THE CANCER LETTER

Vol. 18 No. 11
March 13, 1992

Price $215 Per Year US, Canada.
$240 Per Year Elsewhere

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

Pacific Yew Act Would Result In Duplication, Delays In Taxol Production, Witnesses Say

Legislation intended to promote the availability of the anticancer drug taxol by "requiring the federal government to stop the waste of Pacific yew trees" would result in significant, costly delays and duplication of effort in harvesting yew bark, according to witnesses at a Congressional hearing last week. Rep. Gerry Studds (D-MA) and Rep. Ron Wyden (D-OR) have cosponsored H.R. 3836, the "Pacific Yew Act of 1991," which calls on the federal agencies managing the yew harvest to do what they, in most cases, are already doing. Wyden, who last summer launched

(Continued to page 2)

In Brief

Day, Foti Lead Coalition; Harkin Ends Campaign; UT Southwestern Receives $85 Mil. In Donations

ROBERT DAY was elected president of the National Coalition for Cancer Research for a two-year term. Day, director of the Fred Hutchinson Cancer Research Center, succeeds Albert Owens, of Johns Hopkins Univ. The Coalition this year changed the name of its top elected post from chairman to president. **Margaret Foti,** executive director of the American Assn. for Cancer Research, was elected president-elect. **Francis McKay**, executive vice president of Fox Chase Cancer Center, is secretary treasurer. **Terry Lierman**, executive director of the Coalition and president of Capitol Associates, took a short leave to work on Sen. Tom Harkin's presidential campaign. With Harkin's decision to quit the race this week, Lierman is back in Washington. . . . **$85 MILLION** in donations were announced by Univ. of Texas Southwestern Medical Center recently, including a gift of $25 million for cancer research from an anonymous Dallas donor. In addition to completing funding for a new research building and a center for research in basic cancer biology, that donation funded a new therapy research center that helped attract NCI's Radiation Oncology Branch Chief **Eli Glatstein** to Dallas, the university said. . . . **ENDOWED CHAIR** in breast imaging has been established at the Univ. of California (Los Angeles), with an endowment of $700,000, partly funded by a gift from the Iris and Gerald Cantor Foundation. . . **DIRECTOR OF PUBLIC AFFAIRS,** a new position, has been established by Roswell Park Cancer Institute. Candidates with a proven track record in public and media relations and at least five years of professional experience related to health care or science, are invited to submit c.v. wiht salary requirements to Office of the Institute Director, Elm & Carlton Streets, Buffalo, NY 14263.

825,000 Pounds Of Yew Bark Collected In '91, For 10,000 Patients . . . Page 3

Still Misperceptions On Hill About CRADA Between NCI, BMS . . . Page 4

Report Of SPOREs Cut Premature, Broder Says, Wait For Peer Review . . . Page 5

RFPs, RFAs Available . . . Page 7

Bill To Promote Yew Harvest Would Delay Taxol, Witnesses Say

(Continued from page 1)

Congressional inquiry into the taxol agreements between federal agencies--including NCI--and Bristol-Myers Squibb Co., continued his criticism of the agreements.

With the 1992 yew harvest scheduled to begin in a few weeks, the Forest Service, the Bureau of Land Management, Bristol-Myers, Hauser Chemical Research Inc., and a timber industry representative testified before Studds' Subcommittee on Fisheries and Wildlife, of the Committee on Merchant Marine and Fisheries, that the agencies and the companies that have agreements to harvest the bark and extract taxol already are working to ensure that this year's harvest is successful.

The bill would, among other things, result in duplication of a tree survey, establish committees that in some cases have already been established to perform work that is already being done, require costly and time consuming revisions in timber sale contracts, and require the companies to save materials from the yew tree that at present cannot be used effectively for taxol production, the witnesses said.

Even the General Accounting Office, an arm of Congress that can generally find fault with anything, testified that, "It appears that all parties to the cooperative agreements have taken actions to more fully utilize the bark of the yew tree in fiscal year 1992."

James Duffus, director of National Resources Management Issues for GAO, told the subcommittee: "Both the Forest Service and BLM have established policies to monitor salvage operations to ensure that usable bark buried by logging debris is not overlooked and burned along with other debris. The Forest Service has also instructed its field personnel to ensure that bark from smaller yew branches and stems be utilized."

Some news reports, including a recent article in "The New York Times," have found stacks of yew being treated as logging trash. Anne Heissenbuttel, director of forest planning and policy for the National Forest Products Assn., told the subcommittee that, "This is a trend which has reversed, and companies are making real efforts to protect this resource. In many instances the reports were, in fact, mistaken."

Many trees in slash piles reported as yew were really western cedar, which looks similar. "The problem is certainly much less prevalent than has been reported," Heissenbuttel said.

According to the GAO, Hauser has instructed its collectors to collect bark from all limbs one inch in diameter and larger, and plans to return to previous harvest sites to collect salvageable bark.

"Both Forest Service and BLM officials have informed us that they are working with Bristol-Myers to include provisions in their Pacific yew program plans for fiscal year 1992 to more fully utilize the tree's bark," the GAO's Duffus said. "This will require, among other things, that the two agencies 1) assign responsibilities for ensuring increased utilization among the respective parties to the cooperative agreements, 2) establish utilization standards to determine whether all feasibly collectable bark has been collected, and 3) monitor compliance with the utilization provisions of the program plans."

Wyden: Patients Dying Due To Waste

The Studds bill directs the Forest Service and the Bureau of Land Management to provide for the long term conservation of the yew and a sustainable supply of yew for the production of taxol. The agencies are directed to:

--Complete an inventory of the Pacific yew on the lands under their jurisdiction within six months.

--Establish an interagency yew committee made up of representatives from BLM, Forest Service and U.S. Fish & Wildlife Service to develop a conservation plan for the Pacific yew, as well as interim management guidelines to be implemented until the plan is completed.

--Establish special task forces within BLM and the Forest Service to ensure the proper implementation of the act.

According to a subcommittee memo, the bill also "provides that the interim guidelines and management plan shall include measures to ensure that: when planning Pacific yew harvests, priority is given to harvesting yew in areas of existing timber sales; yew

THE CANCER LETTER

Editor: **Kirsten Boyd Goldberg**
Founder & Contributing Editor:
Jerry D. Boyd

Editorial/Subscriptions Office
PO Box 15189, Washington, DC 20003
Tel: (202) 543-7665 Fax: (202) 543-6879

Subscription rate $215 per year North America, $240 elsewhere. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter.

resources are utilized with little or no waste; yew is cut prior to other timber resources on any given sale and in a manner that allows for resprouting; and yew trees are replanted.

"In addition, the legislation encourages research on Pacific yew ecology and alternative methods for procuring taxol; it seeks to minimize the illegal harvest and sale of yews, and it ensures that collectors are allowed timely access to yew resources. The bill also directs the Administration to report to Congress with recommendations on how to increase the harvest of yew trees if sufficient amounts cannot be harvested in compliance with this act and existing law."

Wyden told the subcommittee that, "If federal agencies were doing the very basic management essentials called for in this bill we wouldn't need to be here today." Wyden held a hearing last summer to examine the Cooperative Research and Development Agreement between NCI and Bristol-Myers (**The Cancer Letter,** Aug. 9, 1991). The focus of last week's hearing were agreements between the Forest Service, BLM, and Bristol-Myers.

Wyden claimed his staff found "significant" waste of yew bark on a trip to the Northwest last summer.

Rep. Harold Volkmer (D-MO) asked Wyden whether Hauser had harvested a sufficient amount of bark to produce enough taxol for the NCI sponsored studies. "If they have, then I don't think there's a problem," Volkmer said.

"My sense is that for 1991, waste was the rule rather than the exception," Wyden said. "We've got people all over the country waiting in line for this drug. There was a significant amount of waste. People die because there's not enough material."

Volkmer continued: "If Hauser can only utilize 800,000 pounds of bark a year, they are not going to be able to give [taxol] to more people. I question whether we can say there are thousands more people who could have gotten this drug."

Volkmer said small amounts of waste at each timber sale are not the major problem. "What we're seeing out there now is decreasing timber sales in the Northwest. If those sales are severely limited, we may have a problem getting enough yew," he said.

825,000 Pounds Of Yew Bark Collected

George Leonard, associate chief of the Forest Service, told the subcommittee that the service "is already meeting the major purposes of the bill, but would not object to its enactment, if amended to eliminate the administrative overlap and complexities implicit in the bill.

"We think it is important that the Pacific yew bark collection process proceed with as little delay as possible," he said.

According to Leonard, only 90,000 pounds of bark were collected in 1990, prior to the agreements between Bristol-Myers and the federal agencies. By the end of fiscal 1991, more than 728,000 pounds had been harvested from seven national forests in Oregon and Washington, and more than 97,000 pounds had been harvested from three national forests in Idaho and Montana, bringing the total amount of collected bark to over 825,000 pounds. That is enough bark to make taxol to treat more than 12,000 patients.

The Forest Service cooperative agreement with Bristol-Myers calls for inventorying yew on National Forest System lands, developing yew conservation guidelines, conducting conservation biology research, and supporting all phases of the bark transfer program. The company paid the Forest Service $882,692 to conduct these activities in 1991, Leonard said.

Cy Jamison, director of the Bureau of Land Management, noted that the FY 1992 appropriations act for the Dept. of the Interior directed the agencies to establish task forces and a yew strategy plan--similar to the requirements in the Studds bill. Leonard and Jamison said the agencies are implementing those requirements.

Jamison said the cost for management and harvest of the yew in FY91 and 92 will total more than $1.5 million, which will be paid by Bristol-Myers.

The agreements with Bristol-Myers "represent an extraordinary long term commitment by BLM to effectively manage the yew for the benefit of cancer research, while ensuring conservation of the Pacific yew as part of an interdependent ecosystem. Enactment of H.R. 3836 has no provisions to facilitate our activities. In addition, we find some of the provisions confusing and objectionable."

Specifically, Jamison said:

--The bill does not clearly require approval of the interior and agriculture secretaries to approve or revise the guidelines.

--Certain provisions of the bill are inconsistent with the Endangered Species Act.

--A Pacific yew inventory for western Oregon will be completed by this August, but the bill requires an annual plan that Jamison said would be duplicative.

--The bill would require costly contract revisions for timber sales that have already been completed but have not been harvested.

"In summary, we believe the program we have developed will accomplish the underlying purposes of the bill without the start up delay and administrative overlap and complexities implicit in this bill," Jamison

concluded.

Dean Stull, chief executive officer of Hauser Chemical Research, testified on the firm's role in the extraction and purification of taxol. "Entering the second year of our program, we expect to see continued improvements in our harvesting methods," Stull said. "We strive to collect all practicable usable bark from public and private lands."

Workers use hand tools and light machinery to harvest bark, he said. After the bark is collected, it goes to a regional processing facility where it is chipped and dried. Then it is shipped to Hauser's facility in Colorado, where taxol is extracted and purified. "Hauser's process to produce taxol yields more taxol per pound of bark than other processes," Stull said.

Hauser is also participating in research to extract taxol from twigs, needles and wood, and synthesis from similar natural products, Stull said. He said the firm has developed a laboratory method for the production of taxol from yew needles and is conducting pilot testing of that method.

Stull also said that within three years, the firm expects to be able to extract and purify taxol from plantation grown trees on a large scale.

Yew Harvest Dependent On Timber Sales

Heissenbuttel of the National Forest Products Assn., whose members hold timber contracts, tried to dispel myths about the yew, including the media reports of waste and burning. Another myth is that the yew is an "old growth" species than can only exist in the wilderness and must have shade. "This is simply not true," Heissenbuttel said. The tree actually grows faster in full sunlight and is capable of regenerating itself either through stump sprouting or by seed.

Heissenbuttel agreed with Volkmer that the major threat to taxol availability in the next few years is delay of timber sales in the West due to court injunction or administrative appeal.

Court orders currently are stalling timber sales in parts of Oregon, Washington, and California due to "uncertainty over management of the Northern Spotted Owl," Heissenbuttel said. "Congress could help ensure a sustained supply of Pacific yew bark by directing the Administration to exempt timber sales which contain Pacific yew from administrative appeals."

Heissenbuttel said her organization recognizes that alternative sources of taxol will be available within five years. "Rather than developing a policy on the harvesting of Pacific yew as suggested in H.R. 3836, we urge Congress to instead support ongoing efforts to develop Pacific yew policy." The bill, she said, might actually delay such a policy.

More importantly, Heissenbuttel said, Congress should provide more funding for research on the Pacific yew, taxol, and alternative sources of taxol.

Rep. Barbara Vucanovich (R-NV), a breast cancer survivor, testified in support of research on taxol and sound management of public lands. She did not support the Studds bill, but avoided outright opposition. "In this time of limited options for women with these diseases, we must ensure that no extra hurdles are placed in the path of cancer research," she said.

Rep. Rosa DeLauro (D-CT), diagnosed with ovarian cancer six years ago, joined Wyden in supporting the bill.

Bristol-Myers vice president for business development Zola Horovitz testified that the firm has agreed to supply NCI with 16 kilograms of formulated taxol in 1992.

"It is absolutely critical that harvesting proceed under this program without impediment or delay for the next two years, so that taxol supplies will be adequate to meet the needs of cancer patients," Horovitz said. "We are confident that, beginning in 1994, our dependence on Pacific yew bark will be reduced."

Two features of the bill concern Bristol, Horovitz said. One, creation of interagency committees and task forces "could prove an unnecessary encumbrance." Two, the provisions mandating collection of needles and small limbs, which are not approved as a source for taxol. "We share the sponsors' concern about waste, and have already begun an aggressive search for alternative sources of biomass," Horovitz said. "We are considering every practical alternative to the use of Pacific yew bark, *but our primary goal is to* eliminate dependence on biomass collected from the wild at the earliest possible time."

The perception that NCI has "given away" taxol to Bristol-Myers still is fashionable in the halls of Congress, the Studds hearing demonstrated.

Wyden told the subcommittee that the NCI-Bristol CRADA "had at its core a handful of sweetheart deals which could greatly benefit Bristol-Myers." Wyden also maintained that, "The Cancer Institute got off to a slow start in research to produce alternatives" to taxol production from yew bark.

Rep. Peter DeFazio (D-OR) said in an opening statement that the yew "grows on public lands, yet the government has entered into secret collusive agreements with private firms" to develop taxol.

Studds said the orphan drug designation for taxol

for ovarian cancer "gives Bristol-Myers a free monopoly."

Rep. Robert Smith (R-OR) wanted to know why the effort to harvest yew bark did not begin earlier than 1991 if scientists knew about taxol's activity in 1988.

Div. of Cancer Treatment Director Bruce Chabner was present to explain the history of taxol and the CRADA. "The extent of the activity of the drug wasn't clear," he said. The drug had major side effects, and there were production problems, which were worked out between 1988 and 1991. "None of us knew the yew would be valuable until late '88 or early '89," Chabner said. There are usually 50 drugs in development at NCI in a given year, he said.

"I wish I had been clairvoyant three years ago and known taxol would be so active," Chabner said. "There was one report, in 25 patients, of a 30 percent response rate. That wasn't enough to set off a land rush."

Here is a summary of Chabner's testimony:

Taxol was isolated in 1971 from the bark of Taxus brevifolia. It showed minimal activity in initial preclinical testing, but later demonstrated a unique mechanism of action and high degree of activity. "At each step, significant problems of production, supply, formulation, and clinical toxicity hampered its development," he said. Activity against ovarian cancer was first observed in 1988.

Federal laws encourage joint research and development between government laboratories and industry. "NCI has followed the policy of seeking partners in private industry to commercialize its discoveries and inventions." In 1990, NCI signed the CRADA with Bristol-Myers to expedite taxol development and generate data to obtain FDA approval. It was awarded following an open competition with scientific review. Four firms submitted proposals, but Bristol was the only major U.S. company with cancer drug development experience that competed, Chabner said. Another was the French firm Rhone-Poulenc-Rorrer, which now has developed a potential competitor to taxol, taxotere.

Under the CRADA, Bristol is doing the expensive production of taxol and is cooperating with NCI on clinical trials. In exchange, NCI provides the firm exclusive access to taxol data, and reserves the right to publish its taxol studies. There is no patent protection on taxol.

"NCI does not have the capacity to develop and market taxol as a prescription drug on its own, nor does any other government agency," Chabner said. "Nor has NCI the legal authority to market drugs.

"While BMS has obtained orphan drug status from FDA for taxol in ovarian cancer patients, other companies are free to pursue the development of taxol for other diseases. In addition, NCI is vigorously attempting to develop other taxol-like drugs. These would be available through patent licensing on a competitive basis to all pharmaceutical companies."

The CRADA also states that Bristol will set a fair market price for taxol. A similar clause was contained in NCI's license agreement with Bristol for the anti-AIDS drug ddI. "In that instance, we believe that the company established a very favorable price for their product, below that of its major competitive product, AZT," Chabner said.

About 500 patients were being treated with taxol before the cooperative agreements began; this year about 8,000 to 10,000 will be treated with taxol from bark harvested in 1991. Potential population of patients with breast and ovarian cancer who may be candidates for taxol treatment is about 50,000 a year.

"Our supplies are adequate to support several of our highest priority studies, but additional meritorious research could be initiated if the supplies were larger," Chabner said. "I am confident that within two to three years we will no longer be dependent on the Pacific yew as the sole source of this drug."

In July of 1990, NCI issued an RFA for taxol studies. Sixteen grants totaling $2.3 million were awarded last year.

This year, NCI signed an agreement with Rhone-Poulenc to aid in testing of taxotere. The company holds several patents on the compound. "We will join the company in testing taxotere as a single agent and in combination against ovarian cancer, lung cancer, and other common solid tumors," Chabner said. The drug is manufactured from yew needles.

Report Of SPOREs Cut 'Premature,' Broder Says, Wait For Peer Review

Will NCI Director Samuel Broder's first major initiative for the 1990s be cut back before it has even begun? Not if he can do something about it, it seems.

The question of funding for the Specialized Programs of Research Excellence in breast, prostate and lung cancer was brought up at last month's meeting of the Div. of Cancer Treatment Board of Scientific Counselors by board member Paul Carbone.

NCI Deputy Director Daniel Ihde, standing in for Broder that day, said seven SPORE grants would be funded. Board member Donald Kufe noted that plans for the initiative called for funding nine SPORE grants--three in each disease site--and asked for an explanation.

"The costs of the applications that came in were higher" than NCI had anticipated, Ihde told the board.

Broder, contacted this week, said the report of the diminishment of the initiative was "premature."

"We have not yet reviewed the applications," Broder told **The Cancer Letter.** "Any final decision about funding levels is premature. The SPORE initiative remains an extremely high priority activity. You might be in for a surprise."

The SPOREs, new grants under the Cancer Centers Program, were established to make major research efforts in the three most prevalent disease sites. Congress provided $17.5 million to fund the SPOREs in FY92.

NCI's original projections called for funding of $22.5 million annually.

According to Broder, the final funding level for the program "will be a function of the enthusiasm of peer review."

NCI received a total of 48 SPORE applications: 19 for breast, 20 for prostate, and nine for lung.

"Everyone has been gratified by the seriousness and depth of the response to the initiative," Broder told **The Cancer Letter.** "NCI, the intramural scientists and all of the people in the extramural community who make up the National Cancer Program, the whole country, can be proud of them. We've gotten very interesting applications in all of the disease areas."

Broder continued: "We will look very carefully at every possible way to make sure good applications are funded. Bear in mind that under the current system, SPORE applications not funded in the current fiscal year can possibly be picked up in the next funding period, but I'm not making any promises."

Broder said he could not confirm Ihde's statement that the budget requests contained in the applications went over NCI's predictions. "The appropriateness and validity of funding requests is a legitimate matter for peer review to decide," he said.

Awards are expected to be made by Sept. 30. Meanwhile, NCI staff are coordinating the massive review job. Each SPORE application has several individual research projects that require separate review.

Kirt Vener, chief of the Prevention, Epidemiology and Control Review Section, Grants Review Branch, is heading the SPORE review process, assisted by three executive secretaries.

'Unusual' Process; 165 Reviewers

Vener told **The Cancer Letter** that a two-stage review is planned for the breast and prostate SPOREs. An initial review panel will look at the research projects proposed and will evaluate proposals on the basis of scientific merit and whether the projects meet the "translational" objectives--the ability to translate basic science to clinical research and, ultimately, treatment. The initial review panel--one each for breast and prostate--will put together the equivalent of summary statements.

Four to six weeks later, the applications will go to the breast or prostate parent committee. This committee will review the entire application, including the career development, developmental research, and institutional commitment sections, and will assign the final priority score.

"That course of action is somewhat unusual, because of the large number of applications we received," Vener said. He estimated that there are more than a hundred research projects proposed in the breast SPORE applications alone. "For one committee to review all the projects and the entire application would be a Herculean task doomed to failure," he said.

Review of the lung SPORE applications will require only one committee. In the nine applications, there are about 65 to 70 proposed projects, Vener said.

NCI is close to naming all 165 of the reviewers--60 each for breast and prostate, and about 45 for lung, Vener said.

One complication: many of the top investigators in each of the diseases have thrown their hats into the ring.

"We cast the net wide for reviewers," Vener said. However, not all institutions have applied for each type of SPORE, so NCI will be able to use a reviewer on the lung committee, for example, whose institution applied for the breast SPORE.

"A tremendous contribution has been made by the scientific community to help us with the review," Vener said. "This is more complex than we are used to dealing with at NCI."

The FY92 cutback in NCI's travel budget will not affect the SPORE review, Vener said, since the reviews will be held in the Washington area. The travel restriction applies to NCI staff leaving Bethesda, not to consultants traveling to Bethesda.

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-CP-21096-21
Title: Prospective cohort study of cancer among men and women in agriculture (field stations)
Deadline: Approximately April 20

NCI's Occupational Studies Section, Environmental Epidemiology Branch, is seeking contractors to perform the above named project. This contract will create field stations for epidemiologic studies in states that produce grain and livestock and/or producers of other nonperishable commodities with a significant proportion of minority farmers. It is anticipated that at least two field stations will be necessary to create a large cohort (approximately 156,000 persons) that can be followed prospectively for 10 years or more to obtain detailed information on agricultural exposures, diet, cooking practices and other factors of etiologic interest for cancer and other diseases.

Field stations shall be located in states with population based cancer registries and pesticide applicator registries with at least 20,000 registrants. It is desirable but not mandatory for the state to also have a birth defects registry. The study is designed so that we can also investigate biomarkers of exposure and disease. The entire cohort will include farm owner/operators (70,000), their spouses (56,000) or commercial and noncommercial applicators (30,000). The cohort will be assembled by enrolling applicators as they come to obtain or renew a pesticide application license at the Agricultural Extension Service Office. The spouses of farm applicators will be invited to enroll in the cohort when their spouse is enrolled. It is anticipated that it will take three to four years to assemble the entire cohort since licenses are renewed on a three-four year cycle in many states. The types of support to be provided by the contractor in the conduct of the studies include: study initiation and liaison, use of study materials and procedures to be prepared by the coordinating center contractor, data collection, data preparation, data processing, drawing blood and collecting urine from cancer cases and their controls in a non-clinical setting, study monitoring, quality control and reporting. These task may vary.

Communication between the contractor and NCI will often be on a daily basis with regularly scheduled conference calls to be held monthly and meetings with the NCI project officer in Rockville, MD, every six months. The contractor must be capable of supervision the administration of self administered questionnaires by cohort members at multiple sites (30-100 locations) within the state. Many of the questionnaire administration sessions may be scheduled concurrently. Personal computers shall be used wherever possible for data processing and manipulation. The NIH/DCRT computer facility (which has IBM computers) shall be accessed by remote terminals to be provided by the contractor on their own premises. The contractor shall provide monthly and annual progress reports, monthly budget reports and a final technical progress report. Other deliverables shall include computerized data, raw data and biologic specimens.

The estimated level of effort to be provided is 100,375 total direct labor hours for the entire period of performance for the entire cohort developed at all field stations. Direct labor hours at individual field stations should be estimated in proportion to the number of cohort members that can be enrolled into the study (the entire cohort is estimated to be 156,000 study subjects). The contract will be a cost reimbursement, completion type for a 60 month period.
Contract specialist: Barbara Shadrick
RCB Executive Plaza South Rm 620
301/496-8611

RFP NCI-CP-21102-13
Title: Dietary fat, cooking practices, indoor radon and lung cancer risk among women
Deadline: Approximately April 20

NCI's Div. of Cancer Etiology is seeking an organization capable of performing a study entitled "Dietary Fat, Cooking Practices, Indoor Radon, and Lung Cancer Risk Among Women." This study is intended to expand upon observations derived from an earlier study conducted on nonsmoking women with lung cancer in Missouri. The main objectives of the new study are to 1) evaluate the relationship between specific types of dietary animal fat and lung cancer, and 2) study the dose response relationship between indoor radon and lung cancer cases and the controls. The RFP will contain a mandatory requirement that offerors document that the geographic region proposed has a geographic region wide population based tumor registry that will yield 700 female lung cancer cases in one year and document access to this registry.
Contracting officer: Sharon Miller
RCB Executive Plaza South Rm 620
301/496-8611

RFAs Available

RFA CA-92-02
Title: **Radiologic Diagnostic Oncology Group IV**: Ovarian cancer and pediatric solid tumors
Letter of Intent Receipt Date: March 24
Application Receipt Date: May 26

The Radiation Research Program in NCI's Div. of Cancer Treatment invites applications for cooperative agreements to establish a multi-institutional scientific group in order to optimize staging and followup of pediatric solid tumors and ovarian cancer.

Nonprofit and for profit organizations and institutions, foreign and domestic, are eligible to apply.

Awards will be made as cooperative agreements (U01), a funding mechanism in which substantial NCI programmatic involvement with the recipients during performance of the planned activity is anticipated.

Approximately $800,000 in total costs per year for three years will be committed to fund applications. It is anticipated that six to eight institutions plus the headquarters component will be funded to establish RDOG IV.

The objective of this RFA is to invite applications to perform centrally coordinated multi-institutional cooperative clinical trials to determine the most effective imaging algorithms required to stage and monitor ovarian carcinoma and pediatric solid tumors (other than those of the central nervous system). The successful applicants will form RDOG IV. The results of the RDOG IV studies should have a direct and immediate impact on patient care. Additionally, considerable health care cost saving is expected due to elimination of unnecessary diagnostic studies. Sufficient numbers of patients, including minorities and women, for significant imaging trials must be available.

RDOG was formed by NCI in September 1987. The objective is timely evaluation of current and emerging imaging modalities in the management of patients with cancer. The development of multi-institutional clinical trial groups allows for rapid patient accrual within a short period of time. This in turn ensures rapid evaluation and optimization of imaging techniques for diagnosis, staging, and serial monitoring of cancer.

RDOG has had a significant impact on clinical research in radiology. This is the first time that multi-institutional clinical trials in diagnostic imaging have been conducted in a centrally coordinated fashion with strict quality control and analysis of cost-effectiveness. Ultimately, RDOG study findings would be useful for

design of therapeutic protocols and formulating clinical and medical insurance reimbursement policy.

Since its establishment, RDOG clinical research has been important for the development of optimal imaging algorithms for prostate and lung cancer (RDOG I) and pancreatic and colon cancer (RDOG II). Recently an RFA (RDOG III) was issued to study musculoskeletal and head and neck tumor imaging, and seven additional institutions have been funded. The specific focus of this solicitation is to establish RDOG IV to study pediatric solid tumors and ovarian cancer.

Inquiries may be directed, and letter of intent sent, to Dr. Faina Shtern, chief, Diagnostic Imaging Research Branch, Radiation Research Program, NCI, Executive Plaza North Suite 800, Bethesda, MD 20892, phone 301/496-9531.

RFA AI-92-05

Title: **Preparation for AIDS/HIV Vaccine Evaluations**

Letter of Intent Receipt Date: March 30

Application Receipt Date: May 13

The purpose of this RFA is to support developmental projects designed to establish collaborative studies, involving U.S. and foreign institutions, that 1) provide baseline data for determining the feasibility of conducting AIDS/HIV vaccine trials in international settings and 2) prepare international sites to conduct HIV vaccine efficacy trials. The National Institute of Allergy & Infectious Diseases anticipates initiating clinical trials of AIDS/HIV vaccines as early as December 1993 at domestic sites and shortly thereafter at international locations.

Applications may be submitted by domestic for profit and nonprofit organizations, public and private, units of state and local governments, and eligible agencies of the federal government. All applicants must demonstrate the existence of a collaborative relationship with a foreign institution and the potential for productivity in the area of epidemiological research related to HIV/AIDS vaccine testing. Applications from minority individuals and women are encouraged.

Support will be through NIH Exploratory/Developmental Grants (R21). Total project period may not exceed two years. NIAID has set aside $3 million for funding the total costs for the initial year of this RFA. The total first year cost of individual applications, including direct and indirect costs, may not exceed $600,000 per year. It is anticipated that five to six awards shall be made for the first year.

The specific objectives of this RFA are to:

--define the incidence of HIV infection in population groups at high risk of acquiring HIV infection;

--identify selected biological and behavioral cofactors of adult and/or perinatal transmission of HIV;

--collaborate in research that studies the distribution of genetic and antigenic variants of HIV in different population groups; and

--strengthen the infrastructure and field management capacity needed to undertake potential future HIV vaccine efficacy trials.

All applicants must satisfactorily address the following issues:

1. Applicants must demonstrate the extent to which a potentially productive institutional relationship has been established between the U.S. and foreign institutions that will be responsible for the Preparation for AIDS/HIV Vaccine Evaluations (PAVE) project.

2. Since most of the research will be conducted in a foreign country, funds must be allocated accordingly. NIAID has determined that at least 70 percent of all direct costs must be spent in the foreign country.

3. Applicants must assure that research participants will be provided treatment for sexually transmitted diseases, consistent with the standards of care for the country in which the PAVE is located if the participants are diagnosed with an STD in any component of the PAVE.

Inquiries and letter of intent may be directed to Dr. Robert Fischer, Epidemiology Branch, DAIDS, NIAID, 6003 Executive Blvd., Solar Bldg., Bethesda, MD 20892, phone 301/496-6177, fax 301/402-1506. For overnight and courier service, use "Rockville, MD 20852" in place of "Bethesda, MD 20892."

NIH Funding Strategies For FY 1992

NIH announced that the "core principles" described below would guide its Institutes, centers and divisions (ICDs) in making funding decisions on research project grants in fiscal 1992:

"Noncompeting RPGs:

--The award of noncompeting grants at committed levels is the cornerstone of the NIH Financial Management Plan and is the basis for credibility with Congress and the scientific community.

--The total costs of the cohort of noncompeting grants, on the average, may not exceed 4 percent more than the prior budget period, taking into account one-time, non-recurring costs such as equipment.

--Every effort will be made to accommodate shifts in the fiscal situation. If conditions are such that funding at the committed levels is not possible, the ICDs will obtain the approval of the NIH Director before taking any action to reduce the size of the noncompeting awards.

"Competing RPGs:

--The average costs of competing grants in one fiscal year will not increase by more than the Biomedical Research and Development Price Index over the average costs of competing grants in the previous fiscal year (including Small Business Innovation Research grants).

--In making funding decisions, ICDs should consider the total costs of a grant, especially for applications with percentiles at the margin of the funding level.

--An appropriate funding level for each award may be achieved by making budgetary reductions based on recommendations of the initial review group and advisory council/board, reviews by program and grants management staff for cost allowability and reasonableness, and, if necessary, programmatic adjustments. Programmatic adjustments may include reductions in investigator effort, adjustments of specific budget items, and/or decreases in the number of specific aims.

--Award reductions of 25 percent or more below the level recommended by the initial review group on a single grant application may require a revised statement of specific aims and a revised budget from the principal investigator, properly countersigned by the institution, which must be reviewed and approved by the ICD program and grants management staff. Program staff, in consultation with the principal investigator and grants management staff, will decide if revised specific aims are required.

--For competing continuation grants, one factor in arriving at the award amount will be the level of support in prior years and the extent to which the ICD can permit growth within the existing constraints on increases in average costs.

--The average length of research project grants will not exceed four years (excluding SBIRs).

"Indirect costs: The NIH Financial Management Plans propose that the effective indirect cost rate for competing and noncompeting awards would become the ceiling rate for the remainder of the recommended period of support. Implementation of the ceiling on the rate of indirect costs is being deferred. However, the Dept. of Health & Human Services and the Office of Mangement & Budget are considering this and other options for government wide policies with respect to indirect costs."