THE CANCER LETTER

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Breast Cancer Coalition To Congress: 'Find A Way To Fund The War;' Bypass Level Is Not Enough

It looked as though Fran Visco was demanding money for a disease other than cancer.

She did not exchange nods with other cancer activists, did not shmooze with the lobbyists who accompanied them. Instead, Visco sat down with a group of women, several of them wearing ribbons

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In Brief

Sullivan Rejects Oregon Medicaid Rationing Plan; Howe To Head National Marrow Donor Program

OREGON'S MEDICAID rationing plan was rejected this week by HHS Secretary **Louis Sullivan**, who said the controversial program to expand Medicaid services to the poor by excluding some services appeared to violate the Americans with Disabilities Act. Sullivan said the state's decision about which services to exclude "was based in substantial part on the premise that the value of the life of a person with a disability is less than the value of a life of a person without a disability." The plan would have excluded cancer treatment for Medicaid beneficiaries who have less than a 10 percent chance of five year survival (**Cancer Economics,** March 1992). . . . **CRAIG HOWE** has been named chief executive officer of the Minneapolis-based National Marrow Donor Program. Howe was associate professor of medicine and director of the bone marrow transplant program at Medical College of Virginia. . . . **AMERICAN CANCER** Society Clinical Research Professorships were awarded to to **Rodney Withers**, Univ. of California (Los Angeles) and **Alan Solomon**, Univ. of Tennessee Medical Center. Each will receive $250,000 for five years. **Dartmouth College** received a $1 million special institutional grant from ACS to establish a Center for Psycho-Oncology Research, under the direction of **Peter Silberfarb**. . . . **PACIFIC YEW ACT** has passed the Senate by voice vote and awaits signing by President Bush. The House passed the bill on July 7. The act provides for management of the yew tree, the source of the drug taxol. . . . **CHILDRENS CANCER** Group is seeking a pediatric oncologist-hematologist for the position of associate chairman for group operations. This new position will report to the group chairman and be responsible for operational management of the group and its office in Arcadia, CA, in association with USC School of Medicine. Appropriate clinical activities and academic appointment can be arranged. Experience in cooperative clinical trials required. Prospective applicants may write to: Chairman, Children's Cancer Group, PO Box 60012, Arcadia, CA 91066-6012.

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Breast Cancer Coalition Goes Against 'The Rules,' Demands $300 Mil. More

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emblazoned with "$300 million more," the slogan of the Breast Cancer Coalition over which Visco presides.

Taking the stand before Senate Labor, HHS, Education Appropriations Subcommittee, the diminutive 44-year-old Philadelphia trial lawyer and breast cancer survivor assumed the tone unheard of when cancer groups come to ask Congress for money:

"When the men in suits all but destroyed the savings and loan system in this country, the nation's economic stability was threatened and this Congress responded with billions of dollars.

"Because our cities are in danger of extinction, this Congress has found a way to appropriate emergency funds for the urban crisis.

"When this administration decided to wage a war, you found $7.5 billion to fund it.

"Women have declared war on breast cancer and you had better find a way to fund that war.

"Women refuse to fight with other diseases for which no funds are available. That would be going by existing rules, and too many women die under those rules.

"It is not enough that we can all say breast cancer aloud. And it is not enough to say you want to help us.

"We will no longer be passive. We will no longer be polite. We can no longer afford to wait while Congress gets around to significant, decent funding for breast cancer.

"We implore you: you must find a way to appropriate the additional $300 million for breast cancer research now. We can accept to less."

From the perspective of professional societies, NIH and NCI, this is an outlandish figure that would increase spending on breast cancer to $433 million, almost double the bypass budget level of $220 million, which NCI says would meet all opportunities in breast cancer research in FY 1993.

"I think that if they had taken the same tactic, but asked for something more in line with the bypass budget, we would have been more supportive of them," said a lobbyist for one of the professional societies.

With the congressional appropriations cycle half-over, the Breast Cancer Coalition has not been able to bring additional funds into the cancer program. However, this is not to suggest that the coalition has been ineffective. Strapped for funds yet unable to say no to a vocal constituency, Congress has done what it could: mandate a diversion of funds from existing NCI programs.

Last week, the House Appropriations Committee, apparently in response to pressure from the Breast Cancer Coalition and its supporters in the Congressional Caucus for Women's Issues, mandated a $40 million increase in NCI's spending on breast cancer research. Altogether, $70 million was reallocated to breast, cervical, ovarian and prostate cancer programs (**The Cancer Letter**, July 31).

For years cancer researchers looked wistfully at the appropriations hauled in by the politicized AIDS activists. What would happen if cancer patients became as politicized? Would more money suddenly be found for cancer?

Now the time for wondering has passed.

Like it or not, breast cancer patients have moved beyond battling paternalistic surgeons. Politicized and militant, they are taking on Congress, the President and NCI.

From Stop the War to Stop Breast Cancer

It is certainly a phenomenon where political style and political tactics are firmly rooted in demographics: the kids who once opposed the war are starting to get suspicious mammograms.

"The nature of breast cancer is such that it is starting to affect people who grew up in the sixties," Visco said to **The Cancer Letter**. "We are activists. That's our nature."

This shared political temperament made it natural for the new generation of cancer advocates to accept the lessons of AIDS activism.

"From AIDS activists we learned what would happen when you open your mouth and make demands," Visco said. "That's where we are now, and that seems to be what the people in power respond to. We are grateful to AIDS activists for showing this to us."

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The newly politicized stance is reflected in the coalition's rhetoric.

"I recognize how starkly dissimilar my [Senate] testimony was from other testimony given that day," Visco said. "I thought it was time to give this kind of a speech. I thought it was time for them to understand that we are serious, that we mean this, and that we are not going to go away."

The Breast Cancer Coalition was started early in 1991 by leaders of CancerCare, Cancer Patients Action Alliance, Faulkner Breast Center, Mary Helen Mautner Project for Lesbians with Cancer, National Coalition for Cancer Survivorship, National Alliance of Breast Cancer Organizations, Women's Community Cancer Project and Y-ME. Since then, 160 organizations, including the American Cancer Society, joined the coalition.

Last October, the coalition decided to flex its muscles by deluging official Washington with letters demanding additional funds for breast cancer research. The goal was to generate 175,000 letters, one for each woman diagnosed with breast cancer last year.

Instead, over 600,000 letters were generated. About 140,000 letters, addressed and delivered to the White House, are yet to be acknowledged by the Bush Administration, said Sharon Green, head of Y-ME and one of the founders of the Breast Cancer Coalition.

After some negotiations, a White House staff member showed up at the side entrance of the Old Executive Office Building to accept the boxes. According to Green, the staff member stood idly while late stage breast cancer patients were placing the boxes on the conveyor.

"Our feeling was, they are probably on the way to the shredder," Green said to **The Cancer Letter.**

Room for 'Moderates?'

The $300 million figure was derived last February, after the coalition held a conference on prevention, epidemiology, basic and clinical science.

Following the conference, the coalition's "research task force," which includes activists as well as physicians and PhDs, arrived at the number.

Among the recommendations considered was one by Virginia Soffa of Vermont's Breast Cancer Action Group. By comparing incidence vs. federal spending on AIDS and breast cancer, Soffa interpolated that breast cancer research should get $4.3 trillion to reach equivalency with AIDS.

While reasonable to some activists, the $300 million figure amounted to heresy in the eyes of the groups committed to pursuing another ambitious goal: closing the gap between NCI's bypass budget and the funds appropriated to the Institute.

Some patient advocacy groups, most prominently, Nancy Brinker's Susan G. Komen Foundation, chose not to join the coalition. The American Cancer Society, also a supporter of the bypass budget, chose a different strategy.

"We knew from the outset that there would be events in which we would not care to participate," said Joann Shellenbach, spokesman for ACS and a member of the Breast Cancer Coalition board. However, the benefits of being part of an emerging political force outweighed the potential costs, she said.

"We've reached a level of understanding with their national board," Shellenbach said. "It's the local chapters with whom we have problems to iron out."

Along with the National Coalition for Cancer Research, ACS is on record asking for a $170 million increase for the entire NCI in FY93 and is opposed to diverting funds from existing NCI programs.

Later this month, at a meeting in Washington, a group of members of the society's public issues committee will gather to decide the future of ACS membership in the coalition.

"I suspect that we will give it another year," Shellenbach said. "The coalition and ACS have disagreed on certain matters, but we haven't been embarrassed. We've disagreed, we've been comfortable about doing it."

Joanne Howse, the Breast Cancer Coalition's Washington lobbyist and partner in the lobbying firm Bass & Howse, said she would like to see ACS remain in the coalition.

"If they decide to leave, from my perspective it would be a serious loss," Howse said. "But again, they obviously have to be supportive of all cancers and they have their own political considerations."

T-shirts at Rayburn

Earlier this year, under questioning by Rep. William Natcher (D-KY), NIH Director Bernadine Healy said that "despite NIH's enormous support of women's health research, I think it would be destructive to planning and destructive to the broad goals of the NIH to have $500 million [including $300 million for breast cancer] earmarked specifically for women's research."

Similarly questioned by Natcher, NCI Director Samuel Broder asked: "Sir, are you asking me for my professional judgment?"

NATCHER: "Yes, I am."

BRODER: "Our FY 1993 bypass budget request for breast cancer was approximately $220 million."

These statements notwithstanding, Howse said she is convinced that Broder "is not going to turn the money down if it's there."

The infusion of $300 million for breast cancer

research could force NCI to operate more efficiently, she said.

"When they tell us how long it takes to get the grants out, women become very impatient," Howse said to **The Cancer Letter.** "Let's get the money out. Let's not create the kind of bureaucracy that can't get the money out efficiently. Let's do something different."

Visco is similarly confident. "We can show [Broder] that the money would not be wasted," she said.

As the Breast Cancer Coalition stood by its demand, the $300 million figure made its way into a letter signed by 20 members of the Congressional Caucus on Women's Issues. Later, the figure appeared in the NIH reauthorization bill.

Then, as members of the Labor, HHS, Education Appropriations Subcommittee went to a closed session to mark up the FY93 budget, women in T-shirts inscribed with demands for "$300 million more" lined the halls of the Rayburn House Office Building.

"We aren't doing street theater, we aren't interrupting meetings like ACT-UP," said Y-ME's Green. "What we do is line the halls. They knew we were there. We did not have to shout."

Most recently, the coalition's goals got another boost when Democratic presidential contender Bill Clinton told a group of breast cancer patients that he supported the $300 million increase.

Looking for Funds

Howse said she was disappointed to see "one disease played against another disease" in the House report.

"You can't get any money from Labor, HHS," she said. "There isn't any money there. We want to get it elsewhere." Most likely, the group would call for cuts in the defense research and development budget, she said.

"We believe that we don't have to take money from other diseases," Howse said. "We are trying to figure out a way to increase the pie for breast cancer research. What we would like to see is that we increase the pie for everyone, so we are seen as heroines."

So far, attempts to cut the superconducting super collider and the space station have failed in Congress, and if the cuts are made, it is far from certain that in the current fiscal climate Congress would apply the funds to anything other than deficit reduction.

Be that as it may, the Breast Cancer Coalition is preparing for its next political action:

Not revealing the details, Howse says only that a large number of coalition members will come to Washington on Sept. 9, the first day of Senate markup of the HHS budget.

In Congress

House Preserves Space Station; Societies Support $170 Mil. Raise

The cancer program suffered another setback last week as the House voted to preserve funding for the space station. The amendment to kill the $30 billion project was expected to be followed by a move to put about $350 million into health research.

The amendment to kill the $30 billion space station, introduced by Reps. Bob Traxler (D-MI) and Bill Green (R-NY) was rejected by a 237 to 181 vote. It was to be followed by an amendment by Rep. Richard Durbin (D-IL).

In another apparent setback, the Senate Appropriations Committee restored the funds for the $8.25 billion superconducting super collider.

Observers say that even if these or other projects get the ax before the end of the appropriations cycle, it appears doubtful that the funds would be applied to anything other than deficit reduction.

Earlier this year, cancer program lobbyists expressed hopes that Sen. Dale Bumpers (D-AK) would introduce a series of amendments that would cut the defense and space budget and divert a portion of the savings to medical research.

Whatever Bumpers' ultimate plans, the bills Bumpers introduced last month (S 2930 through S 2934) mention no diversion of funds to medical research. The entire $10 billion he proposes to cut from the FY 1993 budget would be applied to deficit reduction.

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Advocates of the cancer program addressed the Senate Labor, HHS Appropriations Subcommittee, reiterating their request for additional $170 million for NCI over the President's FY 1993 budget request.

"The House has recommended the NCI funding level $11 million below the President's request," said Ellen Stovall, executive director of National Coalition for Cancer Survivorship.

"This is most unfortunate since the Congress made progress last year in restoring the funding base of NCI. Overall the House provided an increase of 3.1 percent to the entire National Institutes of Health with only a 2.4 percent increase allocated to the National Cancer Institute. We urge you not to repeat the pattern of NCI receiving an increase below that of the rest of the NIH."

Stovall spoke on behalf of the National Coalition for Cancer Research.

▶Speaking for the American Society of Clinical

Oncology, Sharon Murphy, chief of the Div. of Hematology/Oncology at Children's Memorial Hospital in Chicago and member of ASCO's public issues committee, said that "there remains a tremendous shortfall in funds for large scale clinical studies."

"In the past year, due to limited resources, some clinical research teams have already been forced to cap patient accruals and delay the initiation of studies," said Murphy.

The President's budget proposal and the spending levels recently approved by the House threatened the much needed increases for clinical trials. Murphy asked for no less than $17 million in additional funds for clinical trials and "report language urging relevant authorizing committees to advocate health insurance policies that do not hinder patient participation in clinical research."

▶Funding for the cancer centers program is no further along in terms of actual buying power than it was ten years ago, said Jerome Yates, chairman of the board of the Assn. of American Cancer Institutes and associate director for clinical affairs at Roswell Park Cancer Institute.

Yates said that of last year's $32.5 million increase for the cancer centers, $17.5 million was applied to the Specialized Programs of Research Excellence and $750,000 was deducted for 12 planning grants for new centers. The remaining $14.3 million increase for the 58 centers was reduced by "take-backs."

"We suggest that a specific funding line for SPOREs be incorporated into the budget and bill report language be developed specifically separating the traditional center core grants and the SPORE programs," Yates said.

AACI requested that the cancer centers get $18 million and SPOREs $10 million above the President's budget request.

News Roundup: ACS Board

Panel Suggests Limited Test Of Paid Advertising By ACS

An American Cancer Society Panel of outside experts in advertising, media, and public service, established to make recommendations regarding the Society's use of paid advertising, has suggested that ACS "go forward with a limited, careful test of paid advertising to gauge its usefulness as a supplement to public service announcements and sponsored advertising campaigns."

The recommendation follows more than two years of agonizing over the issue by the ACS Board of Directors Communications Committee.

The panel was chaired by committee members George Dessart and Victor Bloede. It included Michael Moore, executive vice president, DMB&B Inc. Advertising; Nancy Clott, senior vice president/media administration, the Advertising Council; Harvey Dzodin, vice president/commercial standards, ABC; Wally Schwartz, former television network president; and Charlotte Ottley, president elect, National Broadcast Assn. for Community Affairs.

The panel's recommendations for a paid advertising test were:

*The project should be designed to test a very specific, hard hitting educational message.

*The ads should have a call to action that would allow a means of measurement, such as calls to the 800 numbers.

*The test should be conducted in a very small, self contained media market.

*Pre and post awareness testing should be conducted.

*The project should actually be considered an experiment in paid advertising, since ACS will also be gauging the impact on intangible factors such as impact on existing PSA time, and the ability to buy time for one message and still pitch PSAs supporting other themes.

*To save money, the paid experiment might include only live radio scripts and newspaper ads, two relatively inexpensive media with good measurability and impact.

ACS divisions have been asking the national office for guidance on use of paid advertising, having encountered increasing resistance from some elements of the media in use of free public service announcements. Sponsored advertising, in which businesses and other entities buy time or space for the ACS message, is an answer to the lack of funds for advertising but it has many of the same problems as use of ACS paid advertising.

The panel discussion made these points, which include some suggestions for divisions considering use of paid or sponsored advertising:

--Because they are created to be used at the whim of the media as all purpose time fillers, PSAs by necessity are forced to be so general that they actually fail to effectively target any specific audience segment. In a move to paid or sponsored advertising, care should be taken to properly target message and audience. Very, very targeted ads work better.

--Any move into paid advertising is a major leap for people not well trained in the very technical skill of media buying.

--A move into a paid campaign will require ACS to create real marketing plans, taking into consideration action objectives, media mix, results measurement, and media buying strategies. It seems ACS has not had to do this in the past, because the Society had no real control over its campaigns.

--Another danger in a move to paid advertising: The public really doesn't like to believe that advertising works in influencing behavior. People see advertising as an extravagance indulged by corporations. A nonprofit's move into paid advertising could cause bad public perceptions about the way ACS uses its money, especially in these times of intense cynicism toward the government, the economy, and charities. Most people believe ACS raises funds to find cures for cancer, not to buy ads.

--The message communicated through paid ads will be very important in terms of positive or negative public opinion about using this medium. It should be used for very hard hitting, factual educational information, not for softer messages like the Food Fight, and certainly never for fund raising projects.

--Paid advertising may never be an option for national campaigns. The trend in all advertising is to localize the message as much as possible. National will be required to coordinate and train divisions, but the actual implementations should all occur locally.

--It appears that ACS is unfamiliar with the total costs of even a small, local paid ad campaign. The Society should go into this with its eyes open as to just how expensive this move could be.

--Because of its general lack of focus on market segments, television, as a paid medium, especially a network wide campaign, may always be ineffective for the Society, in addition to its relatively prohibitive cost.

--The talent fee schedule for actors and creative people producing PSAs for the Society, even radio PSAs, is much lower than those for paid ads. Production costs for paid ads will go up accordingly.

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Support for the newly established Behavioral Research and Consultation Unit was discussed by the ACS Public Issues Committee at its recent meeting in Portland, OR.

"The unit requires long term financing," Denman Hammond said. "Where will the funding come from? The research pool, competitively? Administration expenses? This is a broad, multifaceted program. What is the overall fiscal picture? How will it impact the budget?"

"Those are good questions," Senior Vice President for Research John Laszlo said. "My view is that this is a research function and therefore is allocated to research. The Public Education Dept. has asked the unit to help design a program, and if that requires a full time person, that will have to be provided out of the Public Education budget."

"Let the unit get started, and let the financing develop as demands are placed on the unit," Gerald Mueller said. "A lot of it is likely to end up with a research allocation."

"At this point, most of this is likely to end up in the pay if (that is, if additional money above the ACS budget estimate becomes available) column," Larry Fuller said.

"But this needs to be supported," Hammond insisted, "not just put in the pay if category year after year. There should be a long term commitment."

• • •

Hammond brought up the possibility of ACS support for the various clinical cooperative groups. He noted that the National Surgical Adjuvant Breast & Bowel Project receives $100,000 a year from the Society and asked the rationale for that support.

"That preceded me at ACS by a decade and a half," Laszlo said. "It's a relatively small amount, and I guess it gives us a part of the action, like a minor stockholder. It provides NSABP with some flexibility. I don't think we would fund something that way now."

"I can understand why breast cancer is important to the Society," Hammond said. "NSABP is an important group. But is it not reasonable to suggest that other groups could come in with specific projects and ask for some support?" Hammond was chairman of the Childrens Cancer Study Group for more than 20 years and now is president of that group's foundation which raises money for it.

"We're open to any research suggestion," Laszlo said. "I would love to see them submit grant proposals, particularly those for creative, innovative research."

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Prostate cancer recommendations: Some members of the ACS board's Medical and Scientific Committee were reluctant to accept the recommendation which came out of the ACS workshop on prostate cancer last year suggesting that the Society take on prostate cancer as one of its high priority programs.

After President-Elect Reginald Ho presented the report from the workshop to the committee, one committee member argued against adding prostate cancer "without concern how this impacts our other priorities. Prostate cancer is not my highest priority."

Hammond pointed out that the committee was being asked to refer the recommendation to the

Planning Advisory Council, "the appropriate committee to consider this issue."

Robert Schweitzer felt otherwise. "It is most appropriate for this committee to make this recommendation," he said. "PAC needs the medical background and advice of this committee. If we find that the most common cancer in males is not a priority, that should come from this committee."

"We don't have the scientific data base to push ahead now with prostate cancer as a priority," Eyre said. "This would be primarily screening, and no impact on mortality has been proven."

Robert Hutter agreed that there was no statistical evidence yet, but added "we're in the position of the public demanding some action. By making it a priority, it would put ACS in a leadership position."

Gerald Murphy, group vice president for medical affairs and chief medical officer, noted that an ACS report on prostate cancer detection will be available in September.

"We had an excellent conference on prostate cancer," Mueller said. "It is clear that basic science is moving rapidly to address the problems. We ought to be in front."

Despite the opposition, the motion to refer the recommendation to PAC was approved unanimously.

A summary of the recommendations:

--As the second most diagnosed cancer in men after skin cancer, prostate cancer is highly prevalent.

--Because the populations in which prostate cancer is most likely are so clearly drawn, it is possible to effectively and efficiently target those populations for screening and early detection.

--Because the at risk group is one of the most rapidly growing segments of the American population, the numbers of persons in needed of prostate cancer detection and treatment and the impact of programs to address those needs will grow rapidly in the coming years.

--Because the greatest risk for prostate cancer is in the elderly and especially in American black men, and because low socioeconomic status is associated with late diagnosis of cancer, prostate cancer should be a priority for focus in the American Cancer Society's programs addressing cancer in the socioeconomically disadvantaged, cancer in the elderly, and pain control initiatives.

--Because methods of early detection are reasonably priced and increasingly widely available, programs of professional education and public education, targeted to at risk populations, should have a meaningful impact on the use of these methods.

--Because early detection spares suffering and saves lives from prostate cancer, a priority program to address prostate cancer should have meaningful results in prostate cancer control.

--Because the need for focus on prostate cancer has already outdistanced existing programs to address those needs, as evidenced in the excess deaths and excess late diagnoses, the dilemma is immediate and pressing and it is incumbent upon the American Cancer Society to act promptly, within the confines of the best information available from its many resources.

--Because the American Cancer Society has the resources and the mandate to achieve such a priority, it is the organization that can best do so.

RFAs Available

RFA CA-92-20

Title: **Epidemiology of ovarian cancer**

Letter of Intent Receipt Date: Oct. 15

Application Receipt Date: Nov. 12

NCI's Div. of Cancer Etiology invites grant applications for innovative interdisciplinary epidemiologic studies to better understand the etiology of ovarian cancer and the means of prevention.

Applications may be submitted by domestic and foreign, non-profit and for-profit institutions.

This RFA will be supported through the NIH traditional research project grants (R01) and Interactive Research Project Grants (IRPG). For IRPGs, a minimum of three investigators with related research objectives may concurrently submit collaborative, cross-referenced individual research project grant applications that share a common focus. Applications may be from either a single institution or a consortium of institutions. The earliest anticipated date of award is July 1, 1993. The total project period for applications submitted in response to the present RFA may not exceed five years. The estimated funds (total costs) available for the first year of support for this initiative is $2 million. The expected number of awards is five to eight.

This initiative permits a range of epidemiologic and interdisciplinary investigations of ovarian cancer including, but not limited to:

*Epidemiologic studies of:

--the long-term effect of combination oral contraceptives, with special reference to age at initial use and age at cessation of use, on ovarian cancer risk by pathologic type;

--the relationship between hormone replacement therapy and ovarian cancer risk;

--the use of fertility-promoting drugs, ovarian stimulants, or in vitro fertilization in relation to ovarian cancer risk;

--the interrelationship of tubal ligation, hysterectomy, and hormone levels to ovarian cancer risk;

--the association of unilateral oophorectomy and age at oophorectomy with ovarian cancer risk;

--the influence of diet and physical activity and their interaction on ovarian cancer risk;

--the relationship of exposure to potential oocyte toxins, such as talc, galactose, caffeine, smoking, and other agents, to ovarian cancer risk among women who use and those who do not use oral contraceptives.

*Molecular epidemiology studies exploring differences in genetic predisposition to ovarian cancer due to variations in

susceptibility genes, hormone metabolism, DNA repair activities, chromosome sensitivity to mutagens, or other factors.

*Molecular epidemiologic studies using existing registries of ovarian cancer families.

*Analytic studies of ovarian cancer to determine the impact of changes in exposure due to migration from low- to high-risk regions and/or to secular changes in lifestyle and environment.

*Studies of racial/ethnic differences in the histologic and cytologic parameters of ovarian cancer that may reflect differences in exposure or susceptibility.

*Population-based studies of the correlation of estrogen and progesterone receptor content of ovarian tumors with histologic type, grade, clinical prognosis, and exposure history.

Inquiries and letter of intent may be directed to: Dr. A.R. Patel, Extramural Programs Branch, Epidemiology and Biostatistics Program, Div. of Cancer Etiology, National Cancer Institute, 6130 Executive Boulevard, Executive Plaza North, Suite 535, Rockville, MD 20892; phone 301/496-9600.

RFA CA/ES-92-23

Title: **Biotechnology transfer to epidemiologic studies in cancer**

Letter of Intent Receipt Date: Oct. 22

Application Receipt Date: Nov. 19

The Extramural Programs Branch in NCI's Div. of Cancer Etiology, and the Scientific Programs Branch, Div. of Extramural Research and Training, National Institute of Environmental Health Sciences (NIEHS), invite investigator-initiated research grant applications to further the effective use of biomarkers of exposure or susceptibility in future epidemiologic studies of cancer etiology.

Applications may be submitted by domestic and foreign non-profit and for-profit institutions, public and private. This program will be supported by traditional research project (R01) grants and Interactive Research Project grants (IRPG). The earliest anticipated date of award is July 1, 1993. The total project period may not exceed three years. The estimated funds (total costs) available for the first year of support for this initiative is $1.5 million. The expected number of awards is five to seven.

Successful grant awardees under this RFA are strongly encouraged to participate in an annual program meeting of one or two days' duration in Bethesda, MD, during the first and third years and in Research Triangle Park, NC, during the second year. The respondents must request sufficient funds within the budget to accommodate expenses for one to two participants at these meetings. The application should include a statement indicating a willingness to comply with this requirement.

Traditional methods in epidemiology have estimated exposure to carcinogens on the basis of surrogate measures. These have included, for instance, questionnaire data on lifestyle factors such as diet and smoking, record of job titles or past employment in a particular industry, or interview information on use of medications.

Appropriate biomarkers can reduce misclassification of exposures, increase accuracy, and enhance study power to resolve exposure-cancer relationships.

Exciting opportunities have emerged from the recent revolution in molecular biology and genetics. Laboratory advances offer unprecedented capabilities to measure carcinogenic factors at the cellular or molecular level and to detect their interaction with cellular constituents. A variety of biomarkers show significant promise of improving exposure assessments, identifying inherited and acquired host susceptibility, and detecting cellular and subcellular events representing predisposing disease states, intermediate outcomes, and early stages of cancer (e.g., sister chromatid exchanges). To date, most of the evidence about biomarkers has been derived from experimental systems, with only limited testing in human subjects in well-controlled field studies.

Pilot studies in small populations of humans have demonstrated the utility of certain biomarkers: cellular assays indicating pathobiological responses to carcinogens and techniques that assess inherited or acquired host susceptibility factors. However, a wide range of interindividual variability and methodological issues remain to be resolved before these procedures can be applied to large-scale epidemiologic investigations.

The goal of this initiative is to stimulate investigations designed to validate and apply biomarkers of exposure or susceptibility in epidemiologic research in cancer etiology. For biomarkers demonstrated to have utility, assessment of the extent of intra- and inter-individual variability is important. Validation procedures should consider determinations of range of normal values, as well as sensitivity, specificity, and predictive value. The influence of biological variables such as age, sex, race, ethnicity, nutritional status, preexisting disease, and lifestyle should be appropriately addressed.

Inter-institutional collaborations between laboratory scientists from several disciplines and epidemiologists are encouraged to promote integrated planning of study protocols and experimental methods as well as the conduct of research. Extension of an ongoing epidemiologic study by the addition of a laboratory component can be proposed. Laboratory investigations will be acceptable if human subjects or specimens are being tested. Whenever possible, research design should utilize shared laboratory and specimen resources. Ease of study conduct and expense, as well as collection, storage, and transport problems should be considered. Projects will be evaluated on their potential for enhancing the understanding of cancer etiology and strategies for prevention. The program particularly encourages studies with relevance to breast, ovarian, prostate, and cervical cancers.

The initiative permits a range of investigations in molecular epidemiology relevant to cancer etiology, including, but not limited to:

--Demonstration of the feasibility of developed biomarkers for epidemiologic research (e.g., heterocyclic amine food mutagens, benzene-DNA adducts, thymine glycol, mutation of the hypoxanthine guanine phosphoribosyl transferase (HGPRT) gene);

--Validation of biomarkers in exposed and unexposed population subgroups (e.g., ethnic and minority populations, family units, occupational cohorts, patients taking chemotherapeutic agents or other medicinal compounds);

--Determination of levels of agreement of mutually confirmatory methods of analyses for measuring the same biomarker (e.g., DNA adducts by physico-chemical, immunoassay, and post-labelling methods) with consideration of inter-and intra-laboratory variability;

--Comparison of biomarkers or combinations of biomarkers in different sources of specimens such as human cells, tissues, organs, and body fluids;

--Determination of specific sampling conditions (e.g., timing, seasonality, repetitive or serial testing) in a chronobiologic fashion including host/environmental factors with/without interactions (e.g., dietary, viral, hormonal) that may influence validity, reliability, and reproducibility;

--Establishment of background or reference levels in normal or unexposed populations.

Inquries may be directed to: Dr. Kumiko Iwamoto, Extramural Programs Branch, Epidemiology and Biostatistics Program, Div. of Cancer Etiology, NCI, Executive Plaza North, Suite 535, Rockville, MD 20892; phone 301/496-9600; or Dr. William A. Suk, Scientific Programs Branch, Div. of Extramural Research and Training, NIEHS, Research Triangle Park, NC 27709; phone 919/541-0797.