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DCPC Board Finally Approves Prescribe For Health Concept On 7-4 Vote, Okays RFA On Micronutrients

The controversial "Prescribe for Health" initiative developed by NCI's Div. of Cancer Prevention & Control finally won concept approval from the division's Board of Scientific Counselors, although still not without opposition. The board

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In Brief

Robert Young Named President Of Fox Chase; Elion, Hitchings Share Nobel Prize With Briton

ROBERT YOUNG, who has been director of the Centers & Community Oncology Program in NCI's Div. of Cancer Prevention & Control for a little more than six months, will be the new president of Fox Chase Cancer Center. Young will take up his duties at the prestigious center Dec. 15. That position has been vacant since John Durant left in April. Young's departure will dismay cancer center and Community Clinical Oncology Program participants who have been delighted with the leadership he has shown and his quick grasp of the issues. Young had been chief of NCI's Medicine Branch for 14 years, during which time he established an international reputation in clinical investigation of ovarian cancer and lymphoma. He is currently president elect of the American Society of Clinical Oncology. "Bob Young is a real patient's doctor," an NCI executive said recently. "They love him. I know that if I had cancer, I would want him as my doctor." DCPC Deputy Director Joseph Cullen said he has been "super impressed with Bob since he joined the division because of his intellect and immediate understanding of cancer control and prevention issues. This is an immense loss for us, and a great gain for Fox Chase". . . . **GERTRUDE ELION** and **George Hitchings** will share the 1988 Nobel Prize for Medicine with Briton **James Black** for their research which has led to development of some of the most important drugs, including anticancer and antiviral agents. Elion and Hitchings worked together at Burroughs Wellcome starting in the mid-1940s, focusing on cellular metabolism. They developed 6-mercaptopurine and thioguanine, among the first successful drugs for treatment of childhood leukemia. Both are retired from Burroughs Wellcome but remain active. Elion is a past president of the American Assn. for Cancer Research and is a current member of the National Cancer Advisory Board. Black, of King's College Hospital in London, is the first scientist to use drugs to block receptors.

Prescribe For Health, Two Other Concepts Approved By DCPC Board

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approved the concept 7-4, with two abstentions, when it was presented for the third time, in a considerably revised and less costly form.

The board had rejected the concept last May, directing the staff to revise the evaluation component of the program which some members felt was too expensive (**The Cancer Letter**, May 13).

The staff came back with changes in evaluation methods which sliced the overall budget from an average of $4.1 million a year to $2.1 million a year over five years.

DCPC Director Peter Greenwald said that despite the split vote, the division would proceed with developing the RFA. NCI executives sometimes are reluctant to go ahead with a project without a strong consensus on concept approvals. Greenwald added that the concerns of board members would be taken into consideration in writing up the RFA.

The project is aimed at utilizing intermediary organizations to encourage primary care providers to undertake prevention and early detection measures in the course of their practices.

The board gave concept approval to two other projects--a $900,000 per year, four year grant supported program to study the relationship between blood and tissue micronutrient levels in individuals at varying risk of developing cancer; and an extension of the Chinese Academy of Medical Sciences for nutrition intervention studies in Linxian, China. The latter is a joint effort with the Div. of Cancer Etiology.

The board disapproved two other concept proposals--reissuance of an RFA to support two additional Clinical Nutrition Research Units (three awards have been made from the previous RFA, to the Univ. of Alabama, Memorial Sloan-Kettering Cancer Center and UCLA); and for grants to support public health department approaches to increasing the use of cervical cytology and mammography among unscreened women age 40 years and over.

In addition to the changes in evaluation methods, the revised ~~Prescribe for Health~~ concept made these major changes, as described by Edward Sondik, acting director of the Cancer Control Science Program:

--The emphasis has been sharpened on evaluating the potential of intermediary organizations to bring cancer control regimens to their primary care medical practices.

--Increased flexibility has been provided for applicants in proposing study design and evaluation methods.

--Applicants will be requested to address intervention design, implementation and evaluation (i.e., no separate intervention and evaluation units).

"This proposed initiative is an integral part of NCI's strategy to reduce cancer incidence and mortality through the effective application of cancer control regimens of demonstrated efficacy," Sondik said. "If this cooperative agreement succeeds in identifying effective ways intermediary organizations can involve their memberships in cancer control, we will have opened an important new channel for the delivery of cancer control regimens. As noted in the concept, as much as 70 percent of individuals in need of cancer control services could be reached through this communication and organization channel."

Recent studies suggest that intermediary organizations, with influence over routine primary health care delivery to adults such as large health maintenance organizations, specialty boards, third party payers, and physician professional societies, may be effective in improving the diffusion of disease prevention regimens to primary care medical practices.

In the area of smoking cessation, routine minimal (35-40 seconds) advice to quit smoking delivered by a physician has been found to increase one year quit rates approximately five percent over spontaneous quit rates. Physician counseling (three to five minutes) increased quit rates an additional three to five percent over advice alone. Nicotine gum, when offered with physician advice to quit, has resulted in quit rates double those found among smoking patients receiving physician advice without gum. Providing written materials to patients and following up initial interventions for reinforcement appear to further enhance quit rates.

Screening for cancers of the breast and cervix have been proven effective in reducing mortality from those diseases. Other cancer screening procedures such as sigmoidoscopy and fecal occult blood testing may reduce morbidity and/or mortality. Research indicates that when primary care physicians recommend these procedures to their patients, a majority accept and complete the recommended procedures.

Despite that evidence, recent studies suggest that these activities are frequently not practiced by primary care physicians. Over 50 percent of smoking adults report that they have never received physician advice to quit. Over 50 percent of primary care physicians report that they never recommend mammography to asymptomatic women. Twenty seven percent of physicians report that they performed Pap smears with less frequency than recommended by the American Cancer Society.

The Prescribe for Health RFA will ask intermediary organizations to submit cooperative agreement proposals for demonstration and evaluation of interventions for implementing cancer control regimens in primary care medical practices. The organizations will design, conduct and evaluate the interventions. Applicant organizations will be restricted to using cancer control regimens for smoking cessation and screening that have been approved by a policy advisory committee to be established by NCI. Approved regimens will be adapted from those found to be efficacious in previous research.

Applicants will be encouraged to develop interventions with multiple components based upon state of the art health promotion research. The interventions that applicant organizations proposed to test should be designed to be sustained beyond the period of NCI funding of the project. Primary care practices targeted by these proposed interventions should include practices serving low income and minority populations.

Major questions to be addressed in the evaluation are:

* To what extent will intermediary organization intervention improve adoption of cancer control regimens by primary care medical practices?

* To what extent will these interventions improve maintenance of cancer control regimens by primary care medical practices?

* What will be the quality of implementation of cancer control regimens by primary care medical practices (e.g., to what extent will providers comply with guidelines for Pap smear performance)?

Applicants will be strongly encouraged to test the effectiveness of their interventions with randomized designs in which all affiliated practices are the unit of analysis. Proposals for nonrandomized, quasi-experimental designs will be asked to justify nonrandomization and provide for a more rigorous assessment of factors which potentially confound the evaluation. The use of measures of primary care medical practice other than provider self report will also be strongly encouraged, such as billing records, practice audits, and patient records.

It is anticipated that collaboration on intermediary organization proposals by a variety of organizations will be necessary to adequately address the evaluation criteria for this initiative. Such collaboration will be encouraged among applicant organizations. Because of the need to improve cancer prevention and control in both free for service as well as prepaid health care settings, a balance among these settings will be sought in the selection of participating intermediary organizations. In an effort to achieve such a balance, no more than one award will be made to an HMO. A pre-application conference will be held to assist potential applicants.

An ad hoc advisory group will be convened to provide ongoing oversight to the project. This group will consist of one or more members of the DCPC Board of Scientific Counselors and outside consultants with appropriate scientific and medical expertise. The group will review cancer control regimens, intervention methods and materials, evaluation instruments and pilot studies prior to full scale implementation and provide periodic progress reports to the DCPC board.

Intervention methods and materials, evaluation instruments, and cancer control regimens will be selected, reviewed and adapted by a steering committee with the cooperative participation of NCI staff and consultants, principal investigators and their study teams, and designated representatives of intermediary organizations.

Prescribe for Health will be implemented in two stages. In stage 1 (year 1), intermediary organization interventions will be pilot tested, cancer control regimens will be selected, reviewed and adapted as necessary. Evaluation instruments will be developed and pilot tested. The results of stage 1 will be reviewed by the policy advisory committee before proceeding with stage 2 of the project. Stage 2 will consist of full scale implementation (years 2-4) and evaluation (years 2-5) of intermediary organization interventions.

NCI estimated that two awards will be made, one to an HMO and one to another intermediary. Estimated total cost for stage 1 is $1.5 million; for stage 2, $2.5 million the first year, $2.6 million the second, $2.7 million the third, and $1.5 million the final year.

Board members still had some reservations about the project.

"I've always had a problem with this concept and I still do," Mary-Claire King said. "I have yet to be convinced that working through the sort of intermediary organizations that you propose to work through will in fact help" achieve long term cancer control objectives. She suggested that a pilot study be conducted to determine if the approach could be successful.

"I am less happy (with the new concept) than I was with the previous one...This time you have dropped the evaluation of individual patients," she said, adding that the revision has "weakened rather than strengthened" your ability to test interventions.

William Mayer, DCPC project officer, said the concept was changed to allow more flexibility for applicants, and that it is not intended to preclude individual patient evaluations. The RFA would encourage that kind of evaluation, he insisted.

He also cited the success of three similar studies. One is "Project Insure," an insurance company project that he said resulted in increases in the number of patients screened. Another study by an HMO showed that interventions through intermediaries can change utilization of screening tests. A third is the Florida diabetes project, which found that it is possible to change preventive care of diabetics by working through intermediaries.

Board member Robert McKenna also expressed doubts about whether the intervention could be effective. Discussing American Cancer Society efforts to work through intermediaries in order to impact on cancer prevention, he said such efforts have met with limited success.

"History tells me that Pap smears were not sold through the physician, but by public education--demanding that their physicians perform the test." Mammography represents a similar situation, he said. "You've got to sell this so the patient demands it from the physician."

McKenna also cited the importance of working with industry and insurance companies in order to increase screening measures.

"Industry is right in taking part in cancer control for their employees," he said, suggesting that NCI work with industry. He also advised NCI to collaborate with insurance companies "because all these tests that you want to recommend may not" be covered by insurance companies. Patients may also be reluctant to pay for the tests themselves. "It's got to be part of the health care system."

McKenna also suggested that NCI spend money "trying to prove that early detection saves lives and dollars. We need the data...I'd rather take this $11 million and put it into several different pies, and let all the professional societies do what they should be doing, let the cancer society take a role in continuing to try.

"It's a very important issue...but I think we're just duplicating what they (ACS) are doing, and I don't think you're going to succeed any more than they have."

Mayer again asserted that other studies have shown that such interventions can be successful in changing medical practice.
He also said a concept is on the drawing board relating to the cost effectiveness of cancer screening and early detection.

Board member Donald Hayes, however, said he was more supportive of the concept than he had been previously because of the positive results of Project Insure.

Board member Donald Iverson, who noted that he has been supportive of the concept "all along," said that although "primary practitioners have not been very responsive" to other efforts, "I'm not sure we can afford to write them off."

Reimbursement An Issue

Board member William Darrity agreed, saying "If anybody's more of a cynic about primary care physicians than I am, I don't where" they are. "I'm very cynical, but on the other hand, I don't think we can write this group off...We really have to look and see what we can get out of this," he said. "Let's go with it. I give my wholehearted support."

McKenna again raised the issue of reimbursement for screening, particularly in light of the fact that 30 percent of Americans have no health insurance and that another 20 to 25 percent are covered by Medicare or Medicaid, which doesn't cover most of the tests proposed. "The concept of paying for early detection is not" accepted by major insurers. "We're all talking about doing things that aren't reimbursable." Pap smears aren't technically reimbursable, but physicians state the test was performed because of an infection or cervicitis. Mammograms are reimbursed by physicians stating the test is done for fibrocystic disease as well.

"We've done polls that say (primary physicians) won't do some of this stuff" in spite of ACS screening recommendations.

"I am all supportive, but I don't think it's going to work."

Mayer said NCI has received a good deal of interest from insurance companies about the proposed project. "We envision that the insurance company would be one of the potential intermediary organizations" in the project. He also said such an intermediary organization "may be able to bring weight to bear on policy issues." For example, the American College of Physicians' advocacy of adult immunization led to Medicare reimbursement. "Policy outcomes from this kind of effort are not inconceivable."

Board Chairman Paul Engstrom pointed out that although a number of states have already approved mammography screening, the rate of screening is low. In the HMO where he works, mammography is covered for women 40 years old and over, but the rate is less than 40 percent. Other board members cited long waits for mammography at other HMOs.

The relationship between blood and tissue micronutrient levels in individuals at varying risk of developing cancer.

This is a new project, to be supported by traditional research grants. Four awards are anticipated, with an estimated total annual cost of $900,000, for four years. Mark Messina is the project officer.

A number of micronutrients are under investigation for possible roles in modulating cancer risk. Prominent among these are selenium, calcium, vitamins A, E, and C and betacarotene. Recent evidence suggests that the folate status of individuals might influence carcinogenesis. Epidemiologic studies are often the first to identify a relationship between a specific dietary component and cancer risk. These studies rely upon dietary intake assessment and blood levels for evaluating the relative risk associated with a particular nutrient.

The problems associated with dietary intake assessment are well known. Although a widely used biologic measure of nutrient status, blood levels cannot always be assumed to reflect micronutrient levels in specific tissues. To date, very little is known about the relationship between blood and tissue micronutrient status and cancer risk. Blood levels of many nutrients remain fairly constant over a wide range of dietary intakes. Response to dietary intake differs among tissues and between tissues and blood.

The view that localized or tissue specific nutrient deficiencies not indicated by systemic evaluation may play a role in cancer has been previously suggested. Given that carcinogenesis evolves initially in specific tissues, it would be expected that the nutrient status of tissues rather than of blood may play a critical role. In fact, carcinogens themselves are likely to interfere with the nutritional status of target tissues by increasing the need for a particular nutrient or by direct destruction.

Relatively little work has been done in this area, but there is evidence indicating tissue micronutrient analysis holds great promise for identifying relationships between nutrition and cancer. The ability to assess tissue micronutrient levels would greatly improve the current understanding of the relationship between diet and cancer by providing a basis for determining the appropriateness of using blood as an indicator of tissue nutritional status; an epidemiologic tool for identifying the relationships between nutritional status and cancer; a method of monitoring changes in tissue micronutrient levels for use in intervention trials; and a possible explanation for the large variation in response to dietary supplements given as chemopreventive agents.

In this project, tissues and blood from individuals at varying risk for developing cancer are to be analyzed for micronutrient content. When possible, the tissue sample should be sufficient for multiple micronutrient analyses, and the procedure should not entail undue risk to the subject's health.

Micronutrients to be analyzed should include but are not limited to betacarotene, folate, vitamins C and E, selenium and calcium. when needed, methodology is to be developed by the grantee for obtaining human tissue suitable for micronutrient analysis. The grantee also will be expected to develop methodology, when needed, for micronutrient analysis of of tissue samples.

Holland asked if the concept would be used to encourage research solely for methodology development.

Messina said no, that in some studies of micronutrients and their relationship to cancer, the methodology is already out there.

McKenna asked why it would not include people with cancer. Iverson agreed with him, pointing out that "we don't know that these people are going to necessarily develop cancer."

Board member Frank Meyskens said, "There have been at least a couple of studies now...to address the question of whether micronutrients go down acutely at the time of cancer versus" change five or 10 years before.

"The question of the relationship of serum measurement or analytes to tissue analytes is extremely important" because tissue and serum levels may not be related.

In addition, the process of carcinogenesis is local. "Adding to the increased attempt to relate that to at risk puts a level of complexity that may not be possible to do."

"If you're going to look at risk, then you're looking at at risk of what? Of preneoplasia or for at risk of cancer? If you're looking at the tissue of preneoplasia and seeing what happens there and comparing it to normal tissue and comparing it to serum, that's fine. If you're looking at it in terms of at risk of cancer later on, I think that's an entirely different and much more complex venture."

Greenwald said, "What Mark is proposing is that we look at the validity of serum levels and what happens in tissue levels in people who may have a higher risk of cancer...I don't see what's so complicated about that."

Holland said he agreed with McKenna. "I don't see how you can do this, as if you can identify with a level of importance, a precancerous condition if you don't know" why the vitamin C level is increased in breast cancer, for example.

If investigators "could measure a level in esophageal dysplasia," for example, Greenwald said, they would "have a more sound basis for designing clinical trials" such as the intervention study underway in China.

Hayes asked why the proposed mechanism was an RFA versus an RFP.

Greenwald said an RFP would be much more structured, and that NCI wanted to encourage creative investigator initiated research.

"I don't think there's any question about the first part, methods are very important," Iverson said. He added that the issue of varying risk levels will affect population size and increase costs.

Iverson's motion that the concept be modified to focus on methods development and not require investigators to study varying risk levels was adopted by the board.

The proposal for two additional clinical nutrition research units was rejected largely because Board members felt the money could be better spent elsewhere.

"Could you tell me how you view funding two additional half million dollar units and deactivating" five cancer centers?" Holland asked. He was referring to the shortfall in the cancer centers core grant budget, which either will leave five existing centers unfunded or will necessitate a 20-30 percent cut from recommended levels.

Greenwald said NCI has no authority to move cancer control funds to the cancer centers budget. He defended the units as helping to build up nutrition as a science.

"I still have great difficulty as Jim said, in how you set your priorities," Board member Lloyd Everson said. "You're looking at cutting five cancer centers. How can you justify trying to set up something else?"

"Despite the fact that there are categorizations of funds...I have not had a very persuasive case made to me for this being a good way to spend a million dollars," Hayes said. He recommended that the concept be sent back so DCPC staff could provide "further justification" of the units.

"We should really know how the existing units are performing," Engstrom agreed. "That would determine whether there is need for more units or more concentration by staff on the units we currently have."

Greenwald warned, however, that future applications should not be judged on the basis of old ones.

Board member Donald McCormick defended the units' expansion. "None of the present cancer centers that I'm aware of have significant activity addressing the area of nutrition...I am persuaded that there are some interesting connections."

Greenwald also pointed out that DCPC is "striving to build a nutrition lab" within NCI, and that extramural activities would add a balance to the intramural efforts.

The Board was not persuaded, however, and voted to disapprove the concept.

The Board rejected the concept for public health department screening essentially because of its limited scope.

McKenna supported the concept, but pointed out that many public health departments have difficulty providing such services. In Los Angeles, indigent patients face a two to three year wait for mammography.

"I don't think that this proposal underwrites any of the screening procedures, so I think that departments aren't going to be any better off unless they have more staffing" to undertake such efforts, Board member Virginia Ernster said.

Holland opposed the concept, suggesting that a consortium of state and local health department chiefs be formed instead. Such a group could hold conferences on education, early detection, and how to best invest their resources, he suggested.

Sondik said that information such as how best to organize such programs is not currently known, and that the demonstration projects would provide an example to other state health departments.

When Holland stressed that the project would reach only three locations, Sondik said the information could be used to assist other departments "five years down the line."

"I might not be here in five years," Holland said. "And there will be an awful lot of women who won't be either in the 47 states who are not funded."

Suggesting that NCI use the funds to hold seminars and conferences for public health department officials, Holland said, "It is pie in the sky to think that you will have an impact on the entire country unless there is a change in the availability of these procedures for women in the lower economic group...I think three demonstration projects in three isolated areas of the country won't have any impact in Peoria."

Iverson asked that the concept be broadened in order to allow nonpublic health department clinics, such as neighborhood health clinics, to participate.

While expressing sympathy for the concept's goals, he said he could not support it because it does not determine the capability of public health departments to conduct such programs, and identify what barriers currently exist. "If those can be documented, then you know how you can have effect...if there's no capability, then I think we're making a mistake."

In other matters, Sondik told the Board that NCI's annual cancer statistics upddate will be released during a day and a half meeting with a panel of researchers and members of the press. NCI will not release the statistics during a half hour presentation to the National Cancer Advisory Board, the past practice. The Office of Cancer Communications is planning the meeting.

Wynder's Low Fat Adjuvant Breast Cancer Study Finally Funded By NCI

Ernst Wynder has long believed that a sharp reduction in dietary fat could prove to be as effective as adjuvant chemotherapy in improving survival of breast cancer patients. He proposed, first to NCI's Div. of Cancer Treatment and then to the Div. of Cancer Prevention & Control, that a randomized trial be undertaken to investigate that hypothesis.

A preliminary study was established, but it randomized patients either to CMF chemotherapy or to a low fat diet. Some investigators who had agreed to participate backed out on further reflection, contending that for patients at higher risk for recurrence (those with positive nodes), withholding chemotherapy was unethical.

Wynder disagreed, citing figures from Japan which he said demonstrate that recurrence rates there are significantly lower than in the U.S., even without adjuvant chemotherapy, which he attributed to the lower fat intake of Japanese women.

At that time, DCPC was in the process of setting up the Women's Health Trial, which would have tested whether dietary fat reduction would result in lower incidence of breast cancer in high risk groups. Much of the controversy that swirled around WHT was based on the alleged inability of the investigators to adequately monitor compliance. That issue spilled over onto Wynder's adjuvant study, and with the other problems, NCI withdrew its support.

Challenge Accepted

When the DCPC Board of Scientific Counselors decided against going ahead with Wynder's study, it was suggested that he try the traditional investigator initiated route. Wynder took up the challenge, and last month, his application for cooperative agreement support was funded.

Wynder, president of the American Health Foundation in New York, is principal investigator. Coprincipal investigator is Rowan Chlebowski of Harbor-UCLA Medical Center. Other participating institutions and their PIs are Methodist Hospital-Baylor, William Insull; New England Deaconess Hospital, George Blackburn; Memorial Sloan-Kettering Cancer Center, David Kinne; Evanston Hospital, Janardan Khandekar; Emory Univ., Martin York.

The nutrition unit is headed by Marilyn Buzzard at the Univ. of Minnesota, and the statistical unit is headed by Robert Elashoff at UCLA.

The trial, called Women's Intervention Nutrition Study (WINS), will be limited to postmenopausal patients with resected stage 1 or stage 2 breast cancer. Postoperatively, patients will be randomly allocated either to a program designed to reduce dietary fat intake (to 20 percent of calories from fat, about half the normal U.S. diet), or to a dietary control group.

The controversy over CMF is avoided, thanks to the more recent studies which have demonstrated that tamoxifen is at least as effective as chemotherapy in many subgroups of postmenopausal patients. Tamoxifen, relatively nontoxic, will be given to all patients for five years.

Three hundred patients will be accrued with a primary objective of examining adherence to the dietary program. Secondary objectives include identification of behavioral variables, which can be used as individual predictors of dietary change, and monitoring biochemical parameters, which may correlate with food record measures of dietary change.

All patients will be followed for disease free and overall survival.

The award is for about $500,000 a year in direct costs, for four years.

FDA Vs. NCI: Nothing Has Changed; 'Waste Of Time' To Talk, Einhorn Says

It has been a year since Frank Young, commissioner of the Food & Drug Administration, appeared at a meeting of the NCI Div. of Cancer Treatment Board of Scientific Counselors and promised that whatever differences existed between the two agencies would be resolved.

Other FDA officials at that same meeting expressed surprise that NCI executives felt major differences existed at all.

At last June's meeting of the DCT Board, Carl Peck, director of FDA's Center for Drug Evaluation & Research, and John Johnson, oncology group leader, appeared in place of Young. Their response to NCI's complaints was no more satisfactory to NCI staff than it ever had been.

DCT Director Bruce Chabner again brought up the problems with FDA at this month's meeting of the Board. Those problems essentially are lack of responsiveness to NCI concerns.

NCI drew up a position paper in February

that called on FDA to consider the use of parameters other than survival benefit in approving new drugs, Chabner reminded the Board. "Dr. Carl Peck expressed general agreement with this position in his response to the Board in June, and promised that a written reply to the paper would follow. However, a formal reply has not been received to date.

"We continue to be frustrated by the delays in the approval of flutamide. This drug was tested in combination with leuprolide for prostate cancer, and a prolongation of survival, as well as improved progression free survival, has now been shown in the national intergroup prostate trial."

"Inappropriate" Committee

The flutamide new drug application, however, was not reviewed by FDA's Oncologic Drugs Advisory Committee but instead by the Advisory Committee on Endocrine Drugs, "to my mind an inappropriate forum to review this agent," Chabner said. That committee voted against approval, and FDA, even after reviewing new data indicating a survival advantage, "has confirmed its decision to withhold approval," Chabner said.

"I wrote to Dr. Young and Dr. Peck pointing out my reasons for disagreeing with that decision. Dr. Peck responded, saying that he saw no reason for changing the decision."

Another difference is brewing, with a draft proposal released by FDA for modifying the drug development process for cancer and AIDS, Chabner said. "The key elements of this proposal are:

"1. Early, prephase 2 conferences between sponsors and FDA to define definitive controlled phase 2 trials that can lead to new drug approval, prior to phase 3.

"2. Postapproval phase 3 testing.

"We are somewhat uncertain as to the meaning of the proposed controlled phase 2 trials since, in cancer, phase 2 trials are by definition uncontrolled and are usually undertaken to identify the categories of disease in which the drug is active. Phase 2 trials are then followed by definitive comparative studies of a phase 3 nature. It is our concern that the FDA proposal may simply be redefining phase 3 as perhaps phase 2 and a half. If, on the other hand, Dr. Young is saying in effect that the establishment of definite antitumor activity in a disease is sufficient for approval, then we heartily agree."

Lawrence Einhorn, a member of the DCT Board, has served on the FDA Oncologic Drugs Advisory Committee and has been involved in developing NDAs for a number of drugs.

"I've been working with FDA too long to be an optimist" about the problem, Einhorn said. "If we can appoint an NCI director in a relatively short time (an expected three months after Vincent DeVita's resignation), it is unconscionable that Dr. Peck can't learn his job in a year." Peck had blamed the fact that he had been in his job for only 10 months for not responding completely to the NCI position paper.

"It's a waste of time to have a dialogue with FDA," Einhorn continued. "There has been no change at all." He suggested the Board consider a resolution calling for a new system, to bypass FDA in the cancer drug approval process.

Chabner noted that Vice President George Bush had asked the President's Cancer Panel to form a committee to examine the extent to which governmental regulation is slowing the development of new effective therapies for cancer and AIDS. The committee is being organized.

"I think this is a possible avenue to get relief," Chabner said. "I think the committee will be sympathetic. We've been asked to testify. It is likely that a member of this Board will be on the committee."

Chabner will not have to go far to find examples of what he considers undue delays on FDA's part which hamper clinical research.

Steven Rosenberg's initial protocols for interleukin-2/lymphokine activated killer cell therapy were held up for weeks by FDA. That might be understandable, considering the toxicities that developed with that regimen.

It should be a different story now, with the experience gained using IL-2. Rosenberg's latest regimens using tumor infiltrating lymphocytes have been considerably less toxic. But FDA is still plodding along, business as usual.

Rosenberg told the Board that FDA has been holding up for six weeks his protocol using TIL with IL-2 and interferon, "which certainly won't be more toxic," he said.

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