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Cancer Program Advocate Mary Lasker, 93, Prodded Government, Scientists For Cures

Great commotion accompanied Mary Lasker's visits to Capitol Hill.

"Mary and her entourage came down the halls," Terry Lierman, former Senate staff member, recalled Mrs. Lasker's 1974 visit to Warren Magnuson (D-WA), chairman of the Senate Appropriations Committee.

"Everybody was standing at attention and the Senator was getting ready and prepped for it. I had never seen anything like it before.

"You would have thought the Queen of England was coming."

(Continued to page 2)

In Brief

Sondik Is Acting NCI Deputy Director; $21 Mil. Gift Supports Univ. Of Chicago

EDWARD SONDIK has been appointed NCI acting deputy director, replacing Daniel Ihde, who left the Institute last month. Sonkik has been deputy director of NCI's Div. of Cancer Prevention & Control. A search committee is being formed to recommend a permanent replacement. . . . **ROBERT MILLER**, chief of the Clinical Epidemiology Branch, in NCI's Div. of Cancer Etiology, retired last month. He will be a scientist emeritus in the Epidemiology & Biostatistics Program. . . . **HAROLD VARMUS**, NIH director, has established a laboratory at NIH, to be operated under the auspices of NCI's Div. of Cancer Biology, Diagnosis & Centers. . . . **THE RICHARD DUCHOSSOIS** family has given $21 million to the Univ. of Chicago to build the Duchossois Center for Advanced Medicine, an outpatient and diagnostic care center. The gift also will endow a professorship to honor **John Ultmann**, professor of medicine and nationally recognized cancer specialist. The gift is the largest dollar amount ever received by the university from a family and the largest to the medical center's $160 million campaign. Groundbreaking is scheduled for June and completion for late 1996. The family owns Duchossois Industries Inc. . . . **LUCIA JORDAN DUNHAM**, 87, a retired researcher in the pathology laboratory of NCI, died Feb. 21 in Bethesda after a stroke. Dunham retired from NCI in 1974 after 23 years as a medical officer. . . . **EDMUND GEHAN**, chief of the biometrics section, Dept. of Biomathematics, M.D. Anderson Cancer Center, has been appointed director of biostatistics, Lombardi Cancer Research Center, Georgetown Univ. Medical School. . . . WILLIAM COOK, associate director, Univ. of Alabama at Birmingham Comprehensive Cancer Center, has been promoted from co-director to director of the center's X-Ray Crystallography Shared Facility.

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Lasker Created ACS, Boosted Federal Health Research Effort

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Besides being regal in manner, Mary Woodard Lasker, who died last week at 93, undertook benevolent projects on a scale fit for royalty:

- In 1943, Mrs. Lasker and husband, advertising mogul Albert Lasker, launched a campaign that in effect created the American Cancer Society on the foundation of an organization of physicians many of whom were reluctant to take up the cause of cancer research.
- Having created a mammoth voluntary organization, the Laskers forced into lobbying for increasing federal funding of research. This led to an unprecedented boost in funding of National Institutes of Health. Subsequently, Mrs. Lasker's lobbying led to the enactment of the 1971 National Cancer Act and subsequent increases in funding for the cancer program.
- The Laskers also established an award whose recipients frequently go on to win the Nobel Prize. Altogether, 51 scientists who won the Lasker award became Nobel laureates.

Mrs. Lasker's other cause, gardening, was funded on an equally grand scale.

In Washington, she paid for 10,000 azaleas planted along Pennsylvania Avenue, 900 Japanese cherry trees around the tidal basin and over 1 million daffodils planted at Rock Creek Park and on the Virginia side of the Potomac. In New York, her gardening projects included a 20-block stretch of Park Avenue, Central Park and the grounds of the United Nations. The latter was donated in memory of Albert Lasker, who died of cancer in 1952.

THE CANCER LETTER

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On some years, Mrs. Lasker's purchases of tulip bulbs in Holland were second only to those of the Queen of England.

Mrs. Lasker was a driven crusader who followed scientific journals and science policy publications, showed up at markup sessions of congressional committees, made appointments to see NCI officials, got involved in hiring and firing decisions at ACS and, on occasion, placed 2 a.m. telephone calls to her associates.

"She had nothing to gain personally. It wasn't a selfish thing at all," said Paul Rogers, who was the subject of Mrs. Lasker's lobbying as former chairman of the House health subcommittee. "That was the source of her credibility.

"The American people lost their best health advocate in Washington when Mary died," Rogers said to **The Cancer Letter**.

Mrs. Lasker's admirers are given to quoting her one-sentence pronouncements. One such pronouncement has theological overtones: "I am opposed to heart attacks and cancer and strokes the way I am opposed to sin."

Forced Federal, Science Partnership

Mrs. Lasker realized that scientists and the government needed to work together and that prodding was required to force them into a partnership. Initially, many of the physicians who belonged to the precursor of ACS, the American Society for the Control of Cancer, were opposed to committing the society's funds to research as well as to lobbying the government to underwrite biomedical research.

However, with the Laskers' involvement, the society's budget climbed from $356,000 in 1943 to $10 million three years later. Opposition dwindled.

Later, the Laskers' lobbying contributed to an exponential growth of the federal government's research spending. In 1945, the US Public Health Service spent $2.4 million on research. In 1960, research spending was $400 million.

"Mary used to say, 'You can get more money out of the government in one day than you can get by going door-to-door for ten years,'" recalls Helene Brown, a long-time friend of Lasker's.

In 1971, when ACS was interviewing candidates for the job of a Washington lobbyist, one candidate, Nathaniel Polster, recalled a two-round interview.

First, he met with the society's executive vice president, then he was sent to Mrs. Lasker's apartment

Mary Woodard Lasker

overlooking the UN. "I spent a good piece of the afternoon there," Polster said to **The Cancer Letter**. "As far as I was concerned, she was doing the hiring."

Once Polster got the ACS contract, Mrs. Lasker took it upon herself to acquaint him with her views on how Washington works and to take him on lobbying rounds on Capitol Hill.

Mrs. Lasker' lesson No. 1: "If you can't get it on a three-by-five-inch filing card, you've lost the message."

Doing the rounds with Mrs. Lasker, Polster was struck by the depth of her relationships with House and Senate members. For instance, he learned that Mrs. Lasker had encouraged Tip O'Neill to go on medication for his hypertension.

"She walked into O'Neill's office and said, 'Are you taking your pills?'" Polster recalled.

"And O'Neill said, 'Damn right I am,' and pulled the pills out of his desk."

Campaign contributions were only one part of Mrs. Lasker's Capitol Hill strategy. Her own contributions were relatively small, usually between $500 and $1,000, which she gave to Democrats and, as she put it, "even Republicans." ("There are a few good ones," she used to say.)

However, if a politician was useful to her, Mrs. Lasker was known to make introductions to other donors, whose contributions added up to a far greater sum. "You have to remember, this was before political action committees," said Victor Weingarten, a former White House aide who ran Lyndon Johnson's campaign to beautify America.

"She got a lot of leverage out of a small amount of money," Weingarten said to **The Cancer Letter**. "It would be difficult for someone to recreate that kind of power today."

When she tracked bills, Mrs. Lasker was anything but circumspect. "She would come to markups, and she would either get the first seat in the front row or she would stand up so nobody could miss her," said Lierman, former staff director of Senate Appropriations Committee.

A grand dame with a bouffant hairdo, wearing a sable coat, is easily noticed anywhere, especially at markup sessions closed to the public. However, no session was closed to Mary Lasker, former Capitol Hill staff members recalled. Making such appearances took audacity, but even greater audacity would have been required to have her removed.

"Whenever people asked Mary why she lobbied, she would say, 'It's my money. I have a right to help determine how it's spent,'" said Lierman.

Mrs. Lasker took a more than casual interest in what was going on at NCI.

"When I first became director of the Div. of Cancer Treatment, it did not take her long to call me for an appointment," recalled Vincent DeVita. "I was a brash young man then, and no philanthropist, no matter how well thought of, was going to tell me what to do.

"But she came into my office, and I saw immediately that she was a person who made sense," DeVita said to **The Cancer Letter**. "I was a convert within minutes."

Chief Obsession Was A Cancer Vaccine

The following year, Mrs. Lasker's requested $200 million above the President's budget proposal for NCI.

"Mrs. Lasker, $200 million is a lot of money," DeVita said while accompanying her on Capitol Hill.

Not to worry, Mrs. Lasker replied. "You are going to get half of what you are asking for." Indeed, that year, NCI received $100 million over the President's budget.

Mrs. Lasker's chief obsession was finding a

vaccine that would eliminate cancer. Once, in 1981, Kristin White, a reporter, sent her an advance copy of a news story on the discovery of the HTLV-1 virus at the NCI laboratory directed by Robert Gallo.

"You realize, of course, what this means," Mrs. Lasker said in a telephone call to White. "It means there will be a cancer vaccine."

To accelerate that development, Mrs. Lasker organized a seminar of leading scientists to discuss the implications of the discovery, then scheduled a lobbying trip to Washington. "I am going to speak to Mrs. Reagan, and I am going to take her to NIH and meet with Dr. Gallo," Mrs. Lasker said to White.

Weeks passed and White heard nothing of Mrs. Lasker's meeting with the First Lady. Finally, White picked up the phone.

"Mrs. Reagan is not interested in science," Mrs. Lasker said. "Her father was a surgeon."

Following this condemnation of the First Lady and surgeons, Mrs. Lasker apparently felt obligated to add something nice:

"But Mrs. Reagan is a wonderful housekeeper. I have never seen the White House look so pretty," Mrs. Lasker said.

Mrs. Lasker's own housekeeping strategies were something of an amusement to White.

"Whenever I would go to Mary's for lunch, we would have a soufflé and a dainty salad—a ladies' lunch," White said to **The Cancer Letter** . "But whenever men were present, there would be a magnificent mixed grill.

"Mary was a little sexist and thought men needed meat. In many ways she was a woman of the 19th century."

Hence, the paradox of Mary Lasker: a lady of the 19th century at ease with the concepts of the 21st .

"She Had Nothing To Gain"

Being hired by Lasker was akin to being chosen for service by the queen.

Once in 1981, an airline ticket mysteriously appeared in Lierman's mail. Just a ticket. No explanations.

"I really did not know what it was for," said Lierman, who at the time was working for a venture capital and real estate firm.

A day later, Lierman got a call from Mrs. Lasker, who was staying in California. "You are about to receive some airline tickets from me in the mail," she said. "I'd like you to come to see me.

"If you believe in fate, that's how my path crossed with Mary Lasker," Lierman said.

"I was born 20 miles from where Mary Lasker was born. I went to the Univ. of Wisconsin; she went to the Univ. of Wisconsin. She started the NIH and nourished it; my first job was with the NIH. She lobbied the Senate appropriations committee; I was staff on appropriations committee. Everything in my life was following Mary Lasker."

Lierman took the job, which he eventually developed into the National Coalition for Cancer Research.

"I think the singular reason Mary had such impact was that she had absolutely nothing to gain from doing what she was doing," Lierman said. "Here is a wealthy woman who could easily have spent her years in the south of France having a wonderful time, and instead she devoted her life to the struggle to conquer disease and disability.

"At a time when America has few heroes, she was a giant."

NCAB Asks NCI To Abandon Promulgation Of Guidelines

Three months ago, NCI abandoned guidelines on breast cancer screening. Now, the National Cancer Advisory Board wants NCI to abandon the idea of offering guidelines altogether.

In a resolution adopted last week, the board stated:

"Inasmuch as cancer research is the primary mission of the National Cancer Institute, the NCAB recommends that the NCI not involve itself independently in the setting of health care policy."

The impetus for the resolution was last year's controversy over the 1988 consensus guidelines on breast cancer screening. When NCI drafted new guidelines that proved as controversial as the 1988 version, the NCAB asked the Institute to keep the older version in place until better data became available (**The Cancer Letter**, Nov. 26, 1993).

NCI did not follow that advice, but abandoned the attempt to write new breast cancer screening guidelines. Instead, the Institute offered a "summary of scientific fact" discussing the lack of consensus regarding mammography screening of women under age 50 (**The Cancer Letter**, Dec. 10, 1993).

Last week's resolution recognizes that NCI does not have the authority to dictate treatment and

screening decisions to doctors and the public, said Sydney Salmon, director of the Arizona Cancer Center and the resolution's sponsor.

"The FDA can speak for the government on drugs, but NCI cannot speak for the government on health policy," Salmon said.

NCI's Role To Generate Information

Agreeing with the NCAB, NCI Director Samuel Broder said the Institute is not seeking a health policy role.

"We need to protect our core function, which is to generate knowledge about cancer," Broder said. "In one era, we were under a strong mission of both the generation of knowledge and its implementation. In an era of health care reform, setting guidelines is not a function NCI should play."

In the late 1980s, NCI went along with the consensus guidelines developed by the American Cancer Society and other organizations "pending the results of clinical trials," Broder said. This put NCI in an uncomfortable position when the trial results were not definitive, he said.

"Where the Institute has a lot of difficulty is when we make a promise," Broder said. "Then we're talking pure policy and not science."

NCI should avoid this kind of "promissory notes," stick to the facts, and leave socioeconomic issues and health policy to other government agencies, including the Dept. of Health & Human Services US Preventative Health Services Task Force and the Agency for Health Care Policy and Research, Broder said.

Not Equipped To Move Beyond Fact

The board passed the resolution on a vote of 14-0, with one abstention, that of Zora Brown, a breast cancer patient advocate.

Last November, Salmon offered a similar resolution but withdrew it because the board appeared to oppose it.

Over the past few months, NCI officials and advisors have said that the Institute is not equipped for issuing recommendations that go beyond scientific fact.

Helene Brown, of the Jonsson Comprehensive Cancer Center, UCLA, and a member of the Div. of Cancer Prevention & Control Board of Scientific Counselors, was the first NCI advisor to publicly suggest that the Institute get out of "the guidelines business" (**The Cancer Letter**, Oct. 29, 1993).

"NCI does not have a process to issue guidelines," NCAB member Erwin Bettinghaus said to the board last week. "There was no process in 1987 and there is no process now."

The Institute's abstention from making guidelines does not mean that public groups should do likewise, Broder said.

"I am very comfortable with organizations like the American Cancer Society making recommendations from their point of view," Broder said. "Many issues that prompted us to write guidelines [in the past] will be solved by health care reform, in one way or another."

Harold Freeman, chairman of the President's Cancer Panel, said NCI should be able to advise the public to eat more fruit and vegetables, or not to smoke. That advice is included in HHS health recommendations, said DCPC Director Peter Greenwald.

NCAB member Charles Wilson cited the PSA screening test for prostate cancer as an example. "We can say it has value and has a place, but health policy research can define better the population for which it is most useful," he said.

NCAB Criticizes Coverage Of NCI Screening Statement

National Cancer Advisory Board members said they had been surprised by the media coverage of NCI's "statement of scientific fact" on breast cancer screening.

"Every single media outlet said it is a change in guidelines," said Erwin Bettinghaus, dean of the College of Communication Arts & Sciences, Michigan State Univ.

"I thought the statement was completely misinterpreted, from The New York Times on to every newspaper in the country," NCAB Chairman Paul Calabresi said.

Did news organizations fail to grasp the subtle difference between a change of guidelines and an abandonment of guidelines?

The New York Times article on Dec. 5 said NCI had "changed its formal guidelines for breast cancer screening and dropped the recommendation that women under 50 should have regular mammograms." More to the point, the article's headline was, "Avoiding Mammogram Guidelines."

The story quoted NCI officials saying that the Institute was not promulgating new guidelines and deliberately chose to get out of the guidelines business on this issue.

The Washington Post reported that NCI "changed its existing guidelines for mammography screening and no longer recommends that women aged 40 to 49 have mammograms on a regular basis to detect breast cancer." The story quoted Broder explaining that the Institute was simply stating facts. An ACS official was quoted saying NCI's statement was a statement, not advice.

If, in fact, reporters were having trouble understanding the controversy, it was not helped by NCI's press release, issued about 4 p.m. on Friday, Dec. 3. The release consisted of two paragraphs on the NCI statement, three paragraphs of lean background material, and one paragraph explaining that the statement is "a successor to a 'working guideline' formulation drafted in 1987."

At its November meeting, NCAB members requested that the Institute delay action on guidelines until more data became available and until NCI could develop sensitive public education materials.

NCI did not adopt that recommendation.

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Bettinghaus, ending his six-year term on the board last week, said he wanted to give Broder a gift that would "arm you with a greater ability to argue your case," particularly regarding health care reform.

The gift: an autographed copy of Bettinghaus's textbook, Persuasive Communication.

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Bynum honored: The NCAB last week passed a resolution honoring Barbara Bynum, director of the NCI Div. of Extramural Activities from 1981 until her retirement last month, for her "exemplary contributions in furthering the National Cancer Program."

Bynum served as executive secretary of the NCAB and was responsible for scientific review of extramural research. The resolution also cited Bynum's "visionary role in NCI's efforts to encourage minority participation in a range of cancer research activities," and her "grace, humor, intellect, caring and vision."

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Five NCAB members have served out their terms, but will continue on the board until President Clinton names replacements. They are: Erwin Bettinghaus, David Bragg, Walter Lawrence, Samuel Wells, and Brenda Johnson.

Capitol Notes

Harkin, Hatfield Propose $5B Medical Research Trust Fund

A proposal to extablish a new stream of revenue for medical research was introduced by Sens. Tom Harkin (D-IA) and Mark Hatfield (R-OR) earlier this week.

The bill calls for establishing a "trust fund for health research," to be financed through a 1 percent surcharge on insurance premiums as well as through a voluntary check-off on tax forms.

The goal is to raise as much as $5 billion to $6 billion in new funds for biomedical research. The measure (S 1472 and S 1473) was introduced as an amendment to the Administration's health care reform plan.

Sens. Edwards Kennedy (D-MA) and Nancy Kassebaum (R-KN) appear as co-sponsors of the Harkin-Hatfield measure. In the House, an identical bill was introduced by William Coyne (D-PA).

"The great philanthropist Mary Lasker said, 'If you think research is expensive, try disease,'" Hatfield said at a press conference announcing the introduction of the amendment. "These words capture the motivation and message of our legislation."

As introduced, the Administration's health reform plan is focused on the costs of health care and does not address the need for biomedical research, Harkin said at a press conference.

"Unfortunately, until now the thrust of the health care debate has been over how to pay the health care bills—not how to prevent them," Harkin said. "Unless we address the main cause of skyrocketing costs—disease and disability—any steps we take on health care reform will be about as effective as rearranging the deck chairs on the Titanic."

Harkin and Hatfield said their amendment is not contingent on the passage of any of the competing health reform plans.

"We will attach it to any moving vehicle," said Hatfield. In fact, the surcharge can be instituted even the health care system remains unchanged, he said.

If the fund is enacted, within three years all corporate and regional alliances would be obligated to contribute 1 percent of the health insurance premiums they collect. Also, tax forms would be changed to give taxpayers the option of donating their overpayments to health research.

The new funds would then be automatically allotted to each of the NIH institutes. Five percent of

the funds would be used for extramural construction and renovation of research facilities as well as for the National Library of Medicine and Office of the NIH Director.

Harkin-Hatfield proposal was endorsed by over 200 associations, including the following cancer groups:

—Albert and Mary Lasker Foundation
—American Association for Cancer Research
—American Cancer Society
—American Society of Hematology
—American Society of Therapeutic Radiology and Oncology
—Association of Pediatric Oncology Nurses
—Candlelighters Childhood Cancer Foundation
—FDA Council
—Fred Hutchinson Cancer Research Center
—Leukemia Society of America
—National Breast Cancer Coalition
—National Coalition for Cancer Research
—Susan G. Komen Breast Cancer Foundation

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FDA Open To Tobacco Regulation: In a letter to the Coalition on Smoking OR Health, FDA Commissioner David Kessler said the agency was open to regulating tobacco products.

The letter, based on several recent studies, said cigarette manufacturers have the technology to reduce the nicotine level in their products. However, instead of doing so, they are maintaing—or boosting—the nicotine content, presumably to make their products more addictive.

The letter said Congress should provide direction to the agency "to resolve, once and for all, the regulatory status of cigarettes under the Food Drug and Cosmetic Act." Cigarette manufacturers have not been required to prove the safety and efficacy of their products.

"This new evidence is a smoking gun," said Rep. Mike Synar (D-OK), author of a bill that would give FDA authority to regulate tobacco. "The FDA's disclosures indicate tobacco companies have been making their products more addictive and deadlier by the manipulation of the nicotine content."

Synar's bill, HR 2147, co-sponsored by Rep. Richard Durbin (D-IL), would give FDA authority to regulate the advertising, promotion, labeling and content of tobacco.

"I am appalled and disgusted that any inductry would so callously disregard the health of our nation for purely selfish economic gain," Synar said. "This is one more clear indication that Congress must take the lead in giving FDA the clear guidance on how to regulate this deadly product."

DCPC Board Oks New Grants For Prevention Investigators

NCI's Div. of Cancer Prevention & Control Board of Scientific Counselors have given concept approval to a new grants program for prevention and control investigation.

The board agreed to set aside $1.5 million in fiscal 1995 to fund grants designed to help young prevention and control investigators win their first NIH research project grant (R01).

The board also gave concept approval to new grants in chemoprevention clinical trials. (More DCPC concepts will be published in next week's issue.) Following are the concept statements:

New Investigator Grants for Cancer Prevention and Control Research. Proposed RFA, first year award $1.5 million, four years, announcement expected in May, awards in July 1995.

There is ongoing concern over the declining number of young investigators entering and remaining in academic research related to cancer prevention and control. These investigators are a critical component in translating phase I and II prevention and control research from both epidemiological studies and the laboratory and the clinic to broader venues such as physician practices, HMOs, and communities. These investigators must maintain a broad perspective and knowledge concerning epidemiology and clinical and basic science while developing new delivery and intervention approaches that are hypothesis driven. They are highly interactive with basic, clinical, and epidemiological researchers in related disciplines. This translational investigator is considered distinct from the investigator who has a PhD or equivalent training and concentrates on basic or epidemiologic research or the clinician who participates in cancer research by entering patients on clinical trials.

The American Society of Preventive Oncology has been addressing the problem of the decreasing number of academic prevention and control investigators. One of the problems identified is the lack of suitable mechanisms for the training and funding of young investigators involved in translating basic, epidemiological, ,and clinical research into prevention and control applications. There is no specific program available to train these investigators in the design and conduct of cancer prevention and control studies and trials. The traditional grants

mechanisms often do not fit the needs of young prevention and control investigators for the support of their research. The R29 grant mechanism requires the investigator to devote at least 50% effort to a five year project and the budget is limited to approximately $70,000. Most pilot prevention and control studies do not require five years but it is impossible to support the various study components needed within the budget limitations of an R29 grant. Young prevention and control investigators usually do not have the publication or research track record to be competitive for R01 grant support. Thus, very few prevention and control research proposals are submitted by these investigators. DCPC would like to reverse this trend and encourage new prevention and control investigators in the conduct of translational research.

This initiative would encourage qualified prevention and control investigators to develop R01 grant applications for the conduct of studies translating phase I and II epidemiological, basic, and clinical research into new approaches to the prevention and control of cancer. Grant applications must include trials and interventions involving human subjects and be designed to ultimately reduce the incidence of particular cancers or improve cancer survival. The trials and interventions must have a strong rationale and be based upon phase I or II research conducted by the applicant or others which support the underlying hypotheses. New intervention trials employing such channels as micronutrients, new dietary regimens, policy change, pharmacologic agents, or behavioral or psychosocial change mechanisms, whether used as a single agent/modality or in combination, are appropriate. The research plan should be focused on the trial or intervention proposed. Laboratory studies to monitor patients or to study the mechanism of action of agents may be included as appropriate.

The principal investigator must be an physician or PhD who is working independently but at the beginning stages of his or her research career. The principal investigator must never have been designated previously as PI on any PHS supported research project (except R03, R15, or K series awards). At least 25% effort must be committed to the research project by the principal investigator. The total direct cost award for the 4-year R01 grant period may not exceed $500,000 ($125,000 per year). The sponsoring institution must acknowledge that the PI is the independent leader of this investigative effort.

Chemoprevention Clinical Trials Involving Modulation/Function of Genes and/or Gene Products. Proposed new RFA, $2 million per year, five years, three to six awards per year. Program director: Winfred Malone.

The goal of this initiative is to stimulate and facilitate investigator initiated chemoprevention research involving agents that may effect gene expression and cellular growth, and encourage development of short-term clinical trials that evaluate the modulation/function of gene products by chemoprevention agents.

This proposed RFA would support clinical trials which are directed toward examining the role of gene or gene products in assessing risk or modulation by chemopreventive agents. One or more intermediate endpoints might be evaluated initially to determine baseline parameters, and subsequently to serve as a follow-up after the administration of the chemopreventive agent.

These studies may be developed in phases, including a pilot phase, which could later proceed to a full scale intervention. The main emphasis should be on small, efficient trials aimed at improving future research designs providing biologic understanding of what is happening or providing better, more quantitative and more efficient endpoints. After successful completion of the pilot phase (i.e., demonstrated modulation of marker endpoints by intervention), subsequent studies could include a clinical trial monitoring the test system, cancer incidence or mortality endpoints, and the designated agent.

For the pilot phase the proposed trial must describe the relevance of the marker test system to clinical cancer prevention, the rationale for the selection of the study population, and potential intervention agent. The project could result later in the markers and agent being evaluated in a fullscale, double-blind, randomized, risk reduction clinical trial.

New Receipt Date For RFA

RFA CA/ES/AG-94-005

Title: **Breast Cancer Research Programs In NCI-Designated Cancer Centers**

Application Receipt Dates: February 17 and March 29

This notification provides a second receipt date for submission of applications in response to RFA CA/ES/AG-94-005. Applications will be accepted on the original receipt date of Feb. 17, and March 29. The purpose of providing additional time is to allow all potential applicants to consider addressing two additional areas in their applications. These areas pertain to (1) the need to include in the application a discussion of the involvement of the Cancer Center and Director in continuing oversight of the developing breast cancer program and (2) an opportunity to include a research subtheme focussed on Long Island breast cancer research issues.

Applicants who have submitted applications for the Feb. 17 receipt date may submit an addendum with information pertaining to either or both of the areas only. The addendum should be clearly identified with the title of the project in the original grant application and submitted by March 29 to: Dr. Gail Bryant, Div. of Extramural Activities, NCI, Executive Plaza North Room 635-J, Bethesda, MD 20892, Tel: 301/402-0801.