential of the drug tamoxifen to prevent breast cancer in high risk patients, was suspended earlier this year.

According to NCI officials, the trial is operated in a manner that in fact makes it autonomous from the cooperative group, with participating institutions answering to Leslie Ford, chief of the NCI Community Oncology and Rehabilitation Branch.

About half of the 300 centers that had been involved in the trial before its suspension have been approved to resume accrual, NSABP interim chairman Ronald Herberman said to **The Cancer Letter**.

"They are coming on line very quickly," Herberman said. "It's happening as quickly as participating institutions can get the protocol through their Institutional Review Boards."

Last month, the trial's protocol was amended to require that women entering the trial undergo a sampling of the endometrium in addition to a gynecological examinations.

DCE Advisors Okay $24 Million Worth Of Recompetitions

Advisors to the NCI Div. of Cancer Etiology gave concept approval last month to recompetition of nine competitive contract programs worth about $24 million over the next three to five years.

The contracts support large epidemiologic studies carried out by the Epidemiology and Biostatistics Program and the storage of chemicals and biological resources overseen by the Chemical and Physical Carcinogenesis Program.

The DCE Board of Scientific Counselors gave concept approval to a new procurement, worth $2 million over four years, for master agreement orders to conduct studies of cancer etiology in health maintenance organizations.

The concept statements follow:

Studies of Cancer Etiology in Health Maintenance Organizations. Concept for a new contract, total $2 million over four years, master agreement orders, DCE Environmental Epidemiology Branch, project officer: Robert Hoover.

Objectives are: 1. To assemble a pool of pre-paid health plans that have been in existence long enough and have record-keeping systems appropriate for the conduct of epidemiologic investigations of cancer risks in relation to exposures which are likely to be routinely reported within such plans. 2. Based on the emergence of testable hypotheses and the availability of funding, to initiate collaborative investigations into the carcinogenic risks of specific drugs, radiation, medical procedures, and correlated exposures.

Four basic studies are envisioned, including descriptive, case-control, cohort, and case-cohort studies. The specific sample sizes for individual investigations would depend upon the prevalence of exposure and the relative risk of concern. It would be most useful to focus on plans that have had at least 20 years of experience in providing outpatient and inpatient medical services for a defined population, and for malignancies to have been ascertained for the population over this period. It would also seem necessary that the base population of such a plan be large enough to test cancer-related hypotheses, e.g., in excess of 150,000 individuals annually, averaged over the last 15 years.

Repository for Storage and Distribution of Biological Research Resources. Recompetition of contract held by Quality Biotech Inc., total $2 million over five years. DCE Biological Carcinogenesis Program, Biological Carcinogenesis Branch, project officer: John Cole.

This contract has operated and maintained the BCB repository facility for receipt, storage and distribution of biological reagents. There are 20 mechanical freezers, 4 liquid nitrogen cryopreservation containers and 1 walk-in cold box in 3,000 sq. ft. of air-conditioned floor space.

During FY94, over 20 reagents comprised of more than 1,000 vials were received and stored at the repository. During the last three years, the contractor made more than 700 shipments to domestic laboratories and over 100 shipments to foreign laboratories comprised of more than 6,200 vials of biological reagents.

The objective of this concept is the recompetition of the current contract for the continued operation of the BCB repository. Payback funds will provide a method to offset some of the costs.

A variety of tumor virus reagents are available for distribution including known and suspected oncogenic viruses from humans, subhuman primates, cats, mice and chickens, antisera from over 200 different species-antigen-treatment combinations, and more than 230 monoclonal antibodies and associated reagents derived from avian and mammalian retroviruses. In addition, over 13,000 human sera specimens from donors with malignant and nonmalignant diseases, family members associated with donors with malignant diseases, and normal individuals are available for distribution.

The successful offeror will operate and maintain the BCB repository facility and provide a centralized location for storage of biological reagents.

Chemical Carcinogen Reference Standard Repository. Recompetition of contract held by Midwest Research Institute, $2.467 million over five years. DCE Chemical And Physical Carcinogenesis Branch, project officer: Harold Seifried.

The objective of this concept is to recompete the contract for the operation of the Chemical Repository. The successful contractor will maintain the repository and provide a centralized source of well-characterized and documented reference compounds for carcinogenesis researchers. Safe storage will be provided for stock quantities of chemical carcinogens, anticarcinogens, and related chemicals. Upon request and documentation, samples will be prepared, packaged, and shipped to researchers worldwide. Analytical characterization data will be provided, as well as information on stability and the safe handling of each chemical. Repository stocks will be received from the four CPCB synthesis contractors and, when available, from surplus, reanalyzed test chemicals from the National Toxicology Program.

A payback system helps to partially offset the cost for producing the chemical reference standards that are supplied to the repository by the four synthesis contractors. Under the current contract, the repository has shipped over 3,000 samples of chemical compounds and received payment of approximately $440,000 (25% of operating costs).

Resource for Procurement of Human Tissues from Donors with an Epidemiological Profile. Recompetition of contract held by Georgetown Univ., $404,000 over four years. DCE Chemical and Physical Carcinogenesis Program.

This procurement is an integral part of the research program which requires continuing and reliable sources of selected human tissues known to be the primary targets for the human cancer. Malignant and nonmalignant lung, bronchus, colon and pleural mesothelium; blood components and exudate cells and fluids of the lungs and pleural cavity will be collected.

All offerors provide proof of approval for the project from their local Institutional Review Board. The procedural protocol requires (1) collection of medical histories before or after the collection of tissues and cells, and (2) diagnostic

and histologic characterization of tissue specimens from patients hospitalized for suspected disease; (3) collection of alveolar macrophages (by bronchial lavage) and peripheral blood lymphocytes (by venous puncture) from smoking and nonsmoking normal volunteers, and when possible, from lung cancer patients; (4) transport of tissues and all deliverables to LHC; and (5) administering the epidemiological questionnaire to provide relevant occupational and medical histories on each donor.

In the first 3 years of the current procurement, the contractor has provided a total of approximately 282 specimens from 210 patients and normal volunteers, an average of 94 specimens and 70 donors per year. The specimens include 15 lung, 21 colon, and 16 heart and respiratory patients, and 18 normal volunteers annually.

Transplacental Carcinogenesis and Tumor Promotion in Old World Monkeys. Recompetition of contract held by BioQual Inc., $3.3 million over five years. DCE Chemical and Physical Carcinogenesis Program, Laboratory of Comparative Carcinogenesis, project officer: Lucy Anderson.

This project was established in 1974 by Jerry Rice, who continued as project or co-project officer until his departure from the Laboratory of Comparative Carcinogenesis to become director of the Frederick Cancer Research and Development Center last March.

The purpose of the program was to determine whether transplacental carcinogenesis, or tumor promotion in nonsquamous epithelia, can occur in primates. These objectives were fulfilled by Rice and colleagues who demonstrated the occurrence of both transplacental carcinogenesis and liver tumor promotion in patas monkeys. These results have been published in preliminary form and await termination of subjects still alive for complete reporting. The data also establish the patas as a model for chemical carcinogenesis research. This may be the only colony of patas in the world used for this purpose. It may also be noted that there are preliminary indications that the patas may model the human more closely than do the more commonly used macaque species, rhesus and cynomolgus, with regard to certain biochemical parameters (i.e., levels of cytochrome P450 1A2).

With the successful demonstration of transplacental carcinogenesis and tumor promotion, it was appropriate to direct further attention to mechanistic, pharmacological/cellular/biochemical aspects. New initiatives will expand the experimental applicability of the monkey model to human cancer risk assessment/management.

Contract support is required to provide housing, breeding, and experimental manipulation of 140-160 monkeys, which includes 25 cynomolgus monkeys and 20 patas monkeys surviving from previous transplacental carcinogen exposure. The remaining patas monkeys will include about 50 females eligible for breeding, 12 effective male sires, 15 juveniles of various ages developing as replacement breeders, and an additional 18-38 as replacements for the breeding group and for various experimental applications.

The contractor will provide housing for the monkeys in an AAALAC-accredited facility with board-certified veterinary pathologists on staff. The patas will be maintained as a closed, self-perpetuating breeding colony. Housing for breeding and housing of stock monkeys will be in cages designed and approved to meet new guidelines for nonhuman primate social enrichment. A plan for implementation of this need will be a requirement of the recompeted contract.

Biodosimetry for Populations Exposed to Ionizing Radiation. Recompetition of contract held by Oak Ridge Associated Universities, $1.1 million over three years. DCE Epidemiology and Biostatistics Program, Radiation Epidemiology Branch, project officers: John Boice Jr., Ruth Kleinerman.

In June 1993, approval from the BSC was obtained to apply biochemical measures of radiation dose to epidemiologic studies of irradiated populations. Three proposals were judged qualified to conduct the biological assays, but funds were sufficient only to award one FISH or one GPA contract but not both. The purpose of this request is to increase the concept level to obtain the necessary biodosimetry support for expanding the program. Studies include: Chernobyl workers, US x-ray technologists, Sellafield workers, Chinese x-ray workers, and Chinese tin miners. These markers of radiation exposure do indicate prior radiation exposure up to 30 to 40 years ago. The additional amount requested in this concept would be sufficient to award a GPA contract for approximately 6000 analyses and perhaps another FISH contract for 200 analyses.

Cancer Following Bone Marrow Transplantation. Recompetition of contracts held by Fred Hutchinson Cancer Research Center and Medical College of Wisconsin, total $700,000 over three years. DCE Epidemiology and Biostatistics Program, Radiation and Environmental Epidemiology Branches, project officers: Rochelle Curtis, John Boice Jr., Robert Hoover, Donna Shriner, Lois Travis.

In September 1992, we contracted with Fred Hutchinson Cancer Research Center and the Medical College of Wisconsin, the statistical center for the International Bone Marrow Transplant Registry, to evaluate the risk of a new malignancy among 20,000 BMT recipients. The study focused on the risk of secondary cancers, primarily post-transplant lymphoproliferative disorders, developing early in the follow-up period after an allogeneic BMT.

NCI plans to expand the existing cohort to include approximately 28,000 allogeneic BMT recipients and 1,200 autologous BMT recipients from the IBMTR and FHCRC. This second phase would increase the number of 5-year survivors from 3,400 to 6,000 and the number of 10-year

survivors from 730 to 1,700. We estimate that 440 post-transplant malignancies will be available for study, including 220 solid tumors. The addition of the North American Autologous Bone Marrow Transplant Registry, also maintained by the MCW, would provide an additional 12,000 ABMT recipients for study. Other groups with large numbers of patients may have the capability of participating in a collaborative study of second cancers and, thus, multiple contract awards will be considered.

Anticipated costs include updating the follow-up on transplant patients, identifying new primary cancers, obtaining verification of second cancer diagnoses, and obtaining detailed treatment data and transplant characteristics for selected patients. A prospective program for obtaining pathology reports/slides/blocks to document the second cancer will be instituted.

Continuation of Follow-up of DES-exposed Cohorts. Recompetition of contracts held by Baylor College of Medicine, Boston Univ. School of Medicine, Dartmouth Medical School, Univ. of Massachusetts, and Univ. of Chicago, $5 million over five years. DCE Environmental Epidemiology Branch, project officers: Elizabeth Hatch, Robert Hoover, Patricia Hartge, Iris Obrams.

The objective of this procurement is to continue followup of these established DES cohorts to measure the incidence and mortality of cancer, especially cancers of the breast and reproductive system. In addition to examining cancer endpoints, the risk of certain non-neoplastic conditions will also be ascertained. A DES Steering Committee will be formed to oversee and prioritize future research directions. The committee will be composed of members from the DCE Board of Scientific Counselors, NCI, consumer advocacy groups, investigators from each of the currently collaborating centers, as well as scientists with expertise in specific areas of interest, such as immunology and fertility. Plans for the continued follow-up of the cohorts will be developed under the guidance of the Steering Committee.

With a sample size of 6,100 daughters (approximately 70% are exposed) and a power of 80%, the smallest detectable relative risk for breast cancer is 2.0; with a power of 9th, the study should be able to detect a relative risk of 2.2. The budget request includes funds for each of the collaborating centers, as well as funds for support services contracts to aid in coordination of the study, data standardization, data processing and analysis, and laboratory studies.

Continuation of Follow-up of Participants in the Breast Cancer Detection Demonstration Project. Recompetition of contract held by Westat Inc., $2.3 million over three years. DCE Epidemiology and Biostatistics Program, Environmental Epidemiology Branch, and NCI Div. of Cancer Prevention and Control, project officers: Catherine Schairer (DCE), Arthur Schatzkin (DCPC).

The proposed study is a continuation of a follow-up study of a sample of 64,185 of the 280,000 women who previously participated in a five-year multi-center breast cancer screening program, the BCDDP, 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 was initiated at the end of the screening program in 1979-1980. Between 1979 and 1986 information was collected through annual telephone interviews (Phase I). Between 1987 and 1989 one mailed questionnaire was sent to study participants (Phase II). Another mailed questionnaire is being sent to participants between 1993 and 1995 (Phase III).

Proposed is an additional follow-up in 1995-1998 of the 52,700 women expected to be alive at that time. The purpose is to determine the occurrence of a number of endpoints since the last questionnaire and to update information regarding the standard breast cancer risk factors and exposures of particular interest. After several attempts have been made to obtain the information by mail, telephone interviews will be pursued among non-responders.

Support Services for Clinical Epidemiologic Studies Support Services for Epidemiologic Studies. Recompetition of contracts held by Survey Research Associates Inc. and Westat Inc., $4 million over four years. DCE Epidemiology and Biostatistics Program, Genetic Epidemiology Branch, project officers: Margaret Tucker, Dilys Parry.

The GEB studies the role of host susceptibility factors and their interactions with environmental exposures in the etiology of cancer. The mechanism for supporting the personnel needs for field work is through contracts with survey research organizations. Included in these services are the provision of nursing and research assistant support for evaluations of high-risk families and pharmacogenetic studies; the maintenance and administration of a secure medical records room; the development of liaisons with organizations and individuals at a local level whose cooperation is essential for the conduct of the study; the design and development of data collection forms and manuals, including data forms to be used in different cultures and languages; the hiring, training, and supervision of interviewers, record abstractors, phlebotomists, and other temporary personnel as needed; the collection of data; and the coding, keying, and cleaning of data.

This concept is for the recompetition of the contracts which provide major ongoing support services for the GEB. With the incorporation of staff members from the Clinical Epidemiology Branch into the GEB, the four year support

services contract for the CEB has been transferred to the GEB, and will end 9/30/95.

The BSC also gave concept approval to the following non-competitive contracts and interagency agreements:

•Recommendations on Radiological Protection, a new interagency agreement between NCI and the State Department, $99,000 over three years through the NCI Office of International Affairs, to fund the International Commmission on Radiological Protection, of Oxon, UK.

•Epidemiologic Studies of the Mayak and Techna River Cohorts in the Russian Federation, $365,000 over three years, Institute of Biophysics Branch 1, and Urals Research Center for Radiation Medicine.

•Cancer Risk in X-ray Technologists, $750,000 over five years, Univ. of Minnesota, to complete and extend an incidence survey.

•Operation of a Registry of Tumors in Lower Animals, $1.75 million over five years, Smithsonian Institution.

•Industry and Occupation Coding of Death Certificates, $500,000 over five years, National Institute for Occupational Safety and Health.

•Cohort Mortality Study with a Nested Case-Control Study of Lung Cancer and Diesel Exhaust Among Non-Metal Miners, $1.25 million over five years, NIOSH.

•Computerization of Industrial Hygiene Data from Industry-wide Studies Branch Indusrial Hygiene Section Files, $256,000 over four years, NIOSH.

•Pathologic Types of Lung Cancer in Silica and Radon-Exposed Miners, a Pilot Study, $60,000, one year, NIOSH.

RFA Available

RFA CA-95-003

Title: **Cooperative Family Registry For Epidemiologic Studies Of Breast Cancer**

Letter of Intent Receipt Date: Nov. 30

Application Receipt Date: Feb. 17

The Extramural Programs Branch of the NCI Div. of Cancer Etiology invites cooperative agreement applications from investigators to participate, with the assistance of the NCI, in a network of organizations constituting a Cooperative Family Registry for Breast Cancer (CFRBC).

The purpose of the proposed awards is to stimulate a cooperative effort to:

1. Collect pedigree information, epidemiological data and related biological specimens from patients with a family history of breast cancer in order to provide a registry resource for interdisciplinary studies on the etiology of breast cancer, and to encourage translational research in this area.

2. Identify a population at high risk for breast cancer that could benefit from new preventive and therapeutic strategies.

Approximately $2 million in total costs per year for four years will be committed to specifically fund applications which are submitted in response to this RFA. It is anticipated that two to five awards will be made.

Inquiries: Dr. Daniela Seminara, DCE, NCI, Executive Plaza North, Suite 535, 6130 Executive Blvd MSC 7395, Bethesda, MD 20892-7395, Tel: 301/496-9600, FAX: 301/402-4279, E-mail: SeminarD@nihcdce1.gov.

FDA Changes Requirements For Reporting Adverse Events

FDA has proposed changes in reporting requirements for adverse events associated with prescription drugs and biologics. The changes are contained in a final regulation on biological products published in Oct. 27 Federal Register.

The changes would standardize and speed the process of reporting adverse reactions to FDA by clinical investigators and manufacturers of drugs and biologics undergoing clinical trials. According to FDA, the new rules would strengthen the agency's Investigational New Drug regulations by requiring more frequent and complete reporting of possible problems.

Among the proposed changes pertaining to products undergoing clinical trials are the following:

•Sponsors would have to develop, and provide to FDA a written description of, a specific safety monitoring program before the start of any clinical trial.

•Investigators and sponsors would be required to evaluate each adverse event to establish as clearly as possible whether the event was attributable to the product under trial or to other causes.

•In addition to already required annual IND reports, FDA could require drug and biologic sponsors to submit a safety summary of any study on any investigational product. The agency could suspend further clinical trials on a product should the requested safety summary not be submitted.

•Experimental protocols would have to specify and justify the length and type of post-trial medical followup required for people who participated in trials.

•Protocols would have to include descriptions of the specific adverse events that must be reported to the sponsor immediately by investigators.

In addition to these new requirements under the IND regulations, the proposal would make several changes focusing on safety of drugs already on the market. Among these are the following:

•Safety reporting intervals would be set at every six months for the life of all drugs and biologics. Currently, manufacturers are required to report only annually after the first three years a drug is on the market.

•Data on adverse events would have to be reported to FDA from the "international birth date" of a product, rather than from the date of approval in the US.

Comments may be sent to Paula McKeever, Center for Biologics Evaluation and Research (HFM-635), FDA, 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448. Copies of "Guidelines for Adverse Experience Reporting for Licensed Biological Products" are available from McKeever, Tel: 301/594-3074.