THE CANCER LETTER

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HHS Orders Gallo Forum Canceled; Meeting May Be Held After OSI Report Final--Calabresi

In another unusual development in the saga of NCI scientist Robert Gallo, the HHS General Counsel advised the National Cancer Advisory Board's AIDS Committee to cancel last week's meeting in which Gallo was to respond to the NIH investigation of his laboratory.

HHS General Counsel Michael Astrue advised AIDS Committee Chairman Howard Temin in a June 23 letter that "the meeting that you have scheduled for tomorrow to review matters relating to allegations of

(Continued to page 2)

In Brief

NY Judges, Lawyers Form Breast Cancer Alert; Terms Of ODAC Chairman, 3 Members Expire

JUDGES AND LAWYERS Breast Cancer Alert has been formed by six organizations and 26 individuals representing judges and lawyers in New York State. Impetus for the group was the death of State Supreme Court Justice **Sybil Hart Kooper** of breast cancer last year. The group, launched in May at a meeting of the state Women's Bar Assn., has joined the National Alliance of Breast Cancer Organizations with the goal of promoting improved breast cancer awareness. Initiator of the Alert is Associate Justice **Sondra Miller**, who may be contacted at Westchester County Courthouse, 19th Floor, White Plains, NY 10601; 914/285-4910. . . . **FOUR MEMBERS** of the FDA Oncologic Drugs Advisory Committee attended their final meeting this month before their terms expired, including Chairman **Craig Henderson**. Others are **Sandra Horning, Grace Monaco,** and **David Ahmann**. Three new members will be **Judith Ochs,** St. Jude Children's Research Hospital; **James Ingle,** Mayo Clinic; and **Paul Bunn,** director of the Univ. of Colorado Cancer Center. . . . **BRAIN TUMOR** protocol was approved by NIH Recombinant DNA Advisory Committee for transfering a viral gene into tumor cells to make them susceptible to destruction by ganciclovir. NCI's **Kenneth Culver** reported results of the treatment in animals. If FDA approves the protocol, National institute of Neurologic Disorders scientist **Edward Oldfield** and neurosurgeon **Zvi Ram** will use MRI guided stereotaxis to inject the retrovirus into brain tumors in three patients. . . . **THREE YEAR GRANT** for $5 million was awarded to Children's Hospital of Philadelphia and Washington Univ. School of Medicine by Ronald McDonald Children's Charities for children's neural cancer research. . . **TIM RAFTIS** has joined Science and Health Communications Group, headed by **John Grupenhoff**, Washington representative for the Assn. of American Cancer Institutes. Raftis is former research director for Sen. Tom Harkin (D-IA).

Temin Questions Reasons For HHS Order To Cancel Gallo Forum

(Continued from page 1)

misconduct against Dr. Robert Gallo exceeds the statutory authority of your committee and therefore must be canceled.... You need to be aware that unauthorized expenditure of federal funds may expose you and others to various types of liability."

Temin called off the meeting, but protested the HHS action in a statement to NCAB members, NCI staff and reporters who gathered at NIH Building 31.

'Scare Tactics'?

"I would like to find out what actually was the legal basis for them canceling the meeting and what laws would I have broken had I held the meeting," Temin said to **The Cancer Letter.** "Certain people think there were none and that this was just scare tactics."

"It certainly seems Dr. Gallo is being prevented from exercising his free speech," Temin said.

An NCI executive called the HHS order "very bizarre." Never in recent history has HHS taken action to cancel a meeting sponsored by the NCAB.

NCAB Chairman Paul Calabresi told **The Cancer Letter** that after the meeting was canceled he spoke with HHS Secretary Louis Sullivan, who "was primarily concerned with the timing of the meeting." Sullivan advised postponing the meeting until the NIH Office of Scientific Integrity's report on its two and a half year investigation of the Laboratory of Tumor Cell Biology is finalized.

"Dr. Sullivan was explicit about postponing the meeting instead of canceling it," Calabresi said. "He was very accessible and concerned about the scientific community, and made it clear that this was a question of timing. I think we will be able to hold the meeting when the report is signed, probably in a few weeks."

As a former NCAB member, "Sullivan feels very strongly about the function and activities and authority of the NCAB," Calabresi said.

'Neither Legal Nor Appropriate'

"I believe the General Counsel was concerned that this might in some way interfere with the Public Health Service investigation," Calabresi said. "Temin's committee was specifically asked not to reach conclusions about scientific misconduct and was encouraged to provide advice on administration of the laboratory. It was my understanding that Temin sought to obtain information that might help the NCAB in the future in dealing with similar situations."

"Essentially the committee was proposing to hold a misconduct of science hearing, and they don't have the statutory authority to do that," Astrue said to **The Cancer Letter.** "To have a platform for Gallo to discuss allegations of misconduct is neither legal nor appropriate."

Astrue said free speech is not an issue, since Gallo could hold a press conference or discuss the allegations in some other public forum. "There's no legal problem with that," he said.

With regard to Temin's question about the laws he would have violated, Astrue said, "I'm not going to speculate on that. To conduct a meeting where you don't have statutory authority would have opened up a lot of possibilities."

Gallo was not available for comment.

The AIDS Committee had invited Gallo to respond to charges regarding use of the French isolate LAV in development of the blood test for HIV-1 and whether Gallo gave appropriate credit to others and fulfilled requests from other laboratories for cell samples, Temin said.

In its recently completed report, the NIH Office of Scientific Integrity concluded that Gallo did not engage in scientific misconduct, but criticized his "collegiality." OSI did find misconduct on the part of Gallo associate Mikulas Popovic. Another group of reviewers, called the Richards panel, was more critical of Gallo (**The Cancer Letter,** June 12).

The OSI report is awaiting review by the Office of Scientific Integrity Review before final approval by Assistant Secretary for Health James Mason. Until then, the report is not officially available, but copies have been leaked to the press and circulated on Capitol Hill.

The HHS Inspector General is conducting another investigation into whether false information was given when Gallo applied for a patent for the HIV-1 blood test in 1986.

Lawyers for the Pasteur Institute in Paris are seeking to end the 50-50 split with the U.S.

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government of royalties on the blood test, believing that the French should get 100 percent. Outraged by the NCAB's planned public forum for Gallo, Pasteur lawyers sent a protest letter to Mason and planned a competing press conference 15 minutes after Gallo's presentation.

NCAB's Statutory Role

In his statement, Temin explained why the meeting had been scheduled.

"This laboratory is in the midst of great controversy which is widely discussed and is of great interest to the NCAB in its role of overseeing the National Cancer Institute and Program," Temin said. "In light of the NCAB's statutory role in advising NCI, the chairman of the NCAB asked the NCAB AIDS Committee to hold this meeting to enable Dr. Gallo to present, in his own voice, information relative to this controversy and, perhaps more importantly, to permit the Board to have discussion of some of the lessons that can be learned from this controversy about the processes of scientific discovery, scientific management, and scientific administration.

"We would also have been dealing with issues related to the leadership and operation of the Laboratory of Tumor Cell Biology. This would have been a meeting, not an inquiry or investigation. Furthermore, it would expressly not have been a review of OSI nor of the Richards panel nor of any other group or individuals who have previously officially reviewed" the laboratory.

"Dr. Gallo would have been asked to point out what lessons about the norms of scientific conduct were to be learned from this experience, and I also would have asked him to point out what lessons could have been learned about the administration of the Laboratory of Tumor Cell Biology. As originally planned, members of the Div. of Cancer Etiology Board of Scientific Counselors would have been in the audience and this group might if they thought it appropriate, have take up later various administrative issues relevant to the Laboratory of Tumor Cell Biology."

'Sharp Practices'

Temin said the charges are "about relations between scientists, about whether or not Dr. Gallo behaved in an uncollegial fashion." Temin termed uncollegial behavior "sharp practices."

"There is a general consensus that misconduct is improper and should be publicly punished. However, what we would have dealt with if we had met today as proposed was this topic--sharp practices. There is no consensus on what to do about sharp practice and scientific rudeness. No consensus exists on whether or not it should be publicly punished and, if so, on what should the punishment be. My feeling is that we must punish misconduct, but that all we can do is deplore, as much as we can, sharp practice, and try to teach young scientists that these things are not appreciated and are not helpful to science."

Temin read Astrue's letter, then commented: "I would just like to draw not conclusions about free speech--which may be the most appropriate thing today--but I would like to wonder about why such a statement, about such a meeting, to find out what NCI, and by extension, the NCAB, could do about this sharp practice, was so threatening and illegal that it called for such a letter and had to be canceled."

'Just An Innocent Professor'

The meeting's cancelation was an incongruous twist to Temin's stay in Washington last week. First the Nobel Laureate and professor of oncology at the McArdle Laboratory, Univ. of Wisconsin, visited the White House and was lauded by President Bush, who awarded him the National Medal of Science in a Rose Garden ceremony.

Returning to his hotel, Temin received a phone call from Astrue and later, the hand-delivered letter. "I'm just an innocent Midwestern professor," Temin said to **The Cancer Letter.** "I have no idea why this happened."

Breast Cancer Vs. Other Cancers In Showdown Over Appropriations

Women in T-shirts with inscriptions demanding $300 million for breast cancer programs were expected to stand in the hallways of the Rayburn House Office Building this week, greeting members of the Labor, HHS, Education Appropriations Subcommittee as they entered a closed markup session for the fiscal 1993 budget.

The results of the markup were expected to be embargoed for another week and released following the July 4 recess.

According to Capitol Hill sources, the budgetary outlook for next year is so glum that the President's budget request has come to represent the best case scenario for NIH.

Given that arithmetic, the "Rayburn showdown" and other attempts by the 140-member Breast Cancer Coalition and Women's Congressional Caucus to provide additional funding for breast cancer are likely to entail redirection of funding within NIH, observers said.

"We do not believe that increased efforts in breast cancer research should occur at the expense of prostate cancer, childhood cancers, lung cancer, colon

cancer and a myriad of other life threatening diseases," Robert Day, president of the National Coalition for Cancer Research, wrote in a letter to Rep. William Natcher (D-KY), chairman of the subcommittee.

"Any increase in funding should come from new funds, not threaten to harm existing programs," Day wrote.

Joanne Howes, a lobbyist for the Breast Cancer Coalition, said the coalition's goal is to obtain funding, not redirect it. "We don't want to get involved in a cancer vs. cancer dispute," Howes said to **The Cancer Letter.**

"We are making our case to the Appropriations Committee," Howes said. "It will be up to the members to decide where the funds will come from. We don't want them to give us a pat on top of the head and say, 'You have a point, breast cancer is terrible, but girls, we don't have any money this year."

The Breast Cancer Coalition has the membership of over 140 organizations, including cancer centers, hospitals, companies, trade unions and advocacy groups. The National Coalition for Cancer Research represents 16 professional oncology societies and lay organizations.

"We regret that the Administration, the Congress and the people have lost the will to adequately address [cancer] through support of the [NCI] bypass budget," Day wrote in a letter to Natcher. "We believe that full funding of the bypass budget is imperative to prevent us from cutting funds within one research program to initiate or expand another.

"Further, the bypass budget enables us to maintain a balanced research program to address all types of cancer."

The President's $2.01 billion NCI FY93 budget request came $764 million short of the bypass budget, which represents the Institute's professional judgment of the funding it needs to address research opportunities. The NCCR recommended a $170 million increase over the President's budget.

ODAC Recommends Against Another Chemoprotector, Okays Leustatin

The Food & Drug Administration's Oncologic Drugs Advisory Committee has recommended against approval of Adria Laboratories' Zinecard (AKA Dexrazoxane and ICRF-187) for reducing the incidence and severity of cardiomyopathy associated with doxorubicin.

In another action at a two day meeting in Bethesda, ODAC recommended approval of R.W. Johnson's Leustatin (2-chlorodeoxy-b-D adenosine) for treatment of hairy cell leukemia.

It was the second time this year that ODAC recommended against a chemoprotective agent. The committee previously had decided that more information was needed from an ongoing clinical trial of U.S. Bioscience's Ethyol (WR-2721) before it could be approved for protection from toxic effects of platinum and alkylating agents (**The Cancer Letter**, Feb. 7).

The reasons cited in ODAC's decision on Ethyol were that protective effects had not yet been convincingly established. Some members also felt that the key study had been compromised by protocol violations.

At a closed session of the recent meeting, however, ODAC was told that an FDA staff literature review had found a number of studies in which there was evidence that Ethyol had acted as a tumor protector in both chemotherapy and radiotherapy. Those studies had not been presented to the committee when the Ethyol NDA was being considered.

The possibility that Zinecard also may reduce the antitumor effect of doxorubicin was the primary reason for its rejection by ODAC. There was no question, from the studies presented, that it significantly reduced cardiomyopathy without adding to other toxicities. Patients receiving Zinecard frequently were able to tolerate higher cumulative doses of doxorubicin. However, there was no significant improvement in time to progression or overall survival. In one study, there was a statistically significant difference in response favoring the control group.

The major studies cited in the NDA and presented to ODAC were carried out by James Speyer at New York Univ. and Richard Gams at Ohio State Univ. Speyer's study randomized patients with advanced breast cancer receiving the combination of 5-FU, doxorubicin, and cyclophosphamide (FAC) to either Zinecard or placebo. Gams' regimen was a multicenter trial (which also included members of the Assn. of Community Cancer Centers' Collaborative Research Group) which randomized advanced breast cancer patients to either FAC or the combination of cyclophosphamide, doxorubicin, and vincristine, and the further randomized them to Zinecard or placebo.

Gams also carried out a trial with FAC and Zinecard in treatment of small cell lung cancer with doxorubicin combinations.

ODAC voted unanimously that Zinecard does decrease the incidence and severity of cardiomyopathy caused by doxorubicin; that additional assurance is needed that it does not decrease the antitumor effect of doxorubicin; and that it is not approvable for use

with FAC for treatment of breast cancer or with CAV for treatment of small cell lung cancer; and that it is not approvable for a more limited indication.

Recommends 2-CdA for Approval

ODAC unanimously recommended approval of Leustatin (2-CdA) for first and second line treatment of hairy cell leukemia.

The recommendation was based on the results of two phase 2 clinical trials conducted by Scripps Clinic and Research Foundation and M.D. Anderson Cancer Center enrolling 124 patients, and was made on condition that the company provide annual followup data on the drug's efficacy for at least three years.

The trials demonstrated that 2-CdA produces an 87 percent overall response rate, 64 percent complete response rate within the first four months, durable responses out to 7.6 months with two years being the longest response, 7 percent disease progression, and the need for blood transfusions is abolished, according to Esther Rose of R.W. Johnson, who made the company's presentation.

The standard treatment, interferon, results in about a 75 percent total response rate, with only about 7 percent complete responses. Recommended dosage of 2-CdA is 0.1 mg/kg/day as a single seven-day infusion.

Safety data were given for the first 14 days after treatment with 2-CdA. There was a 71 percent incidence of fever, half of which were considered mild, 48 percent incidence of fatigue, and 38 percent incidence of infection.

Five patients died in the study, two within 30 days from the end of treatment; one died of sepsis on day 20, the other of heart disease on day 35 which was not considered to be drug related. The other three patients had persistent hairy cell leukemia; one died of sepsis, one of pneumonia, and one of cardiac arrest.

The committee's deliberations were the least contentious of any of its recent meetings. Committee members had few questions of the sponsor, and FDA reviewer Miguel Conde made only a few clarifications to the company's data.

Committee member Charles Schiffer asked why the drug was given as continuous infusion. Lawrence Piro, Scripps Clinic, said the administration was based on early phase 2 work. "We did not want to backtrack" to test the drug with bolus administration, he said.

Schiffer also questioned the durability of response, noting that the data are not very mature. Harvey Golumb, Univ. of Chicago, a consultant to the company, said 50 percent of patients on interferon need retreatment by 36 months, while Piro showed that only one patient who had been treated with 2-CdA needed retreatment by 20 months after therapy.

Management Survey Finds Problems At ACS, Suggests Major Changes

A management survey of the American Cancer Society national office, performed by Arthur D. Little Inc. under contract with ACS, resulted in a number of recommendations for reorganization and streamlining including reducing the size of the national staff by 10 percent.

The survey was initiated by the ACS Executive Committee last January, with the intention that the results would be available for consideration by the Society's new executive vice president, in concert with the president and chairman of the board.

The survey and recommendations were presented to the Executive Committee and the Board of Trustees at last month's meeting in Portland, when the board also formally offered the executive vice president position to Indiana Univ. professor and former ACS board chairman, John Seffrin.

Seffrin had to skip the last day of the board meeting, but later told **The Cancer Letter** that the Arthur D. Little report "is an incredibly important document" but it is only one of several analyses that will be considered in any reorganization effort.

Seffrin said he considers the recommendation for a 10 percent staff reduction only a suggestion. "I'm not about to make that kind of rif without a far more thorough analysis and discussions with everyone involved." He said he has invited comments on the report from the national staff, especially those who would be most affected by the recommendations. "I hope we can come up with additional ideas on how we can make improvements."

The A.D. Little team interviewed national office staff, division executive vice presidents, and volunteer leaders. Their critiques, observations, and suggestions were limited to the national office, which is the organized staff working under the direction of the national executive vice president. The survey came up with five observations relative to the operation of the national office, two relative to management, four regarding the national office organization, and five on the efficiency of the national office.

Operation

--National office programs with consistent high marks included research ("the jewel of the Society"), the spokesman role on current medical issues, and financial management services to the field.

--Relationships between the national and division staffs are not well developed. There is insufficient working contact, national does not get out to the field enough, and senior vice presidents are not

appropriately visible in the field.

--Field staff would like to have more input into program planning. National should concentrate more on implementing current programs and less emphasis on finding new ones. There is no mechanism to network programs developed and implemented by field units. There is insufficient sense of a consistent national theme. National is frequently late in delivering materials to the field. Professional education programs developed for divisions receive low marks from divisional EVPs.

--Management of fund raising is of particular concern in the field. Effectiveness of residential fund raising is questioned in many divisions. Good fund raising ideas developed by units are not communicated effectively to others. National creates fund raising programs without sufficient unit input. No national fund raising strategy exists.

--Administrative support activities and characteristics are also issues. National has different standards from the field regarding compensation, equipment, and personnel matters such as termination and transfer. There is no regular comprehensive evaluation of national office performance. The field would like a prominent role in such an evaluation.

Management

--Management behaviors cause internal difficulties and inefficiencies. Specifically, there is internal dissension and bickering caused by turf protection; absence of directive leadership; lack of horizontal communications and sharing of ideas. There are 19 departments, each working on its own.

--Management behaviors cause external problems by creating perceptions by field staff that national staff see themselves as superiors rather than servants, and see the field as subordinates rather than customers. National is not responsive to the most important concerns of the divisions or to their criticisms. The internal bickering is a symptom of a lack of direction and leadership.

Organization

--There is no consensus on how to organize the national office staff to carry out the national office's role, improve support to the committees of the board, align it with the strategic direction of the Society, or maximize interdepartmental coordination.

--There is an unresolved debate within the national office regarding the value and approach of organizing staff, functionally (public education, income development, finance), programmatically (prevention, detection, treatment), or according to priority areas of activity (breast cancer, tobacco).

--There is a need to rethink the organizational links between the divisions and national office. Some felt the four area offices worked well. Some question the value of the national vice presidents, particularly in light of their reporting relationship. Some suggest a regional scheme, based on small divisions affiliating with big divisions. Some suggest organizing divisions by size.

--ACS's nonconfrontational culture makes change difficult and slow, which presents a problem in reorganizing and reenergizing the national office.

Efficiency

--There is a consensus among senior management that the national office staff should be reduced, but the estimates vary widely. One senior vice president stated he could reduce staff by 60 FTEs. One suggestion was that a 10 percent reduction in staff would be easy to achieve.

--The perception among divisional EVPs is that the national office is over staffed.

--Staff support to the board committees often appears excessive.

--Several national staff suggested that there are unnecessary information/data processing redundancies among research, information systems, and finance.

--The national office has no systematic measures for or standards of efficiency.

The report listed 12 major recommendations:

1. The national office should focus on serving the volunteer leadership, medical professions, cancer researchers, and the ACS divisions.

2. The national office should concentrate on presenting the national image of the Society, supporting the voluntary governance, providing medical leadership, funding cancer research, and serving the divisions.

3. Board functions should be consolidated and the number of board committees which require staff services from the national office should be reduced.

4. Fewer national office staff should be in attendance at committee meetings.

5. The need to provide professional education programs should be reevaluated.

6. Support should continue for the very well received peer reviewed research program.

7. The 57 divisions should be segmented into four categories for purposes of defining appropriate support from the national office: mega, large, medium, and small. National office organization should be redesigned to serve these groups of divisions and strengthen the link between divisions and the national office by forming four division councils, appointing a vice president for division services for each group of divisions, and assigning

staff from departments to work with each vice president for division services.

8. The nature and level of national office services to the divisions should be determined by expressed division needs; these needs differ from each category of division. It is anticipated that redetermination of needs will result in reduction or elimination of some services and restructuring of others. The highest service priorities for all divisions are research, particularly peer reviewed basic research; mechanisms to collect and share among all divisions the best ideas for programs and fund raising; provision of program and fund raising materials; development of public education programs; publication of professional journals; staff training; advice on medical issues of concern to the public. In addition, each divisional category has a separate list of needs.

9. A number of critical processes in the operation of the national office should be improved, substantially redesigned, or replaced. In other cases, processes which are not in place to serve important customer needs should be developed.

10. National personnel should more closely serve the needs of division staff. This is particularly true for national senior managers who would work more closely with division EVPs. Senior managers should have specific field assignments each year. The annual performance evaluation of senior managements should include an assessment of their attitudes, visibility, and cooperation with divisions and board members. Division EVPs should be involved in key national office activities.

11. National office organizational structure should be revised to increase cooperation and collaboration among senior managers and across department lines by reducing the number of senior managers reporting to the EVP to correspond to the primary roles of the national office; and by creating a matrix organization under a group vice president for division services consisting of a functional chain of command and program oriented teams.

12. Rationalize national office staffing by reducing the number of senior managers en toto; providing an opportunity for the new national EVP to build his own management team; reducing staff in the national office by at least 10 percent following the analysis of critical processes and the needs of the divisions. This will also be facilitated by a reduction in the number of board committees which require staffing from the national office.

'Urgent Consideration'

The Executive Committee and the board approved a resolution receiving the report and referring it to the new EVP, president, and chairman of the board for "urgent consideration and implementation as deemed appropriate." The resolution also called on the Society's leadership to "make a commitment to allow the new executive vice president to select his own management team."

Seffrin said that one theme which comes through most clearly in the report is the need to enhance services to the divisions. "I certainly intend to do that."

The Ad Hoc Committee to Consider the National Office Management Survey was cochaired by Irvin Fleming and John O'Callaghan.

Coalition To Launch Effort For 'Major, Major Increase' In Cigarette Tax

The Coalition on Smoking or Health is considering an effort to sell Congress on a "major, major increase" in the federal cigarette tax from the current 20 cents per pack (due to go to 24 cents next year) to a whopping $5.

"We will have a big fight with the tobacco industry on this," coalition Chairman Alan Davis said in what is probably the understatement of the year. "We have made a lot of progress in public attitude over the last 10 years, and we think this is achievable."

Davis, American Cancer Society vice president for public issues, mentioned the coalition's tentative plans at the recent meeting of the ACS Board of Directors. ACS is a member of the coalition, along with the American Heart Assn. and American Lung Assn. The chairmanship is rotated among the three organizations.

Davis noted that Canada has imposed a $5 tax on cigarettes, resulting in a retail price of about $7 per pack. Since that tax went into effect, cigarette consumption there has dropped nearly 50 per cent. Davis estimated that a similar increase in the U.S. would, "theoretically," result in tax revenues of $150 billion over two years and reduce smoking by 50 percent under current levels.

Davis said that a study by Michigan investigator Kenneth Warner that found that increasing the cost of cigarettes resulted in reduction in consumption, especially among young people. "That hypothesis was proven accurate when the federal tax was increased from eight to 16 cents in 1983," Davis said. Consumption was reduced by 10 percent overall and 14 percent among youths. The tax raised $3.8 billion over two years; Warner had predicted it would generate $4 billion.

Davis extrapolated those figures to a total tax (probably state and federal) of $5 per pack, and came up with the $150 billion, 50 percent reduction in consumption figure. As the consumption falls, of course, the revenue eventually would decline, and the coalition has not developed any hard figures on specific amounts.

Tobacco companies, "while bemoaning tax increases, always add on additional amounts over and above the tax increase," Davis said. "If the federal government does not increase the tax, the price eventually will reach $5 a pack anyway, but the increased amounts will go to industry."

Michael Heron, ACS senior vice president for communications, said that he supports "anything that raises cigarette taxes, but we should go into this with our eyes wide open. We can expect more than just tobacco industry opposition. We ain't seen nothing yet. It will be a well financed effort and will include right wing groups. They will raise issues of freedom of speech, free enterprise, personal freedom. There will be enormous amounts of money fighting it."

Until the last few years, Congress and the Executive Branch were too intimidated by industry lobbying and the power of tobacco state senators and representatives to seriously oppose the industry. The overwhelming evidence of tobacco's adverse health effects finally had an impact, resulting in doubling and then increasing again the federal cigarette tax, stricter labeling laws, banishment of smoking from airline flights and many federal buildings, and restrictions on smoking in military establishments.

A higher U.S. tax would probably curtail the rampant smuggling of cigarettes from the states into Canada, a serious problem.

Lynn Bagnal, ACS Public Issues Committee member from South Carolina, commented on the importance of "enticing state governments to set aside some of the cigarette tax money for health purposes."

"We thought we had our legislation well written in that respect," said Jennie Cook, committee member from California. "But now the governor (Pete Wilson) is trying to take the cigarette tax money to help with the $10 billion deficit."

The Public Issues Committee and the ACS board approved a resolution revising the Society's position on tobacco taxes, and another on restrictions on smoking in public places.

The previous policy on tobacco excise taxes, adopted in 1980, noted that it was ACS policy "to refrain from comment on legislative proposals which have as their principal purpose the raising of revenue." That policy stated added, however, that since higher cigarette costs translated into fewer young people taking up smoking, ACS does support initiatives to increase the cost of cigarettes through increased excise taxes at federal, state, and local levels. Additional language was added in 1982 specifically supporting federal cigarette tax "sufficient to deter consumption."

The new statement drops the language referring to the Society's self imposed restraints on supporting tobacco tax increases. The new language states, "The American Cancer Society supports efforts at all levels of government to increase excise taxes on tobacco products in order to deter their consumption."

The statement on in public places:

"Restrictions on smoking in public places remain a keystone in the overall challenge to achieve a tobacco free society. Establishment of strong public indoor smoking control laws will protect public health by effectively reducing involuntary exposure to environmental tobacco smoke. Ideally, these statutes should include a prohibition of smoking in child care facilities, all school property, all private and public workplaces, health care facilities, public transportation, food service establishments including restaurants, and all other indoor areas open to the public.

"The American Cancer Society supports legislation at all levels of government to protect the health of nonsmokers by eliminating their exposure to environmental tobacco smoke through enactment of comprehensive smoking restrictions."

DCBDC Advisors Ok New Interactive RFA In Breast Cancer Biology

Advisors to NCI's Div. of Cancer Biology, Diagnosis & Centers have given concept approval to a new grant program in breast cancer biology and immunobiology.

DCBDC's Board of Scientific Counselors set aside $1.5 million per year for four years to fund six to eight interactive R01 grants.

NCI divisions have begun moving from the "global" program announcements seeking interactive R01 applications in all aspects of the Institute's research programs to using the interactive mechanism in RFA "set aside" programs addressing a specific need. The interactive mechanism is a step below the program project grants, which have been stressed by Congressionally mandated grant targets.

The board also gave concept approval to recompetition of two contracts. Following are the concept statements:

[Reports on concept reviews by the boards of scientific counselors of NCI divisions provide readers

with advance notice of the Institute's spending plans. Announcements for Requests for Proposals, Requests for Applications, and Program Announcements are published in ***The Cancer Letter*** *as they are released; proposals need not be submitted until that time.]*

Biology and immunobiology of breast cancer: an interdisciplinary approach. Concept for a new RFA, $1.5 million per year for four years; six to eight R01 grant awards. Program director: Grace Shen, Cancer Immunology Branch, DCBDC.

The intent of this initiative is to encourage interdisciplinary approaches to research on the basic biology and immunobiology of breast cancer. The goal of this proposed RFA is to encourage interactive grant applications that address unanswered questions in breast cancer in a multidisciplinary approach. DCBDC would like to support basic research in, but not restricted to:

1. Molecular genetics: Studies of the contribution of changes in the structure or regulation of oncogenes, tumor suppressor genes and other important cellular genes to the development and biologic behavior of breast cancer.

2. Cell biology: Studies of the organization and differentiation of breast epithelial cells during normal development and progression to malignancy, including studies of interactions between normal and malignant epithelial cells and surrounding tissue/stroma.

3. Immunobiology: Studies of the effects of immune responses on breast cancer development and progression, both positive and negative; molecular identification of relevant breast cancer antigens and development of effective strategies for immunologically based prevention or treatment of breast cancer.

4. Endocrinology: Studies of the roles of soluble factors and their receptors in breast cancer development and response to therapy. These may include, but are not limited to, such steroid and nonsteroid factors as estrogen, progesterone, insulin like growth factor, prolactin, TGF-alpha and TGF-beta.

Mechanism of support would be interactive R01 grants. Each interactive group must contain at least three individual R01 applications and address two or more of the major areas of research listed above. Preference will be given to high quality groups of applications with a strong immunobiology component. Applicants will be asked to describe how their integrated approach will provide a more comprehensive understanding of important problems in breast cancer biology.

Maintenance of an animal holding facility and provision of attendant research services. Proposed recompetition of a contract, $3.12 million total cost over four years. Project officer: John Wunderlich, Experimental Immunology Branch, DCBDC.

The current contract provides a facility for holding and breeding experimental animals in support of research carried out by investigators in the Experimental Immunology Branch of NCI. The colony consists of up to 10,000 mice, 40 rabbits, 500 rats and 50 hamsters, cared for according to National Research Council Standards. Quarantine facilities are provided for all animals received from appropriate sources, and the contractor provides routine screening of the colony for common pathogens every three months. The contract also provides breeding of special strains of mice, up to 260 breeding cages, and technical manipulations, particularly, injecting and bleeding animals, collecting mouse tail samples for DNA analysis at NIH, preparing mouse lymphocytes from peripheral blood, skin grafting mice, injecting and harvesting mouse ascites tumors, and palpating mice for detection of tumors.

Facility for housing and preparing virus infected and chimeric mice. Proposed recompetition of a contract, $2 million total costs over four years. Project officer: Gene Shearer, Experimental Immunology Branch, DCBDC.

The contract provides a colony of 3,600 mice, housed in such a way that virus positive, virus negative, immune competent and immune compromised mice can all be maintained and studied within the same facility, without contamination among the various groups of animals. Experimental procedures include: whole body irradiation; the preparation and inoculation of bone marrow, spleen, and lymph node cells; thymectomy; thymus grafting; embryo transfer; skin grafting; viral infection and assay; preparation of influenza virus; immunizations; and bleedings. The contractor is also required to provide weekly animal inventories to EIB investigators, and to deliver sera and cell preparations to EIB laboratories.

Epstein Hits 'NCI Reliance' On Doll, Peto 1981 Report; Greenwald Replies

Samuel Epstein, professor of occupational and environmental medicine, Univ. of Illinois School of Public Health, submitted the following Letter to the Editor in response to an article in The Cancer Letter, May 15, on his presentation to the National Cancer Advisory Board:

At the May 5 meeting with the National Cancer Advisory Board, I criticized NCI's continuing reliance on the Doll and Peto 1981 estimate that 4% of cancers are due to occupational exposures for a wide range of reasons. These include the fact that Peto later in the same year admitted the uncertainty of his estimates and also the validity of other divergent estimates:

"For a variety of reasons no reliable epidemiological studies of most (occupational carcinogens) have been or will be undertaken, therefore the scope for reasonable uncertainty seems large. Perhaps because of this, divergent views have been expressed as to whether occupational factors are likely to account for a 'small' percentage (e.g. 2-4%) or a 'large' percentage (e.g. 20-40%) of all U.S. cancer. (Peto and Schneiderman, Banbury Report No. 9, 1981).

I also criticized NCI's reliance on Doll and Peto and other blame the victim advocates of cancer causation, in virtually equating lung cancer with smoking while ignoring other major non-smoking attributable causes, particularly exposure to environmental carcinogens.

In further criticism of NCI's current reliance on the Doll and Peto 1981 estimate that 35% of cancers (up to 70%) are due to dietary fat is Peto's subsequent retraction of this estimate and admission that it is devoid of any scientific basis.

"(Recommendations for reducing dietary fat) should chiefly be because they will help avoid heart disease, rather than because they may well avoid cancer, ... the evidence in this respect is less secure." (Peto, "Science," 225:1562, 1987).

"(Quoting Peto) We'd like to have definitive evidence (on diet and cancer), but we don't have it. There is nothing in the league with smoking, which is a big and

definite risk factor." (Kolata, "Science," 235:436, 1987).

Finally, I further criticized NCI's reliance, until recently, on the Doll and Peto 1981 report that there is no evidence for increasing cancer incidence rates over past decades other than cancer attributable to smoking. I pointed out that Doll and Peto reached this remarkable conclusion by excluding consideration of blacks and people over age of 65, just those groups among whom more than half of all cancer deaths are reported.

In the circumstances, it would appear difficult to comprehend how NCI policies appear to be so influenced by the Doll and Peto estimates, since it is clear that these are wild guesses and lacking in scientific credibility.

NCI Div. of Cancer Prevention & Control Director Peter Greenwald responds:

NCI believes that environmental carcinogenesis is an exceedingly important topic. That is why we have major research thrusts on chemical and physical carcinogenesis, biological carcinogenesis, epidemiology, and cancer prevention and control. These are the major foci of two of our four research divisions.

We agree that there is uncertainty about the quantitative estimates of what portion of the cancer load is due to different etiological factors, and those related to occupation and pollutants could be underestimates. The reason Doll and Peto (JNCI 66:1191, 1981) often is cited is that this 107 page paper is the most thorough analysis of its type ever done. In a recent supplement to "Cancer Research" (52:2024s, 1992), Doll reaffirmed his dietary estimate, saying, "The estimate that the risk of fatal cancer might be reducible by dietary modification by 35% remains a reasonable guess, but I would narrow the range of acceptable percentages from 10-70% to 20-60%."

If Dr. Epstein or anyone else has new research findings that bear upon this issue, we would look forward to a scholarly review of this information.

Cancer Meetings For July, Aug.

President's Cancer Panel Special Commission on Breast Cancer--July 8, Dallas, TX. Doubletree Park West, 1590 LBJ Freeway, open 9 a.m.-4:30 p.m., topic: "Issues in Basic Research."

Caring, Coping, Conquering Cancer--July 9-10, La Crosse, WI. Contact Lutheran Hospital-La Crosse, 608/791-4744.

Society for Nutrition Education Annual Meeting--July 14-18, Washington, DC. Contact Darlene Lansing, phone 612/854-0035.

Radiation Therapy Oncology Group Semi-Annual Meeting--July 24-26, Philadelphia. Contact Nancy Smith, RTOG, 215/574-3205.

Seoul International Symposium on Cancer Treatment--July 24-25, Seoul, Korea. Contact Dr. Jin-Pok Kim, College of Medicine, Seoul National Univ. Hospital, 28 Yungun-Dong, Congno-Gu, Seoul 110-744, Korea.

Head & Neck Cancer International Conference--July 26-30, San Francisco, CA. Contact Ruth Enquist, phone 507/285-1523.

Environmental Toxicology & Cancer--Aug. 2-5, Towson, MD. Contact International Conclave of Environmental Toxicology & Cancer, PO Box 134, Park Forest, IL 60466, phone 708/748-0440.

International Conference on Cancer Nursing--Aug. 16-21, Vienna, Austria. Contact M. Darley, 2nd Floor, Mulberry House, Royal Marsden Hospital, Fulham Rd., London SW3 6JJ, UK.

Advances in Psychoneuro-immunology--Aug. 17, Budapest, Hungary. Contact J. Szelenyi, Nat. Inst. of Haematology & Blood Transfer, Dept. of Molecular Biology, Daroczi u.24, 1113 Budapest, Hungary.

Supportive Care in Oncology--Aug. 25-28, Brussels, Belgium. Contact Ch. Jacob, Inst. Jules Bordet, Rue Heger Bordet 1, 1000 Brussels, Belgium.

ESTRO Annual Meeting--Sept. 1-4, Malmo, Sweden. Contact ESTRO, Dept. Radiotherapy, U.H. St. Rafael, Capujinenvoer 35, 3000 Leuven, Belgium.

Future Meetings

Novel Approaches to Selective Treatments of Human Solid Tumors: Laboratory & Clinical Correlation--Sept. 9-12, Buffalo, NY. Contact Dr. Youcef Rustum, Roswell Park Cancer Institute, phone 716/845-4532.

National Conference on Cancer Prevention & Early Detection--Sept. 10-12, Chicago, IL. Contact Andy Cannon, American Cancer Society, phone 404/329-7604.

Program Announcement

PA-92-86

Title: **Magnetic resonance spectroscopy and cancer treatment**

Application Receipt Dates: Oct. 1, Feb 1, June 1

NCI's Diagnostic Imaging Research Branch, Radiation Research Program, seeks applications through Interactive Research Project Grants to establish multidisciplinary research in early detection and prediction of tumor response to treatment using magnetic resonance imaging guided magnetic resonance spectroscopy.

Applications may be submitted by foreign and domestic, for-profit and non-profit, public and private organizations. A minimum of three independent investigators with related research objectives are encouraged to submit concurrent, collaborative, cross-referenced individual research project grant applications (R01) that share a common research focus. Applications may be from either a single institution or a consortium of institutions.

The goal of this initiative is to conduct well-focused, prospective clinical studies using currently available, routinely applicable, methodology to begin comprehensive testing of the potential for MRS to predict and/or detect therapeutic response in patients with tumors. The critical issue in these studies is quality control, i.e., setting precise standards for performance and interpretation of spectroscopic studies.

A consensus-based development of the experimental design will include data acquisition, presentation and processing (e.g., standards of MRS performance, well-defined technical requirements, and method(s) of spectral localization, quantification, and data analysis). This announcement seeks to encourage the following research topics: Detection and prediction of immediate treatment response; prediction of final outcome; evaluation of the direct effect of drugs; differentiation of viable tumor from treatment-induced necrosis, edema, and scar. It is also expected that the proposed studies will address: In vivo metabolic characterization of human tumors; correlation of metabolic characteristics with histological features; correlation of metabolic characteristics with clinical and biological behavior.

Inquiries: Dr. Faina Shtern, Chief, Diagnostic Imaging Research Branch, Radiation Research Program, NCI, Executive Plaza North Suite 800, Bethesda, MD 20892; phone 301/496-9531.