THE CANCER LETTER

Vol. 23 No. 32
Aug. 15, 1997

Price $265 Per Year US
$285 Per Year Elsewhere

FDA Declares Taxol Orphan Drug For KS; Can IVAX Break Bristol's Exclusivity?

On Aug. 4, IVAX Corp. received good news from FDA: the Oncologic Drugs Advisory Committee would consider the company's New Drug Application for paclitaxel as a second-line treatment for advanced Kaposi's sarcoma.

On the same day, Bristol-Myers Squibb received even better news from FDA: the agency approved the company's supplemental NDA for Taxol as a second-line treatment for advanced Kaposi's sarcoma.

With the approval, Bristol received the "orphan drug" status and, consequently, seven years of market exclusivity for KS.

These good tidings from Rockville have left many observers scratching their heads: If BMS has been granted seven years of exclusivity

(Continued to page 2)

In Brief

Ginder To Direct Massey Cancer Center; UAB Receives $1 Million For Genetics Chair

GORDON GINDER was named director of the **Massey Cancer Center** at Virginia Commonwealth University. Ginder is the former director of medical oncology and associate director of the University of Minnesota Cancer Center. . . . **UNIVERSITY OF ALABAMA AT BIRMINGHAM** received a $1 million charitable remainder trust to establish the Olivia Turlington Miller Endowed Chair of Cancer Genetics at the **UAB Comprehensive Cancer Center**. The contribution was given by William Miller, founder of AmSouth Bank Corp. International Department in honor of his late wife. . . . **GUIDO TRICOT** was named director of the bone marrow and stem cell transplant program at the **University of Maryland Greenebaum Cancer Center** in Baltimore. Tricot is professor of medicine, oncology, and pathology at the University of Maryland School of Medicine, and the former director of bone marrow transplantation at the University of Arkansas Hospital. . . . **DOROTHEE HERLYN** was awarded an $87,000 two-year grant from the Brain Tumor Society to support her work on a brain tumor vaccine. Herlyn, a scientist in the **Wistar Institute** tumor immunology program, is studying active specific immunotherapy to activate immune systems against the mEGF-R protein. . . . **NCI RESEARCH CONTRACTS BRANCH** has amended RFP NO2-CN-75041-70, "Cancer Control Research Program Support Contract." The proposal due date is changed from Oct. 15 to Sept. 15.

URGENT: Please deliver this FAX edition to the person named on the cover sheet. For transmission problems or information, call 202-362-1809.

IVAX To Present Paxene Data To FDA Advisors Sept. 19

(Continued from page 1)

for KS, why is ODAC reviewing a competing application for an analogous drug for the same indication?

Thus, FDA may have to: (a) tell IVAX that its approval (if it gets one) would not entitle it to sell the drug for the next seven years, or, (b) find a legitimate reason to break the BMS market exclusivity.

IVAX officials were undeterred by the odd circumstances of their upcoming date with ODAC. "We are moving our application forward, and we are going to be presenting our data to FDA on Sept. 19 for Paxene for KS," said Robert Jaffe, director of corporate communications at Miami-based IVAX. Jaffe declined to discuss the application further.

"Either IVAX has something that no one knows about, or they are very naive, or they feel committed because their application is publicly out there, and they feel they have little to lose," a former ODAC member said to **The Cancer Letter**.

"It looks to me like IVAX is trying a stealth approach to the Orphan Drug Act," said a prominent clinical investigator who specializes in drug development. "`Maybe no one will notice if we do this.' I believe they will."

THE CANCER LETTER

An Independent Newsletter

Member, Newsletter Publishers Association

Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg
Staff Writer: Catherine Fiore
Circulation: Rena Guseynova

P.O. Box 9905, Washington, DC 20016
Tel. (202) 362-1809 Fax: (202) 362-1681
Editorial e-mail: kirsten@www.cancerletter.com
Customer service: subscrib@www.cancerletter.com
World Wide Web URL: http://www.cancerletter.com

Subscription $265 per year US, $285 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc.

Founded Dec. 21, 1973 by Jerry D. Boyd

While IVAX officials have not commented on the issue directly, at a Congressional hearing last spring, Samuel Broder, the company's senior vice president, research and development, said FDA should abandon what he characterized as the restrictive role of enforcing patents and doling out orphan drug exclusivity.

"FDA rules and policies unintentionally encourage and could reward the larger sponsor for waiting until the very last moment to put together a study and submit an application whose primary purpose is to block the smaller sponsor from entering the market for seven years," Broder, former NCI director, said at a hearing of the Subcommittee on Health and the Environment of the House Committee on Commerce (**The Cancer Letter**, May 9).

The BMS application for the orphan drug designation and a supplemental NDA were submitted to FDA in early February. The IVAX NDA for the KS indication was submitted in late March. (**The Cancer Letter**, April 18).

While refractory advanced KS involves a small number of patients, the stakes are enormous for the two companies. If the IVAX drug, brand name Paxene, is approved for KS and made available, the door would be open for its use off-label. If Paxene is priced below Taxol, the indication could open a back door to the nearly $1 billion a year market now controlled exclusively by BMS.

Breaking through the exclusivity barrier of the Orphan Drug Act is difficult, though not impossible, observers say. IVAX will have to demonstrate that its drug differs from Bristol's Taxol on the molecular level, or that it is "clinically superior."

Under FDA regulations, clinical superiority has the following components:

- "Greater effectiveness than an approved orphan drug (as assessed by effect on a clinically meaningful endpoint in adequate and well controlled clinical trials). Generally, this would represent the same kind of evidence needed to support a comparative effectiveness claim for two different drugs: in most cases, direct comparative clinical trials would be necessary, or
- "Greater safety in a substantial portion of the target populations, for example, by the elimination of an ingredient or contaminant that is associated with relatively frequent adverse effects. In some cases, direct comparative trials will be necessary; or
- "In unusual cases, where neither greater safety nor greater effectiveness has been shown, a

demonstration that the drug otherwise makes a major contribution to patient care."

According to FDA documents, the agency is prepared to consider only the active ingredient in paclitaxel rather than the drug's formulation, which includes a Cremophor solution, and which is often blamed for at least some of the drug's side effects.

The agency has made this position clear in a letter that notified Bristol that its drug would qualify for the orphan designation. "Please note that it is paclitaxel and not its formulation that has received orphan designation," Marlene Haffner, director of the FDA Office of Orphan Products Development, wrote in a March 25 letter to BMS.

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

Bulk paclitaxel for the IVAX drug is provided by NaPro Biopharmaceutics of Boulder, CO. The two companies are involved in a strategic partnership to develop the drug.

What IVAX Has to Show

Several observers said FDA would be likely to ask ODAC to compare the two drugs. Expert advice could give the agency protection in case its decision is later challenged, these observers said.

Thus, in addition to addressing the usual questions of safety and efficacy of the IVAX drug, ODAC members could be asked to draw comparisons between the drug in question and the Bristol drug.

Since no other treatment for KS existed through much of the BMS trial, Taxol was approved on the basis of two phase II studies. Though the studies were consistent enough to impress ODAC, the prospect of comparing Bristol's phase II data with the IVAX phase II data is likely to appear daunting to the committee members.

"I don't think you can compare their data, because the Bristol studies on KS are not definitive," said a clinical investigator who spoke on condition that his name would not be used. "They lack the benchmark by which to draw a measurement."

The Taxol data were the best ever seen in a refractory population, said Michael Marco, director of opportunistic diseases at the Treatment Action Group, who served as a patient representative on the panel that recommended approval of Taxol for KS.

According to the FDA analysis of the BMS data, Taxol had a 59 percent objective response rate, a performance that leaves room for improvement, said Marco, who has been invited to serve on the panel as it considers the IVAX drug.

"There is 41 percent which could be higher," he said. "We could have 100 percent complete response rate. Of course, that's what we would like."

The question that puzzles many observers is where could a dramatic improvement come from?

The active ingredient in both drugs is basically the same. It has the same generic name and the same chemical name.

Notwithstanding the FDA position of applying orphan drug protection to the active ingredient exclusively, one possible way to achieve a better performance for the drug would have been to improve the formulation.

However, a comparison of the package insert for the BMS Taxol and the clinical brochure for the IVAX drug indicates that the formulations are identical: 6 mg paclitaxel, 527 mg Cremophor, and 49.7% (w/v) absolute alcohol.

A copy of the IVAX clinical brochure and the company's informed consent form which were obtained by **The Cancer Letter** indicate that the two companies are focusing on similar, if not the same, populations. The IVAX informed consent is titled "Paclitaxel in Advanced Refractory Kaposi's Sarcoma: A Phase II Trial of Paclitaxel from Baker Norton Pharmaceuticals." Baker Norton is a subsidiary of IVAX.

The doses of the two drugs overlap, too.

The IVAX regimen calls for the infusion of 100 mg/m^2 of the drug over three hours every 14 days, the brochure indicates. The BMS drug, too, is approved at 100 mg/m^2 over three hours every two weeks.

Another dose on the BMS label is 135 mg/m^2 over three hours every three weeks.

The IVAX trial for KS, which has produced no publications, involves several of the same investigators as Bristol's. Parkash Gill, of the University of Southern California, who is listed as the principal investigator on the informed consent form for the IVAX drug, was among presenters at the BMS ODAC hearing.

According to a clinical trials database maintained by the Community Consortium, a San Francisco Bay Area group of health care providers, the IVAX trial enrolls patients at USC, the University of California at San Diego, the VA Medical Center in Miami, Massachusetts General Hospital, Beth Israel Deaconess Medical Center in Boston, and St. Vincent's Hospital & Medical Center in New York.

Action Plan on Breast Cancer

HHS Official "Obstructed Intent" Of Committee, Report Finds

The Steering Committee of the National Action Plan on Breast Cancer found that established procedure was not followed by the Public Health Service Office on Women's Health in entering an agreement with NCI for use of $14 million in federal funds earmarked to support the Action Plan.

The committee, which governs the public-private partnership, said OWH Director Susan Blumenthal "ignored the committee's intent" to turn the funds over to NCI for peer-reviewed research in breast cancer.

"Dr. Blumenthal's disregard of process in this matter and her continuing tendency to promote the OWH agenda within NAPBC activities is disturbing and disheartening," said a report written by a subcommittee and approved by the full Steering Committee.

"This most recent example of disregard for and obstruction of [the Steering Committee's] intent has seriously eroded the trust, confidence and enthusiasm that are integral to this partnership," the report said.

Government officials who serve on the committee abstained from last week's vote on the subcommittee's recommendations.

Members of the committee were scheduled to discuss the controversy at an Aug. 15 meeting with HHS Deputy Secretary Kevin Thurm.

The NAPBC is led jointly by Blumenthal and Fran Visco, president of the National Breast Cancer Coalition and a member of the President's Cancer Panel.

Congress appropriated $14.75 million to NCI to support the Action Plan for fiscal 1997. At a meeting last November, the committee decided the amount was inappropriate, considering the Action Plan was not designed to become a separate funding agency. The group voted to allow the funds to remain at NCI to support peer-reviewed breast cancer research.

Following the vote, Shalala directed Blumenthal and NCI Director Richard Klausner to develop a plan for use of the funds. Shalala signed a Memorandum of Agreement between OWH and NCI on July 30 (**The Cancer Letter,** Aug. 8).

Despite its requests, the Steering Committee did not receive copies of the agreement until July 31, according to the subcommittee's report. The final version of the agreement did not specify the amount of funds that would be spent on each of 16 activities. An earlier, complete version, signed by Klausner and Blumenthal, was published in **The Cancer Letter** Aug. 1.

According to a memorandum to the committee, written by John Eisenberg, acting assistant secretary for health, the agreement transfers $3 million from NCI to the OWH to support a program to be developed by the Federal Coordinating Committee on Breast Cancer. "The remaining $11 million remains at NCI for research activities," the Aug. 7 memorandum said. Less than $1 million of the funds would support workshops or conferences, Eisenberg wrote.

The edited text of the Steering Committee recommendations follow:

Subcommittee findings:

1. Established Steering Committee procedure was not followed. Since its inception, the SC has acted to guide the disposition and expenditure of NAPBC funds in a public-private partnership.... When the NAPBC's $14 million was voted to be returned to the NCI last November, it was assumed to be subject to the NCI's exclusive direction and control, with disbursement to be guided by established peer-review procedures. The SC discussed its wishes in detail, voted, and felt that its intentions were well understood. Therefore, it did not occur to the SC to give any further instruction about how this $14 million should be spent, and the existence of an alternative plan devised jointly by the NCI and the OWH came as a surprise to SC members. If such an alternative plan had been anticipated, this should have been fully disclosed to and discussed with the SC. The fact that no advance discussion took place and that the MOA was formulated, revised and then submitted to the Secretary for approval, circumvented the NAPBC's operating plan, violating both the spirit of the public-private partnership and the trust of the SC.

2. OWH sought the Secretary's sign-off on the MOA without benefit of SC reaction and opinion. OWH sent this subcommittee a second document in addition to the attached documents, indicating that the MOA was initially developed by the OWH and the NCI prior to April 1997. On April 28, 1997, Dr. Richard Klausner returned to HHS a "Memorandum of Agreement between the National Cancer Institute and the Office of Women's Health to support research initiatives in breast cancer." The SC met in person on Feb. 10 and by conference call on May 23 and June 13, three opportunities for OWH to provide details about the MOA that were not utilized.

The most recent MOA is a revised, final version of the earlier agreement, ready for the Secretary's approval.

It was received by her office on July 24 with her action requested by July 25, prior to the July 28 SC meeting. The Secretary gave her signature approval to the document on July 30, presumably definitive authorization to start work on the 16 activities.

Since the SC had expressed serious concern regarding lack of procedure and had appointed a subcommittee to assist with a prompt response, OWH and others should have informed the Secretary about these facts, and might also have requested that she delay consideration of the document until after a full SC response was available. We have no information about whether the Secretary signed with full knowledge about the SC's concerns and action, or not.

3. We do not agree with the OWH interpretation that the activities described in the MOA are an appropriate use of NAPBC funds. The $14 million appropriation was put in the hands of the NAPBC SC for its use or direction—it was not put under the joint control of the NAPBC and the OWH. Once under the SC's direction, despite the decision to return these funds to the NCI, they remain NAPBC funds. The fact that Dr. Blumenthal initiated the MOA without consultation with the SC ignored the SC's expressed and implied intent. Rather, OWH created or selected activities—the majority of which are under the lead control of OWH—that diverted funding from peer-reviewed breast cancer research.

4. Given violation of procedure, the finalization of the MOA without SC discussion and the inappropriate use of NAPBC funds, we do not consider a detailed review of the MOA to be a useful exercise. The NAPBC has rigorous procedures for initiating new priority areas, establishing cross-cutting initiatives and creating new activities under its current six priorities. The 16 MOA activities were not subjected to those procedures. Offers to involve the SC in the implementation of the MOA should be rejected.

Subcommittee Recommendations:

Given the above findings, we recommend that the SC take the following three actions:

—Call upon the Secretary to reaffirm that all NAPBC funds are subject to the SC's oversight and the guidelines established by its operating plan, and that she supports the spirit of our public-private partnership.

—Formally express the SC's lack of confidence in the public-sector co-chair. Dr. Blumenthal's disregard of SC process in this matter and her continuing tendency to promote the OWH agenda within NAPBC activities is disturbing and disheartening. This most recent example of disregard for and obstruction of SC intent has seriously eroded the trust, confidence and enthusiasm that are integral to this partnership. In considering this recommendation, the SC will need to determine (a) to whom this lack of confidence should be expressed, (b) what form the communication should take, and (c) what actions the SC wishes to take or be taken that would restore the type of leadership which the SC requires. We recommend that all OWH representatives recuse themselves from this part of the discussion.

—Reaffirm to the Secretary the SC's original intent for the $14 million FY97 appropriation: that it be used for peer-reviewed breast cancer research, and be subject to the NCI's exclusive direction and control, with disbursement to be guided by established peer-review procedures.

Professional Societies

Tobacco Industry Should Fund Cancer Research, AACR Says

The American Association for Cancer Research said the tobacco industry should be supporting federally funded cancer research as part of the proposed tobacco settlement.

"The tobacco industry has a moral obligation to support cancer research because of the morbid impact of its products on the people of the world," AACR said in an Aug. 1 statement. "The taxpayers should not be required to shoulder the burden of this research."

The association urged Congress to use public health funds obtained from the settlement with tobacco companies to fund peer-reviewed research on lung and other smoking-related cancers at NCI.

The association asked Congress to ensure that money from the tobacco settlement be provided to:

1. "Markedly increase the cancer research budget of NCI;

2. Underwrite the cost of participation in clinical research trials on tobacco-related cancers that will contribute to curative or preventive new therapies;

3. Supplement, not supplant, current resources provided to NIH and NCI. This must be done by including a trigger mechanism to maintain the integrity of the baseline budget that is provided through direct appropriations," the organization said.

The association said the proposed settlement effects only the US, and urged Congress to do more to decrease worldwide incidence of smoking-related cancers.

AACR also said FDA authority to regulate any substances found in tobacco that are known to be addictive, or are later found to have adverse affects needs to be confirmed, and that no unusual restrictions be put on that authority through the

settlement.

"Providing new research funds through the tobacco settlement for early detection, treatment, and prevention will offer the hundreds of thousands of Americans afflicted with tobacco-related cancers a better health outcome," the association said.

"The AACR takes the position that Congress has the clear mandate to ensure that our national investment in cancer research is intensified in proportion to the devastating effects of tobacco on public health."

Federal Research Funding

Year-To-Year Funding Hampers DOD Program, IOM Study Says

The Department of Defense Breast Cancer Research Program is hampered by year-to-year funding which makes it difficult to assure continuity of research, a panel of experts convened by the Institute of Medicine said in a report last week.

"The fact that the program is funded for only one year at a time has understandably hampered the ability of the program managers to plan for the longer term," the report said.

The 13-member committee was formed to review the DOD research portfolio, review the progress of the program, which was founded in 1993, and recommend areas for future research. Uta Francke, professor of genetics at Stanford University School of Medicine, served as chairman of the committee.

The DOD breast cancer program was shaped with the help of IOM, which in 1993 convened a panel of breast cancer experts asking them to delineate the areas where research could be advanced through involvement of the military.

In the recent report, the IOM panel said it would be premature to evaluate the quality of the portfolio of projects funded by DOD. "Most funded projects are not complete and progress reports were not available to the committee," the report said.

However, the panel praised the programs for the "flexible approach taken for setting priorities annually; the involvement of breast cancer survivors in the grant peer review process; the level of commitment and diligence of the individuals who serve the program in various capacities; the commitment and support of the program director; the low administrative costs that allow the greatest share of funding resources to be awarded as grants; the use of outside experts for evaluation; and the unwavering respect and advocacy for this program among breast cancer advocacy organizations nationwide."

The panel said that year-to-year funding has prevented the program from establishing standing primary review panels, which resulted in the lack of standardization of priority scores across the ad hoc panels.

"Year-to-year funding has also produced too short a time frame between the publication of the announcement of each grant cycle by a Broad Agency Announcement and the deadline for grant applications, and exacted an unduly heavy toll in time and energy on those involved in the various stages of the process," the report said.

The panel recommended multi-year authorization of the program. The excerpted text of other recommendations follows:

● **Develop a plan with benchmarks and appropriate tools to measure achievements and progress toward goals of the BCRP**. This would allow an evaluation of the effectiveness of the different funding mechanisms, with particular emphasis on Innovative Development and Exploratory Award grants and recruitment and training grants. Elements of the process could include examination of records of publications and presentations, success by investigators in obtaining other grant support relevant to breast cancer, and identification and tracking of investigators who were recruited into breast cancer research by BCRP funding.

● **Consider establishing a permanent non-Army oversight committee independent of both the integration panel and the contractors**. The permanent oversight group would be responsible for quality assurance and program evaluation. "The group would report directly to the BCRP Director and would have access to all information needed to oversee and rigorously evaluate the program in an on-going fashion," the report said.

● **Establish measures to ensure the continuation of the current strength of the Integration Panel**. The workload of individual integration panel members should be reduced where possible. The committee believes that the IP represents a new and imaginative concept in planning and monitoring a research grants program. By functioning as a second tier (programmatic) review and council, and reporting to contractors and

predominantly nonscientific administrators within the Army, the IP wields considerable power in deciding investment strategies and funding policy. The unquestionable success of the IP is the result of the high level of dedication and professional excellence of its members.

● **Spell out in more detail in the Broad Area Announcement the types of proposals sought, the programmatic evaluation criteria, and exclusionary parameters**. The concepts of "innovation" and "translatability," espoused in the 1996 funding cycle, need to be developed and defined more extensively. The BAA should be explicit in inviting proposals in currently under-funded areas of epidemiology, psychological, social, and quality of life issues, and health care delivery research.

● **Lengthen the time between release of the BAA and the deadline for submission of proposals**. This would require shortening the time between appropriation and release of funds from the DOD to the BCRP. This recommendation is especially important for large multidisciplinary proposals that require coordination between a number of basic and clinical researchers.

● **Increase the time between receipt of applications and first-tier peer review panel meetings**. This would facilitate assignments of applications to the most appropriate panels and recruitment of the best and most appropriate ad hoc reviewers.

● **Communicate detailed information about consumer participation in the BCRP peer review process to the scientific community**.

● **Move toward establishing standing review panels**. Include some of the same peer reviewers on consecutive committees to increase reviewer familiarity with the procedures and goals of the program and to provide more consistency in rating patterns.

● **Improve feedback to applicants whose applications were not funded**. IP decisions not to fund applications within the funding range (and to fund applications below the funding range) should be fully documented and the rationale should be communicated to applicants.

● **Establish a procedure for resubmission of unfunded applications**. Proposals that have been revised according to the previous scientific peer reviewers' critiques provided to the applicant should be eligible for resubmission in the next funding cycle. Responsiveness to the previous critique should be made an evaluation criterion.

● **Establish a procedure for competitive renewal applications**. In the framework of a long-term BCRP, successful projects should be considered for continued funding. In the review of renewal applications, past progress made while receiving BCRP support should be taken into account as one of the scoring criteria.

● **Revise the application process to make it less cumbersome**. The Army should consider accepting institutional assurances in the areas of human and animal use and laboratory and environmental safety, in the same way other federal funding agencies do.

● **Reduce the time it takes between funding recommendation by the IP and actual awarding of funds to the investigator's institution**. Streamlining of award and contract negotiations could be accomplished by appointing a program officer dedicated to the BCRP and by increasing the number of staff positions.

● **Streamline the annual reporting process and allow awardees more flexibility in changing experimental design and methodology**. It seems counterintuitive to fund a 3-year IDEA grant that is by nature high-risk and open-ended, and yet manage it like a contract with close monitoring of adherence to a statement of work that was defined at the time of the award. Since no preliminary data are required for these awards, the results of initial experiments and/or progress made by others in the field may suggest a more promising research strategy or more appropriate methodology to attain the original goals of the funded proposal.

● **Allow awardees flexibility in use of funds across spending categories**. This would allow the optimal use of available money toward reaching the goals of the project.

The Six Questions

In 1993, the IOM panel that determined the scope of research for the DOD program, identified six questions the program could address.

The questions concerned the causation, prevention, screening, detection, diagnosis, and optimal treatment of and recovery from breast cancer. The 1993 report recommended that DOD direct its research toward answering one or more of the six questions.

"The committee notes that 50 percent of the funding to date has gone to address the first two

questions, and reiterates the continuing importance of the other questions," the recent report said.

The six questions, which the recent report said remain a useful framework for the program are:

● What genetic alterations are involved in the origin and progression of breast cancer?

● What are the changes in cellular and molecular functions that account for the development and progression of breast cancer? Such studies may result in the development of diagnostic tools capable of identifying heritable and acquired changes that can be detected before the cells become invasive, or even in the premalignant phase, and also in knowledge of the likelihood of an in situ cancer's progressing to invasion. Furthermore, novel therapies capable of eliminating or terminally differentiating breast cells carrying the genetic changes predisposing to malignancy could be developed. The development of such gene therapy requires a better understanding of the genetic and immunological basis of breast cancer, with the vaccine approach to prevention and treatment facilitated by knowledge of the new altered gene products and peptides expressed in cancer cells.

● How can endogenous and exogenous risk factors for breast cancer be explained at the molecular level? Studies of interactions of genetic and environmental or other nongenetic factors should be given high priority. This work will require close collaboration of clinical and basic scientists. The natural history of breast cancer and factors that influence prognosis need to be understood at both a histological and a molecular level. Epidemiological studies should evaluate new and existing risk factors at the molecular level with emphasis on hormonal, geographic, and family history variables. Emphasis should be placed on identification of new factors whose molecular mechanisms explain cancer risks not explained by known risk factors.

● How can investigators use what is known about the genetic and cellular changes in breast cancer patients to improve prevention, detection, diagnosis, treatment, and follow-up care? Knowledge of a woman's genetic makeup should facilitate the determination of whether she would benefit from a particular treatment and of what her chances would be for good health and quality of life. Studies to determine the optimal way to counsel women with genotypes that place them at risk will assist in developing informed consent procedures for testing and methods for effectively communicating test results. Implementation of preventive measures in high-risk women requires the full understanding of the natural history of breast cancer and the efficacy of various interventions, stratified by genotype information.

● What is the impact of risk, disease, treatment, and ongoing care on the psychosocial and clinical outcomes of breast cancer patients and their families? Behavioral, psychological, and social research has focused increasingly on race, ethnic, and cultural differences, and the psychological effects of genetic testing for breast cancer susceptibility. Work in these areas should continue where gaps remain.

● How can investigators define and identify techniques for delivering effective and cost-effective health care to all women to prevent, detect, diagnose, treat, and facilitate recovery from breast cancer? The IOM (1993) outlined a number of targets for health services research including: barriers to state-of-the-art health care, health care seeking behavior, patient treatment preferences, and barriers and inducements to participation in clinical trials. These topics remain important. Other areas for investigation have emerged, including access to care, patterns of utilization of health services, patient-provider communication, provider education and behavior, economic and cost analyses, issues relating to policy setting and guidelines, and health care delivery systems.

Use of computer information systems is increasingly important in patient tracking, tissue bank administration, networking genetic information, and facilitating enrollment in clinical trials. These systems require additional investigation prior to widespread implementation because of confidentiality and acceptability issues.

Studies regarding ethnic, cultural, and personal differences in health beliefs and health care seeking behavior will yield important information for those providing care and setting policy. Also necessary is accurate, reliable, unbiased information on direct and indirect costs associated with genetic testing, prevention strategies, screening and diagnostic techniques, or a given treatment; such information is a critical component of realistic health care planning and delivery. An area of urgent importance is the effect of managed care on breast cancer screening, detection, treatment, and follow-up.

RFA Available

RFA CA-97-016

Title: **Minority-Based Community Clinical Oncology Program**

Letter of Intent Receipt Date: Sept. 23

Application Receipt Date: Nov. 18.

The NCI Division of Cancer Prevention and Control invites applications from domestic institutions for cooperative agreements to the Minority-Based Community Clinical Oncology Program. New community and research base applicants and currently funded programs are invited to respond to this RFA. Up to 10 Minority-Based CCOP awards will be made; up to $2.7 million in total costs per year for three years will be set aside to fund applications.

Inquiries: Lori Minasian, DCPC, NCI, 6130 Executive Blvd Rm 300-D MSC-7340, Bethesda, MD 20892-7340, tel: 301/496-8541, fax: 301/496-8667.