THE CANCER LETTER

Vol. 17 No. 31
Aug. 2, 1991

Price $205 Per Year US, Canada.
$230 Per Year Elsewhere

P.O. Box 15189 Washington, D.C. 20003 Telephone 202-543-7665

ODAC Endorses Tamoxifen Trial, With Modification To Ensure Enrollment Of Women At Higher Risk

FDA's Oncologic Drugs Advisory Committee recommended on a 6-1 vote that the NCI sponsored chemoprevention trial of tamoxifen be allowed to proceed, with the stipulation that the eligibility criteria will be tightened to ensure that the study population is at a very high risk for developing invasive breast cancer. If FDA follows the committee's

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In Brief

Three NCI Basic Science Centers Rank In Index Of Citations; Novello: Help More Smokers Quit

THREE NCI SUPPORTED basic science cancer centers rank two, three, and four among the world's biological sciences research laboratories with regard to the number of citations that papers written by their scientists receive. The centers are Cold Spring Harbor Laboratory, La Jolla Cancer Research Foundation, and the Salk Institute for Biological Studies. The citation index was compiled by the Institute for Scientific Information in Philadelphia. While footnote counting has its critics and its limitations, proponents of the method say that as one index of merit, it is at least quantifiable. . . . **SURGEON GENERAL** Antonia Novello has called on health professionals to intensify their efforts to help smokers quit and to prevent young people from taking up the habit. Writing in the May/June issue of "CA--A Cancer Journal for Clinicians," published by the American Cancer Society, Novello said the current rate of decrease in the number of Americans who smoke must be doubled to meet the PHS goal of cutting smoking prevalence to 15 percent by the year 2000. "We must remain ever vigilant. We must remember that more than 400,000 Americans died in 1988 because of smoking," she wrote. . . . **ERNST WYNDER,** president of the American Health Foundation, has been awarded the Officer's Cross of the Order of Merit of the Federal Republic of Germany, by German President Richard von Weizsacker. The distinction honored Wynder's achievements in the public health field in the US and Germany and for his efforts to foster scientific collaboration and exhanges between the two countries. Wynder, who was born in Germany, immigrated with his family to the US in 1938. . . . **PAUL CALABRESI,** professor and chairman, Brown Univ. Dept. of Medicine, and chairman of the National Cancer Advisory Board, recently delivered the second annual Charles Spurr Lectureship at Wake Forest Comprehensive Cancer Center. The title of the lecture was "The Use of Antineoplastic Agents in Non-Neoplastic Diseases."

ODAC Gives Go-Ahead To Tamoxifen Trial, But Seeks Higher Risk Women

(Continued from page 1)

recommendation, the agency would approve an Investigational New Drug application allowing the National Surgical Adjuvant Breast & Bowel Project to proceed with a long term trial of tamoxifen versus placebo in 16,000 healthy high risk women at 70 centers. The IND is required since the trial would test the drug for an unapproved indication.

NSABP plans to address the committee's recommendations and submit a final IND, and has scheduled enrollment of patients to begin in late fall.

The study's primary purpose is to reduce the incidence of breast cancer by 30 to 50 percent in the in the tamoxifen arm. Secondary endpoints are prevention of cardiovascular disease and osteoporosis. The National Heart, Lung & Blood Institute also is sponsoring the trial.

The NSABP draft protocol proposed to enroll any woman over age 60, or any woman aged 35-59 whose risk of developing breast cancer in the next five years is at least as great as that of a 60 year old woman. The relative risk would be determined using the Gail model, a method to determine an "individual risk profile" based on a woman's family and personal history. The younger women would have at least a five times greater risk of developing breast cancer than an average woman.

NSABP Chairman Bernard Fisher said younger women "should not be denied the opportunity to participate."

The committee, however, was troubled by the risk of endometrial cancer and thromboembolic events possibly offsetting any reduction of breast cancer.

"I'm concerned that the serious side effects would balance the incidence of breast cancer you would have by not using the drug," said committee member David Ahmann.

Ahmann referred to Fisher's data on the NSABP B14 trial of tamoxifen versus placebo in 2,800 women at risk of developing contralateral breast cancer. Fisher said 1.5 percent of the women on tamoxifen in that trial experienced serious thromboembolic reactions, resulting in two deaths. He said the deaths occurred after patients had been on tamoxifen for a relatively short time. Six patients on tamoxifen developed endometrial cancer; all were stage 1 "or less," Fisher said. Three of those patients had had prior hormone intake, and none were premenopausal.

Adriane Fugh-Berman of the National Women's Health Network told the committee that her organization opposes any trial of tamoxifen in healthy women until there is more data on the drug's adverse effects.

On the benefit side, the B14 trial demonstrated a 75 percent decrease in the risk of contralateral breast cancer in patients under age 50, and a 40 percent decrease in those over age 50. There were 61 cancers of the opposite breast in the placebo arm and 29 in the tamoxifen arm; significance was .0002. The women were on tamoxifen for at least five years.

But Ahmann said the NSABP draft protocol predicts the therapy "will avert cancer in less than 2 percent of the trial participants. What is the likelihood that adverse events could outweigh clinically significant benefits?" he asked. He also was concerned about the projected 10 to 20 percent dropout rate.

Fisher responded that, "There is not enough information until the trial is conducted. We can't answer this without knowing the data."

"You're asking patients to buy a breast cancer delay with some other event and we need to know the exchange rate. It's imperative for patients to know [the risks]," committee member Steven Piantadosi said.

"We're being asked an extraordinarily difficult question: What constitutes a safe chemoprevention trial?" said committee member Dean Brenner, who was the one vote against proceeding with the trial.

Committee member Grace Monaco said the investigators should carefully address the issues in their informed consent forms. "I have no problem with people taking risks as long as they are informed. We don't know what [tamoxifen] will do or when it will stop working. There are a lot of unknowns," she said.

Fisher said the consent form can be modified to reflect the committee's concerns. But he commented

THE CANCER LETTER

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Editorial/Subscriptions Office
PO Box 15189, Washington, DC 20003
Tel: (202) 543-7665 Fax: (202) 543-6879
Subscription rate $205 per year North America, $230 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter and AIDS Update.

that in the past, review bodies have held up important breast cancer studies such as the lumpectomy trial. "If you feel this is not ready to go, then that is your decision and you are responsible for the next 20 years," he said.

"You will have more data in the next year or two," said Monaco.

"Do you really believe the data will be different in a year?" Fisher replied. "Tell us how long it will be before the data is acceptable." Fisher said NSABP did not come to the meeting to "try to sell anything, but merely to present data."

"I wanted to be sold on this," said committee member Nancy Kemeny. "You probably have the data. Go back and look and present for a simple person what you think will happen."

FDA asked the committee to determine whether the risk was "high enough for the development of invasive breast cancer and/or cardiovascular disease to justify five or more years of therapy." The vote was 2-5 against the statement, with Monaco and Piantadosi in the minority. However, the committee did not recommend specific changes to the enrollment criteria.

Despite their concerns, the committee endorsed the NSABP protocol "with modifications" because of the importance of conducting a trial and NSABP's reputation as a "excellent group."

Committee Chairman Craig Henderson said, "Tamoxifen is already being used in the community for this purpose, so this is a window of opportunity." He called the protocol "an elegant trial, beautifully put together," and agreed with Monaco that "women at high risk should be able to decide for themselves whether to participate."

Last year, ODAC reviewed a chemoprevention protocol submitted by a California group and recommended against that particular study proceeding, but emphasized the need for a trial of tamoxifen in healthy high risk women.

Ahmann and other committee members underscored their respect for NSABP. The NSABP protocol is "a well written, thoughtful protocol prepared by an excellent group," Ahmann said. "It is in sharp contrast to the protocol we evaluated last year."

Later, Ahmann commented that, "It really is difficult for me to believe the study will produce clinically significant results that will affect health care decisions. [However,] if any study is to be done, this is the one that should be done, but I lack enthusiasm for it."

Leslie Ford, chief of NCI's Community Oncology & Rehabilitation Branch in the Div. of Cancer Prevention & Control, said the trial will be done under a cooperative agreement with NSABP, through NCI's Community Clinical Oncology Program (CCOPs). The trial was approved by the DCPC Board of Scientific Counselors with the understanding it would be reviewed again after one year.

NCI Considering Master Agreements With Centers For Clinical Trials

NCI is considering the idea of establishing master agreements with its designated cancer centers in order to conduct innovative clinical trials and prevention and control trials.

The master agreements would be jointly sponsored by the Div. of Cancer Prevention & Control, the Div. of Cancer Treatment, and the Div. of Cancer Biology, Diagnosis & Centers, according to Margaret Holmes, chief of the Cancer Centers Branch in DCBDC.

"Centers are ideally suited for prevention and control and clinical trials," Holmes told the DCBDC Board of Scientific Counselors at its recent meeting. Funding for the master agreements would be "over and above" the centers program's current budget, she said.

Board member Ross McIntyre said the idea "offers flexibility and would speed the linkage" between laboratory studies and clinical research, but suggested that a large number of cancer centers already are members of clinical cooperative groups. Core components such as statistical centers might have to be duplicated, placing those centers with a large number of staff investigators "at a significant advantage" in competing for master agreements over smaller centers, he said.

Holmes said NCI envisions the master agreement "as somewhat complementary with the cooperative groups."

The idea, which may be presented in further detail at the board's fall meeting, is part of NCI's effort to enhance the Cancer Centers Program. Even if funding is not available for the proposed program now, it could be available in the future, said Centers, Training & Resources Program Director Brian Kimes.

"We should look to the future," Kimes said. "We are trying to figure out where we are going to be in a few years. If you have any ideas, please help."

"We are very much in a reactive mode," agreed board member Albert Owens.

Suggestion Of Prevention Working Group

The master agreement proposal grew out of recommendations from the Cancer Centers Program's Prevention & Control Working Group, chaired by Shirley Lansky, director of the Illinois Cancer Council.

The working group met in April to discuss the

promotion of prevention and control research at cancer centers. One major suggestion was that any effort to promote research must be backed with a funding mechanism.

Working group members are Ellen Gritz, UCLA; Robert Day, Fred Hutchinson; Paul Engstrom, Fox Chase; Louis Bernard, Drew/Meharry/Morehouse; Gary Morrow, Univ. of Rochester; and Randall Harris, Ohio State Univ.

Following is an excerpt from the working group's report on its meeting:

Lansky opened the working group deliberations by noting that in 1975 there was a lot of money for prevention and control research and a lot of ideas, but by 1980 NCI, as a formal policy, reduced its emphasis on investigator initiated ideas and concentrated its efforts primarily on large, fairly costly targeted initiatives. Historically, the mega-programs funded by DCPC through cooperative agreements and contracts lasted only when the support was there and the program vanished with the loss of funds. She believed that cancer centers have the greatest staying power in prevention and control research and that the evidence of this is that greater than 50 percent of the prevention and control research grants have been in cancer centers over the last 15 years. She focused the discussion of the group on five major areas:

Cancer center collaborations. For the most part, although individuals in centers often share ideas, there are few collaborations between centers involving specific protocols of research programs. There is the practical barrier of busy people dealing with multiple priorities that works against such spontaneous collaborations, but there are examples where the Cancer Information Service has been the focus for collaborations and the CIS could serve as the focal point for many kinds of research. It was noted that a recent investigator initiated effort of collaboration between the Drew/Meharry/Morehouse Consortium Center, the USC and UCLA Comprehensive Centers and the California State Health Department failed to receive funding. There was some discussion about the CCOP program and how difficult it is to maintain communications. In addition, there was considerable confusion over the difference between a cooperative group and a research collaboration. The consensus was that collaborations between cancer centers can work in those areas where the science is ready for interaction and when there are specific projects identified in which interaction is mutually advantageous for the participating institutions. There was an overall negative feeling about a cooperative group structure for cancer centers. In order to facilitate collaborations among cancer centers, there must be a way of initiating discussions that are project specific, sustaining the interaction through the development of a truly collaborative research enterprise, and then implementing the research (i.e., funding). Perhaps multiple project, multiple site PO1s or interactive multi-institutional R01 packages would be a way to stimulate collaborative research that is cost effective. Clearly, there must be an appropriate funding instrument that facilitates and encourages collaborations.

Perhaps two areas where collaborative research might be ready for multicenter studies are:

1. Development of new innovative approaches for the assessment of cancer risk factors and screening, for which basic scientists can be brought effectively into the problem. Centers are poised and in a perfect position to gather epidemiologic data to conduct risk factor studies. Risk factor data can be collected because cancer centers have access to a large number of patients. Perhaps a group of centers could find a way to collect common information on patients.

2. Development of new approaches to reducing morbidity and increasing the quality of patients' lives.

Another suggestion was for the Cancer Centers Program to coordinate a prevention and control research centers meeting in conjunction with the American Society of Preventive Oncology meeting, or develop a regular research conference using the conference grant mechanism.

Priorities of NCI versus cancer centers. There was considerable discussion between the working group members and DCPC staff relative to the perception that DCPC has focused on large, institute initiated, targeted, costly studies at the expense of innovative, investigator initiated ideas. The working group felt that these larger studies have penalized cancer centers by reducing the funding opportunities for investigator initiated ideas and forcing centers to find other, softer, more unreliable sources of support to do their own research.

If the center mobilizes its expertise for a long term NCI mega-study, when the study ends the cooperative group also terminated their collaboration, leaving no experience or research program that can serve as the springboard for future innovative research. If centers use softer sources of funds for prevention and control research, when the money goes away so do the people involved.

The working group felt very strongly that cancer centers should be encouraged to conduct innovative research and that, if NCI wants to build a strong infrastructure for prevention and control research in cancer centers, it must think about the availability of funding mechanisms to achieve this goal. NCI must distinguish between the conduct of prevention and control research, which centers are good at, and the application of existing technologies for servicing the communities, which cancer centers can participate in but cannot be responsible for.

Collaborations with other organizations. The Centers for Disease Control is becoming heavily involved in breast cancer and cervical cancer screening programs, but these programs are being implemented entirely through state health departments. CDC is doing business in the same way as it has in the past. There should be more communication between the CDC and NCI, especially with regard to the important role cancer centers can serve in the implementation of these screening programs. Since the state health departments do not have cancer prevention expertise, one solution is for the state health departments to place the CDC person in the cancer center. This could be done in a few places on an experimental basis. The CDC program will be better and the cancer center will fulfill its prevention and control research and outreach and service responsibilities more effectively.

There should be more effective linkages among NCI, cancer centers, and the American Cancer Society such that ACS dollars could be more effectively applied to promote prevention and control research in cancer centers.

There was considerable discussion relative to the NCI CCOP program. Cancer centers and CCOPs are difficult to integrate because centers are good at developing new ideas, and cooperative groups, which are run by committees, are good at taking what is feasible into the community. It would be to the advantage of both centers and CCOPs if these functional capabilities could be linked more effectively; that is, linking research ideas more effectively to technology transfer.

The major issue for cancer centers, and the confusing issue, is where does a cancer center's responsibility lie. Responsibility without authority are incompatible. Cancer centers can be an active participant in the community or public health issues; but

there are many examples of successful demonstration projects conducted by centers that could not obtain further support from the responsible public health agencies to continue such projects. In some cases, more damage than good is done when such demonstration projects disappear. Overall, however, there is a lot more going on in public education and implementation of screening technology and there is considerably heightened public awareness. NCI has a much better story to tell than it has been doing.

There could be some broader oversight for cancer control, especially with regard to the responsibilities and roles of the different organizations in and outside the federal government.

Building prevention and control research programs and training new investigators. Vincent Cairoli of the Cancer Training Branch noted that only 60 people were identified in the area of prevention and control research in the NRSA program, that approximately 15 people had received K07 awards since the inception of this award mechanism, and that there were a number of R25 education grants which emphasized training in prevention and control. Several of the working group members were complimentary of the intramural DCPC training course and were interested in knowing how many people have been trained, where they have gone, and what success they have had in establishing independent research centers.

There was considerable discussion about the new NCI R25 initiative to stimulate outreach activities and to incorporate schools of public health into cancer prevention and control education programs. There has been a very mixed experience of cancer centers in their efforts to successfully work with schools of public health. UCLA, UNC, and Fred Hutchinson are examples of good experiences, but there have been difficulties and bad experiences with cancer centers in other institutions. While conceptually the integration of cancer centers and schools of public health is laudable, practically it is only possible if the school of public health wants to work with the cancer center. It was considered essential that the new R25 initiatives should be awarded to cancer centers rather than to schools of public health if the intent is to stimulate cancer center/SPH interactions.

Review and funding of prevention and control research applications at NIH. The working group discussed the value of the P01 mechanism and the investigator initiated R01 applications for prevention and control research. They emphasized two major points: 1) The distribution of the prevention and control research dollar pool for investigator initiated R01 and P01 research relative to institute initiated, targeted, large studies is a critical NCI policy decision. In addition, those who successfully obtained R01 support frequently experienced difficulty in competitive renewal because of the lack of a standardized format for evaluating progress in long term cancer prevention and control research programs. The need for setting milestones for progress in long term prevention and control research is essential. 2) Many prevention and control researchers in cancer centers are therefore very discouraged and are not likely to believe NCI's intent to promote innovative investigator initiated research when past policies appeared to deliberately discourage this kind of research in favor of targeted research.

The program project grant (P01) is of considerable benefit to prevention and control research because it requires collaborations and interactions and much of the future of prevention and control research will depend on effective translational linkages between the basic sciences and more applied research areas in prevention and control. It might be used to encourage cooperation between centers as long as these were investigator initiated collaborations.

The working group was provided the data on the composition and charge of the Behavioral Medicine Study Section (BEM) and the Epidemiology & Disease Control Study Section (EDC), as well as the results of all reviews of NCI R01 grant applications reviewed by these study sections in 1989 and 1990. These are the study sections in which investigator initiated proposals are peer reviewed, and these are study sections which reside under the administrative purview of the NIH Div. of Research Grants. Both the BEM and EDC study sections had mandates which fit the general needs of prevention and control research; however, the study section memberships and expertise are too narrow to meet the needs of cancer prevention and control research applications.

For example, BEM has no strong advocate for cancer research. If two to three individuals with cancer expertise, preferably from a cancer center environment, could be added to the BEM regular roster, it could provide appropriate, objective, expert peer review of NCI applications. EDC has little representation in the cancer area and no expertise in cancer control--all of the membership are expert in etiology.

Kimes noted that there were other alternatives that NCI had discussed internally:

1) One option is to create a study section managed by DEA/NCI that gets handed over to DRG once the application review workload is up, 2) using a new chartered study section in DRG that meets only once a year to raise the application review load is another option. The R03 program was generally very successful and should be continued; R03 applications are totally reviewed by ad hoc review groups or by the existing Cancer Control Review Group in the Div. of Extramural Activities in NCI.

It was noted that ACS receives 80 applications per year and that it supports two study sections which seem to work well. Perhaps it would benefit future strategies in this area by looking into the Prevention, Diagnosis, and Therapy Study Section and the Psychosocial and Behavioral Research Study Section in the ACS.

House Passes NIH Authorization Bill, Overturns Fetal Tissue Research Ban

The House last week passed a bill to authorize funding for NIH that includes a controversial provision to overturn the government's ban on federally funded research using tissue from aborted human fetuses.

President Bush has indicated he would veto the bill, which passed on a 274 to 144 vote, slightly short of the two-thirds margin needed to override a veto.

Rep. Henry Waxman (D-CA), the bill's sponsor, said he was "pleased" with the margin. But the bill's opponents, led by Rep. Christopher Smith (R-NJ) and Rep. William Dannemeyer (R-CA), predicted the veto would be sustained. Antiabortion advocates believe fetal tissue research encourages women to have abortions.

The bill also would reverse a decision by the administration cancelling a nationwide survey of adolescent sexual behavior.

The bill also authorizes funding for NCI, and cancer program advocates have said that the bill does not contain controversial provisions related to cancer funding.

NCI Awards Grants To Physicians For Improving Early Cancer Detection

NCI has awarded grants to primary care physicians and research institutions in a collaborative effort to evaluate methods for implementing NCI's working guidelines for early cancer detection.

It is the first NCI program to fund medical intermediary organizations to improve physician skills in detecting early cancers.

The program, called "Prescribe for Health," uses a set of early detection guidelines NCI formulated for seven types of cancer--breast, skin, colorectal, prostate, testicular, oral cavity, and uterine cervix.

The program will study 348 practices in four geographical areas of the U.S.; this includes about 1,000 physicians and more than 60,000 patients.

Following are the grants NCI has awarded:

--$2.5 million for four years to Clinical Directors Network of Region II, collaborating with Dartmouth Medical School and Albert Einstein College of Medicine to improve early detection among low income and minority patients served by public health clinics. CDN will provide community health centers with training for physicians and staff. CDN is sponsored by the Public Health Service. Principal investigators are Allen Dietrich, Dartmouth; Alan Perla, CDN; and Jonathan Tobin, Einstein.

--$2.3 million, four years, to Univ. of North Carolina to study early detection in rural primary care practices. The study will be conducted in 30 counties in North Carolina, including half in the mountainous western part of the state heavily populated by Cherokee Indians. PI is Arnold Kaluzy.

--$1.6 million to Univ. of Chicago to develop better screening and early detection procedures through health maintenance organizations with physicians serving low to moderate income blacks and Hispanics in the Chicago area. Breast, cervical, colorectal and oral cancers are targeted in the study. PI is Loretta Lacey.

--The Agency for Health Care Policy Research of HHS has funded a fourth grant for $2.5 million for the AMC Cancer Research Center in Denver, which is collaborating with the Copic Insurance Co. of Colorado to study 112 primary care practices to increase early cancer detection by more than 168 physicians. PIs are Stuart Cohen, of AMC and George Thomasson, of Copic.

"Prescribe for Health" is headed by Suzanne Haynes of NCI's Div. of Cancer Prevention & Control. Forrest Pommerenke, a family practice physician at NCI, is the medical consultant for the project.

NCI Early Detection Guidelines

Following are NCI's recommendations for early cancer detection:

Skin cancer--All individuals should be encouraged to examine their skin thoroughly on a regular basis. Primary care physicians should be encouraged to examine the skin as part of the periodic health examination. Further public and professional education should be promoted on the early detection of skin cancers and in particular malignant melanoma.

Breast cancer--Physicians should encourage their female patients in doing monthly breast self exam. Physicians should be encouraged to do clinical breast examinations on all female patients in whom they are doing a periodic exam. Beginning at the age of 40, a mammogram should be encouraged every one to two years until the age of 50, after which it should become annual. In women with a personal history of breast cancer, mammograms should be encouraged annually.

Uterine cervical cancer--All women who are, or have been sexually active, or have reached age 18, should have an annual Pap test and pelvic examination. After a woman has had three or more consecutive, satisfactory, normal annual examinations, the Pap test may be performed less frequently at the discretion of her doctor.

Colorectal cancer--A rectal examination should be included as a part of the periodic health examination. At age 50, fecal occult blood testing should be done annually and sigmoidoscopy should be performed every three to five years. The physician should identify for special surveillance high risk patients, including those with a strong family history of colon cancer or with a personal history of polyps, colon cancer, or inflammatory bowel disease.

Testicular cancer--Periodic (monthly) testicular self examination should be encouraged. Routine palpation of the testicles by a physician during physical examination should be carried out as part of the periodic health examination.

Prostate cancer--Annual digital rectal examination of the prostate should be performed on all males over age 40. More specific education and training should be given physicians in the detection of prostate cancer.

Oral cavity cancer--Oral examination including palpation of the tongue, floor of the mouth, salivary glands, and lymph nodes of the neck should be performed as part of the periodic health examination. Special attention should be given those at high risk due to tobacco and alcohol use.

NCAB Committee To Propose Event Marking Cancer Act's 20th Year

The National Cancer Advisory Board will be asked to consider at its next meeting a proposal to hold a special one-day scientific symposium in honor of the 20th anniversary of the National Cancer Act of 1971 later this year.

The event is proposed by the NCAB's Committee on Activities and Agenda, which discussed the idea at a meeting last week in Arlington, VA. Committee members suggested that the event be held in conjunction with the Board's scheduled meeting in late November. The anniversary of the signing of the Act is Dec. 23.

The symposium would review progress made in understanding and treating cancer over the past 20 years.

"This event comes just once in a decade, and we have made some significant advances," said Board Chairman Paul Calabresi, who also is chairman of the Activities and Agenda committee.

Although other organizations such as the American Cancer Society are making plans to mark the anniversary of the Act with certain events, NCI has chosen to take a "low-key" approach, Calabresi said. No events are planned, but the "Journal of the National Cancer Institute" has marked the anniversary all year with a series of special articles.

"It's a question of style," Calabresi told the committee. "[NCI Director Samuel Broder] doesn't want to make a big hullabaloo and come out with a lot of promises."

"The purpose [of the event] would not be to wine and dine Congressmen, but would be a way to present information.... There have been a number of documented advances," said Board member Sydney Salmon.

All former NCAB members, NCI directors and division directors would be among those invited to the symposium.

Committee members said they would further define the proposal for presentation to the Board at its Sept. 23-24 meeting.

Future Agenda Items

Calabresi, appointed by President Bush earlier this year as Board chairman, asked the committee to suggest topics for future Board meetings. Suggestions included: NCI-FDA interactions, program project grants, "the whole issue of clinical research," drug scheduling and chronobiology, advances in chemoprevention, systemic therapy for prostate cancer, NCI's drug discovery groups, ethical issues in the tamoxifen chemoprevention trial, laser surgery, and new topics in radiotherapy such as proton beam, boron activation capture, and stereotactic radiosurgery.

Several committee members said they wanted more balance between presentations by NCI intramural scientists and those outside the Institute.

John Durant asked for an annual report from the NIH Office of Scientific Integrity on "how many scientists have been accused and found innocent." He also suggested followup on the "town meetings" the Board held a few years ago around the country on NCI's Year 2000 goals for reducing cancer incidence and mortality.

Erwin Bettinghaus said the Board's Committee on Information and Cancer Control is considering whether to hold another round of "town meetings."

"We got a lot of press in each place; there was a major press conference in Washington. It made a fair amount of splash," he said.

The committee also discussed whether all regular NCAB meetings should be held in Bethesda, as they normally have been. The NCAB once held a meeting at Memorial Sloan-Kettering Cancer Center. Under the leadership of Armand Hammer, the President's Cancer Panel held its meetings all over the country. "It had a lot of positive impact," Calabresi said.

Bettinghaus suggested NCAB hold one meeting a year somewhere besides Bethesda. "You go places where you will get the best national press," Bettinghaus said.

DCT Board Has More Fun?

The committee also approved moving the Board's closed session in which it considers grant applications from Tuesday mornings to Monday afternoons during its two-day meetings, and endorsed the idea of allowing more time for committee meetings.

Marlene Malek suggested the Board hold an "informal dinner" the first night of its meeting.

"Oh, I see, a social," said Calabresi. "That would be nice. But it's a big group, so if you hold it at a restaurant, you've got to split up into separate tables, kind of defeating the purpose. And you're forced to eat Chinese when maybe you'd rather have Italian."

"While I was on the Div. of Cancer Treatment board, we had a closed session in a restaurant," said Salmon.

"While I was on the DCT board, we had a session in a restaurant and at [DCT Director] Bruce Chabner's house," said Calabresi.

"If you do it routinely, people will lose interest," said Bettinghaus.

The committee concluded its meeting by deciding to meet more often. "When we meet off-schedule [not in

conjunction with an NCAB meeting] where should we meet?" Calabresi asked.

"Chicago airport is a good place," Durant said. "Next to Terminal 2 is the Skybird Lounge. I've been there many times."

RFPs Available

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

RFP NCI-CM-27721-19
Title: Shelf life evaluation of clinical drugs
Deadline: Approximately Sept. 13

The Pharmaceutical Resources Branch of the Developmental Therapeutics Program, Div. of Cancer Treatment, NCI, is seeking a contractor experienced in analysis and evaluation of clinical pharmaceuticals to provide proper storage, adequate testing and evaluation of shelf life samples of investigational clinical drug formulations, including both injectable products and oral dosage forms, and report the results of such testing. Data provided in these reports will be used for providing NCI and its investigators with information regarding the proper storage and handling of various drug products under investigation, for determining appropriate expiration dates for the products, and to support NCI's Investigational New Drug Applications files with FDA. Storage and inspection of reserve samples as defined by the FDA current Good Manufacturing Practices regulations shall be required. The contractor will be responsible for validating each of the analytical methods in conformance with FDA requirements prior to use. The contract period will be for five years beginning approximately May 1992.

Contract specialist: Zetherine Gore
RCB Executive Plaza South Rm 603
301/496-8620

International Collaboration PA

Program Announcement PA-91-77
Title: Fogarty International Research Collaboration Award
Application Receipt Dates: Oct. 1, Feb. 1, and June 1

The Fogarty International Center), under a program of Central and Eastern European (including the USSR) and Latin American and Caribbean Initiatives, is providing small grants to U.S. grantee institutions to facilitate cooperation and collaboration between U.S. scientists and scientists in these regions. These small grants will provide funds to the foreign collaborators, through the U.S. grantee institution, for equipment and supplies at their home institution, and for travel expenses for both the U.S. Principal Investigator and the foreign collaborator. These awards are intended to support the new and expanded research efforts of U.S. scientists who are Principal Investigators of currently funded NIH research project grants on the general scientific subject of the proposed collaboration.

The main objective of this program is to facilitate collaborative research efforts between U.S. and foreign scientists that will expand and enhance the NIH-supported research program of the U.S. Principal Investigator, while at the same time benefiting the scientific interests of the collaborating foreign scientist. These small grants will provide funds to purchase supplies, materials, and small equipment items necessary to conduct the collaborative research in the foreign scientist's research laboratory at a non-profit public or private institution in the eligible countries. These awards will also provide travel support, as necessary to conduct the collaborative research effort, for the U.S. and/or the foreign collaborator(s). All biomedical and behavioral research topics supported by the NIH are eligible for inclusion under this program. The U.S. Principal Investigator must show evidence of ongoing NIH research support in areas related to the small grant application, and this support must be available during the entire small grant award period. The application must demonstrate that the effort will enhance the scientific contributions of both the U.S. and foreign scientists and strengthen the contribution to the NIH-sponsored research effort.

The small grants will provide up to $20,000 per year for up to three years in direct costs. Funds may be used for materials, supplies, and equipment for the foreign scientist's research laboratory and for travel expenses for the Principal Investigator and/or the foreign collaborator, and their research associates, as justified by the scientific needs of the project. No salaries or stipends for any of the collaborators, students, or technical assistants will be offered under these awards. Applicants must request support to conduct research not already being supported by the U.S. investigator's research grant; however, the research proposal must be an extension of or related to the currently funded research project. The awards will be made to U.S. institutions that will be responsible for the expenditures. The minimum small grant project period will be for one year; the maximum will be for three years. Indirect costs will be calculated on the basis of the off-site rates of the U.S. sponsoring institution. The award of this small grant is non-renewable, and the NIH awarding unit of the "parent" grant is under no obligation to continue support for the foreign grant as a component of a recompeting "parent" grant.

U.S. scientists who are Principal Investigators of NIH research project grants (R, P, or UO1 series) that will be active and funded during the proposed grant award period (up to three years) are eligible.

The small grants will be made for work conducted in cooperation with scientists only in countries
located in the geographical regions commonly known as Central and Eastern Europe (including the USSR), Latin America, and the non-U.S. Caribbean. The foreign collaborator must hold a position at a public or private non-profit institution that will allow him or her adequate time and provide appropriate facilities to conduct the proposed research.

To obtain further information on this program and to request the necessary special application instructions, write, fax, or phone: Dr. David Wolff or Dr. Danuta Krotoski, International Research and Awards Branch, Fogarty International Center, NIH Bldg. 31, Rm B2C21, Bethesda, MD 20892, phone 301/496-1653, FAX 301/402-0779.

For grants management and fiscal matters, contact Silvia Mandes, Grants Management Officer, Fogarty International Center, NIH Bldg. 31, Rm B2C21, Bethesda, MD 20892, phone 301/496-1653, FAX 301/402-0779.

NCI Contract Awards

Title: Synthesis of bulk chemicals and drugs for preclinical and clinical studies
Contractor: Aldrich Chemical Co. Inc., Milwaukee, WI; $2,399,322.