DRS
6/17/88

THE CANCER LETTER

Vol. 14 No. 25

June 17, 1988

Subscription: $175 year North America, $190 year elsewhere

P.O. Box 2370 Reston, Virginia 22090 Telephone 703-620-4646

FDA Reaction To DCT Proposals 'Positive,' But Chabner, Wittes 'Disappointed' In That Response

FDA Commissioner Frank Young did not keep his promised return engagement with the Div. of Cancer Treatment Board of Scientific Counselors, to follow up on the somewhat contentious discussions he and his staff members had with

(Continued to page 2)

In Brief

Cady New SSO President, Rush President Elect; Polackwich, Major Figure In Straus Case, Killed

BLAKE CADY, New England Deaconess Hospital, became president of the Society of Surgical Oncology at its annual meeting in New Orleans. Cady took over from **J. Bradley Aust**, who assumed chairmanship of the Executive Committee. **Benjamin Rush**, New Jersey School of Medicine & Dentistry, was elected president elect. **Alfred Ketcham**, Univ. of Miami, was elected vice president. **Charles Balch**, Univ. of Texas M.D. Anderson Cancer Center, remains as secretary, and **Samuel Wells**, Washington Univ., is treasurer. . . . **ROBERT POLACKWICH**, president of the Tampa Bay Oncology Group and a member of the Univ. of South Florida Medical School faculty, was killed in a sailing accident earlier this spring. His stepson, 19 year old Jonathon Richards, also died when the mast of their catamaran struck electrical transmission lines while they were sailing near Ft. Myers. It was Polackwich who, as a Boston medical oncologist, found what he thought were irregularities in clinical trials data reported by Marc Straus in the late 1970s. Straus eventually was forced to give up participation in NCI supported trials, but not before Polackwich endured severe criticism from various sources for standing by his charges, which were later supported by a government investigation. NCI took a lot of heat from Congress when, a year or so after the charges were made public, it awarded a grant to Straus . Director Vincent DeVita defended that action on the basis that no charges against Straus had been proven, but Straus ' grant later was terminated. . . . **TIMOTHY TALBOT**, president emeritus of Fox Chase Cancer Center, is recovering from surgery performed there. . . . **BOYER YOUNG** Investigator Awards to those at Memorial Sloan-Kettering Cancer Center who show the most promise and productivity in clinical and laboratory studies went this year to Maurie Markman, associate chairman for clinical affairs, and Jeffrey Ravetch, associate molecular biologist, both in the Dept. of Medicine.

FDA Commissioner Skips DCT Board Meeting; NCI Skeptical On Assurances

(Continued from page 1)

NCI staff at last October's meeting of the board. Instead, he sent Carl Peck, director of the agency's Center for Drug Evaluation & Research, and John Johnson, oncology group leader.

They were there to respond to a document drawn up by Robert Wittes, director of DCT's Cancer Therapy Evaluation Program, in collaboration with DCT Board Chairman John Niederhuber and a board committee. The document incorporates DCT's recommendations for criteria to consider in approval of new drug applications for anticancer agents, the major issue in the long standing controversy between NCI and FDA.

The complete document starts on page 4.

Young and some of his staff attended the board meeting last fall in an effort to resolve the escalating controversy over approval criteria. The parties agreed to work on the matter, and Young said he would return at the June meeting, hoping to wrap up an agreement by then.

In a parting shot, Young needled DCT for not giving him a seat at the board table.

They had a seat for FDA this time, but it was occupied by Peck rather than Young, who Peck said "had a previous commitment." Since the meeting date had been set at least a year in advance, some board members wondered whether Young was still miffed.

Young's office told **The Cancer Letter** that he was in California on leave, which had been scheduled four months previously.

His absence may have prolonged the controversy. Peck has been at FDA for only 10 months and admittedly has not yet learned all the ropes.

The DCT recommendations for NDA approval were completed in February and sent immediately to FDA. Four months later, Peck had to say that he could offer only "our preliminary reaction" to the five page document. "A full response from FDA and the Oncologic Drugs Advisory Committee has not been completed."

Peck's approach basically was conciliatory. "Overall, our reaction was very positive," he said. "There is no serious disagreement in principle."

NCI has objected to what it feels has been FDA's undue reliance on survival as an endpoint in evaluating a drug, and to an unswerving demand for data from controlled trials. One of the DCT recommendations (No. 3 under "Assumptions") is that agents intended for patients with refractory disease should not need to be tested in comparative trials against a drug or placebo.

"We are unaware of any requirement for uncontrolled trials that prove effectiveness," Peck said. He noted that FDA had approved AZT for AIDS without completion of a comparative trial. "The fact that it was stopped early did not jeopardize approval."

On issues of relative effectiveness (No. 5), DCT said that "comparative studies should not be required for new agent approval if patient benefit can be established without them."

Peck's response: "We say, how can you demonstrate patient benefit without comparative trials?"

The DCT document calls for use of significant response rates as an acceptable endpoint. "We agree," Peck said, "but what constitutes 'significant'? We think that has to be judged on a tumor by tumor basis."

DCT Director Bruce Chabner disagreed. "I still think we need more discussion about alternate endpoints," he said. "I don't agree that you have to do this tumor by tumor."

Chabner acknowledged that progress is being made between the two agencies. But he said that "there is a difference sometimes between the working level and the upper echelon. Those who are working together day by day have to work with principles. That does not stop us from trying to change some of the principles."

Chabner insisted that "we need faster approval" of NDAs. "It is my belief that much of the important development takes place after a drug is approved for marketing."

Wittes' reaction was stronger. "I'm deeply disappointed in your response," he said to Peck. "The thrust of point No. 3 is rather clear. It involves using patients as their own controls. "You're missing the point. When no standard therapy exists, how can you compare?

"By allowing for general wording, we hoped it would provoke some reflective thinking within FDA," Wittes continued. "Commercial sponsors won't jeopardize millions of dollars by coming to you with creative trials unless you encourage them. . . You always harken back to survival. The whole point of this is to look for endpoints that don't take so long. We need faster approval. Survival is the ultimate endpoint, but it doesn't have to be the only one."

"I'm disappointed that you are disappoin-

ted," Peck responded. "We don't say that survival is the only endpoint."

Wittes wouldn't drop the issue. "In evaluating antiarrythmia drugs, do you demand survival? Or do you look for biological effectiveness in elimination of arrythmia?"

"I haven't been long enough with the agency to respond," Peck said.

Board member William Hryniuk suggested that the FDA Oncologic Drugs Advisory Committee should review the document, as a basis for evaluating drugs. "We need to get FDA and the committee's complete evaluation of this, as a formal mechanism to follow."

The document was sent to members of the FDA committee, and FDA staff had received at least one response. Two members of the committee, Chairman Martin Abeloff and Robert Capizzi were on the DCT committee that helped draw up the document.

"My opening comment was that our overall reaction was positive," Peck said. "We believe the document generally reflects FDA policy. We do need further discussion of approval criteria. This is a good start."

"That's fine," Chabner said, "but one of the problems we'll have is in actual practice." He referred to recent FDA action involving flutamide, when the sponsor sought approval for pain relief from flare responses associated with LHRH treatment of prostate cancer.

The NDA was reviewed by an endocrine committe, not the Oncologic Drugs Advisory Committee. That committee was not familiar with the use of flutamide, Chabner said, so it took the easy way out and asked for evidence of survival benefit. "They reverted to form."

FDA's Johnson agreed that "the flutamide application is a good one to look at. We can't say much about it while it is still under consideration. Time to progression sounds good (as an acceptable endpoint) but we feel it is one of the softest endpoints we look at. Determination of time to progression is not always sharp."

In his opening remarks, Peck noted that Johnson's oncology group includes seven medical reviewers. Of those, five are formally trained in medical or radiation oncology, four are board certified medical oncologists, four have worked at least 10 years in oncologic therapy and two have engaged in clinical oncology practice.

"We rely heavily on the advisory committee system," Peck said. "They give us outside and not always predictable advice. We're not bound to accept this advice, although we ordinarily do." Of the last 11 NDAs submitted to the oncologic advisory committee, FDA went along with 10 of its recommendations. The 11th involved mitoxantrone, which the committee recommended for approval for breast cancer. FDA did not approve it, and the committee later reversed itself after getting additional data.

"Since last October, four NDAs have been submitted (for anticancer agents), three have been acted upon, two were approved, one disapproved and one will be approved as a treatment IND within 30 days," Peck said. "That is rapid turn around. I wish we could say the same for the rest of the center. The average time (from submission to approval or disapproval) is 25 months.

"We view NCI as a sponsor, a special client, as an interested party with motives of the highest order. But we recognize that on occasion, careers and egos are at stake. The Technology Transfer Act provides a powerful incentive for government employees to invent things and transfer them to industry. There are scientists with personal interests in some of the products we are evaluating."

Peck said that it came as a "delightful surprise when I realized that we are promoters of drug development." He concluded, "We can't afford to be adversaries of NCI, and we can't afford a divorce. We actually work well on a routine basis."

Vice President Asks Hammer To Probe FDA Regulation of Anticancer Drugs

Vice President George Bush has written to Armand Hammer, Chairman of the President's Cancer Panel, asking him to investigate whether the Food & Drug Administration's regulation of anticancer drugs has been improper.

Bush, for much of his tenure as vice president, has headed the Administration's efforts to assess the impact of regulatory activities of various federal agencies.

Hammer's reaction to the request has not yet been revealed. NCI executives, who would not speculate on what prompted Bush's request, believe that Hammer probably will call for a meeting or a series of meetings, with presentations to be made by cancer clinical investigators, NCI staff members, industry drug sponsors, and FDA staff members.

"This could be a rehash of what we've been talking about for years," one NCI staff member commented.

Recommendations to FDA Concerning Approval of New Drug or Product Licensing Applications for Antineoplastics

Expeditious approval of anticancer agents that are beneficial to patients is a matter of highest priority. The demonstration that a new drug causes tumor regression and may improve the quality of life of patients who have cancers that are currently incurable should lead independently to approval for marketing, even in the absence of supportive long term survival data. The criteria for approval need to be uniquely tailored to patients who have incurable, indolent or aggressive cancer; those who have failed on prior therapy; or those who have disease for which there is no standard beneficial treatment. This degree of complexity requires participation by sophisticated clinical investigators with expertise in conducting such studies.

Assumptions

1. Safety and efficacy are appropriate requirements for drug approval.

2. Neither safety nor efficacy is an absolute concept in the context of cancer (or any other) treatment. Drugs are neither uniformly curative nor uniformly safe, nor are they ever likely to be. Thus, the approval process must approach flexibly the relation of risk to benefit in cancer patients with different underlying prognoses.

In particular, the approval process should be based on evidence that net benefits result from treatment for defined populations (or subpopulations) of patients. For example:

A. Agents showing significant benefit in patients with refractory cancer might be approved even in the face of very substantial toxicity.

B. Agents that confer modest but reproducible levels of benefit in patients with refractory cancer should be approved if the level of toxicity is minimal.

C. For agents with intermediate degrees of benefit and toxicity, the weighing of this balance is more difficult, but the decision rests ultimately on whether demonstrated benefits to the treated population outweigh adverse effects.

D. Agents that avoid significant and specific organ toxicity may be approvable if they demonstrate benefit equivalent to a standard agent in a particular cancer.

3. Randomized clinical trials in support of an NDA or PLA (product licensing application) are generally the preferred means of drug evaluation. However, in patients who have refractory disease there is characteristically no standard therapy that provides reproducible benefit. In such cases, alternative evaluative designs may be more appropriate medically and ethically. In such situations, clinical trials cited in support of an NDA need not involve a comparative trial against a drug or placebo.

4. The premarketing experience with a drug should be sufficient to characterize its long and short term benefit and toxicity. Sufficient numbers of patients should be treated for long enough durations that uncommon but medically important toxicities, whether acute or chronic, will have a high probability of being detected. One would not have wanted to miss, for example, the cardiotoxicity of doxorubicin. Thus the appropriate length of followup should take into account the expected survival of the patients for whom the drug is intended.

5. Issues of relative effectiveness, i.e. how the new agent compares to other available treatments for the disease in question, are often medically important. Such questions can be addressed either in the pre or post-marketing period in randomized controlled trials. These comparative studies, however, should not be required for new agent approval if patient benefit can be established without them. Pivotal studies for an NDA or PLA may, of course, compare new therapy to standard treatment but they must do this only when the labeling indications sought by the sponsor refer to a patient population for which effective standard therapy exists.

Approaches to the assessment of net benefit to the treated population

Acceptable endpoints include:

1. Survival benefit. Clearly an agent imparting a survival advantage to the treated population should be approved. Such a therapeutic effect is generally best shown in randomized controlled trials (RCT), although the effects of very potent agents or combinations of agents may be apparent even with historical controls (e.g. etoposide for the second line and ifosfamide for the third line treatment of metastatic germ cell tumors).

2. Time to treatment failure (or to disease progression) provides important information relating to drug efficacy and may be a useful parameter supporting approval. Involvement of TTF in the adjuvant setting is generally best shown in RCT.

3. Complete response rate. Across a variety of malignancies, a consistent increase in complete response rates has translated into increased survival and cure rates. Drugs that have reproducible and carefully documented complete response rates should be strong candidates for approval. Even in the presence of substantial toxicity, a significant complete remission rate, with responses of meaningful duration, may well justify drug approval, particularly for diseases having few good theapeutic options.

4. Response rate. Some have argued that virtually any drug with a response rate above some arbitrary level (e.g. 10-20 percent for many solid tumors) should be approved. Clearly any reasonable threshold level should be a function of the tumor type and stage in question (i.e., the threshold response rate for previously untreated indolent lymphomas might be very much higher than that for renal cell carcinoma or melanoma). The problem with this, however, is that it is not meaningful to consider response rate in isolation from duration of response and from the general level of toxicity.

Response rates above a certain level might constitute a basis for approval provided that the responses are of meaningful duration and the toxicity of the agent is not substantial enough to outweigh the beneficial effects.

5. Beneficial effects on disease related symptoms and/or quality of life. Quality of life may be influenced by treatment induced decrease in symptoms of disease and/or reduction in the deleterious effects directly attributable to treatment. The aim here is to show improvement in tumor related symptoms, improved function, decreased reliance on medical support, gain in lean body mass, and other measures of patient benefit, in addition to tumor shrinkage. Such improvement may be demonstrated by:

A. Comparison with standard therapy in a randomized controlled trial. Here one must show equivalence or near equivalence in efficacy for the quality of life benefit to be medically meaningful, since ordinarily one would not want to sacrifice very much in survival for superior quality of life or symptom control. Individual patients and physicians might, however, come to rather different conclusions about the relative value of length of survival vs. a somewhat shorter survival that is of better quality.

B. Comparison of the posttreatment status of the patient with his/her own pretreatment status. This approach has been used recently in the case of interferon alpha for hairy cell leukemia (reduction in transfusion requirement and infection rate after treatment) and in trials of somatostatin analogs in islet cell/carcinoid tumors (reduction in symptoms related to

hormonal secretion). In other disease, other parameters would have to be developed.

Illustrative examples

1. Consider a hypothetical antiestrogen having a response rate in previously untreated postmenopausal ER (+) patients of about 30% (compared with 50-60% for tamoxifen) and about 10-15% in patients who have previously responded to and then failed all other hormonal therapy including tamoxifen. Toxicity minimal.

Comments. For an indication centering on hormonally refractory patients, this drug should be approvable on the basis of a 10-15% objective response rate and essentially no toxicity. It should be very easy to show tangible patient benefit in the responders with an absence of treatment related toxicity. For an indication involving previously untreated ER (+) patients, however, comparison with tamoxifen in a randomized controlled trial should be required. Indeed, the 30% response rate quoted above suggests that it might not be approved for this indication, since it appears to be only half as good as the established agent and has no other advantages.

2. Drug has a 20% response rate in kidney cancer, median duration four months; none lasting past six months. Severe refractory nausea and vomiting, lasting several days after each dose (q3w administration).

Comment. It is unlikely that the totality of data would support a claim of net patient benefit. Perhaps it might be approvable if the responders included patients with symptomatic liver, lung or brain disease who responded remarkably. It seems more likely, though, that the short response durations and the severe nausea and vomiting would militate against approval.

3. Consider a hypothetical cytotoxic activity against MOPP/ABVD failures with Hodgkin's disease. Response rate is approximately 30%, all of which are partial responses. Median durations of responses are five months; none lasting longer than eight months. Toxicity moderate: nausea and vomiting for two to four hours in 60-70%, grade 3 myelosuppression in 75%, urticaria in about 7%. Drug is given q 3 weeks.

Comments. A drug with these modest credentials seems unlikely to increase the effectiveness of initial chemotherapy if incorporated into primary combinations, although admittedly this 30% response rate may vastly underestimate its activity in less heavily pretreated patients. Nevertheless, the drug should be approved for salvage use if the data in this group (i.e. MOPP/ABVD failures) suggests medical benefit. Comparison with standard therapy in the salvage setting should not be required for approval, since there is no standard therapy for this group that is medically meaningful. The basis for approval would be medical benefit to a group of patients for whom few other options exist. It is the sponsor's responsibility to show in its NDA that this 30% response rate, plus the associated toxicities, translated into overall benefit for the treated population. The best way of doing this would probably be to show better symptom control and quality of life in responders, compared to their pretreatment status, without strong adverse effects in the nonresponders.

4. Analog A, a chemical analog of a parent, has a similar spectrum of antitumor effect but with less toxicity (e.g. nausea and vomiting, major organ toxicity, whatever). Completely cross resistant with parent.

Comment. If the sponsor can show net patient benefit, analog A should be approvable for that patient population, without the necessity for comparative trials against parent. The labeling indications of analog A can be written narrowly without reference to the parent. Subsequent comparative trials that can be done in the post marketing period of a comparison is a medically important experiment in the particular clinical context. For example, the relative effectiveness and toxicities of 4-DMDR and daunorubicin, both in combination with AraC, in the initial therapy of acute leukemia, is a medically relevant issue, as is a comparison of cisplatin and carboplatin (each in combination with cyclophosphamide) in ovarian cancer. On the other hand, a comparison of carboplatin and cisplatin (alone or in combination with 5-FU or bleomycin) in squamous head and neck cancer is much less important, because the role of cisplatin itself is less well defined in that disease.

5. Analog B is partially or completely noncross resistant to parent.

Comment. Although this is a chemical analog of the parent, the lack of cross resistance means that the agent is likely to have a different spectrum of clinical activity. Analog B should be developed as a novel structure for both medical and regulatory purposes. Direct comparisons with parent should not be required for approval unless the labeling indication requested is for a disease stage for which parent is effective therapy and analog B is being proposed as a substitute for the parent.

6. New drug with 30% response rate in kidney cancer, including 10-15% complete responses that are relatively durable (median duration of PR about six months and of CR >12 months). Mild toxicity.

Comments. Approve. Should be easy to show patient benefit, which should be presumed anyway because of the complete responses.

7. Same clinical scenario as in 6 above, except that drug administration is complex, requires hospitalization and intensive care, and is associated with significant major morbidity but a very low mortality rate.

Comments. Judgment would obviously depend upon details. Probably not approvable unless both of the following are true: (1) the CRs are impressively durable; and (2) the regimen can be given outside highly specialized centers with adequate safety and maintenance of efficacy, unless a way can be found to limit sale and distribution to qualified centers.

RFAs Available

RFA 88-CA-12

Title: Data based intervention research for public health agencies

Letter of intent receipt date: June 30

Application receipt date: Sept. 7

The Div. of Cancer Prevention & Control of NCI invites applications for cooperative agreements in support of projects that will serve as models of data use in the planning and evaluation of statewide cancer prevention and control programs.

This RFA is designed to stimulate the development of cancer prevention and control intervention programs on the state and local level based on a thorough analysis and evaluation of the variety of data sources related to cancer control that exist in the state. The four phased project includes (1) identification, appraisal and analysis of existing population specific data sources related to cancer control; (2) the development or modification of a cancer control plan; (3) initiation of new or modification of existing cancer prevention and control programs as specified in the plan; and (4) a period for evaluation of process and outcome.

Applicants must be state or territorial health departments (including the District of Columbia). Local health departments or agencies within the jurisdiction with primary responsibility for cancer control activities may apply through the state or territorial health department. Health departments currently funded under the NCI grants "Cancer control technical development in health agencies" or "Data based interventions for cancer control" are not eligible to apply for this grant. Prospective applicants are asked to submit a letter of intent.

Awards will be made as cooperative agreements. Funding is limited to a maximum of seven years.

Approximately 10 awards are anticipated depending on the quality of applications and the availability of funding.

Copies of the complete RFA and additional information may be obtained from, and letters of intent directed to, Dr. Leslie Boss, Program Director, Cancer Control Applications Branch, NCI, Blair Bldg Rm 4A01, Bethesda, MD 20892, phone 301/427-8684.

RFA 88-HL-17-L
Title: Cellular growth factors and oncogenes in developing lung
Letter of intent receipt date: Sept. 15
Application receipt date: Dec. 9

The Structure & Function Branch of the Div. of Lung Diseases, National Heart, Lung & Blood Institute, announces the availability of an RFA on the above subject.

This program will support basic research on the mechanisms by which polypeptide growth factors and oncogenes regulate cell growth and proliferation in normal developing lung during the prenatal and early postnatal period. The use of molecular biologic approaches is strongly encouraged. It is expected that research applications will encompass a variety of approaches and require expertise from a wide range of disciplines including pulmonary cell biology, biochemistry, molecular biology, cancer biology, developmental biology and pulmonary physiology and medicine.

It is anticipated that six grants will be awarded under this program. The specific amount to be funded, however, will depend on the merit and scope of the applications received and the availability of funds.

The earliest award date for successful applications will be July, 1989. Awards will be made to foreign institutions only for research of very unusual merit, need and promise.

Copies of the complete RFA may be obtained from, and letters of intent directed to, Dorothy Berlin Gail, PhD, Chief, Structure & Function Branch, Div. of Lung Diseases, NHLBI, Westwood Bldg Rm 6A07, Bethesda, MD 20892, phone 301/496-7171.

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 Blair Building room number shown, National Cancer Institute, NIH, Bethesda, MD 20892. Proposals may be hand delivered to the Blair Building, 8300 Colesville Rd., Silver Spring, MD, but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-97575-72
Title: Primary rodent production centers
Deadline: Approximately Aug. 15

The Developmental Therapeutics Program of NCI's Div. of Cancer Treatment is seeking organizations with the capabilities and facilities for producing large numbers of inbred rodents which are genetically sound and free of pathogenic organisms. To be considered for the contract award, offerors should meet the following criteria:

1. The principal investigator and other key personnel must have experience and expertise in the production of the highest quality rodents free from pathogenic organisms.
2. The facility must be available at the time of contract award, capable of producing highest quality rodents at tasks specified levels.
3. Organizational experience in pertinent areas of quality rodent production including pedigreeing procedures, isolator production, etc., at a scale commensurate with tasks performance.
4. Willingness to participate in grantee reimbursement cllections.

It is anticipated that three awards will be made at the various task levels. Only one award will be made to any organization.

Contracting Officer: Jacqueline Ballard
RCB Blair Bldg Rm 228
301/427-8737

NCI Reorganization Proposals Create Opposition Among Some Advisors

We train hard, but it seemed that every time we were beginning to form into teams we would be reorganized. I was to learn later in life that we tend to meet any new situation by reorganization; and a wonderful method it can be for creating the illusion of progress while producing confusion, inefficiency and demoralization. *--Caius Petronius, A.D. 66*

Alan Yagoda, Memorial Sloan-Kettering Cancer Center, said later he did not have NCI's unending series of reorganizations in mind when he led with the Petronius statement in his presentation at the symposium on the status of cancer treatment at the American Assn. for Cancer Research meeting last month. It was in an entirely different context, involving progress in cancer treatment.

There were some in the audience, however, who immediately related the 2,000 year old bit of wisdom to the latest NCI reorganization proposals. Those who felt that it described the NCI situation are not being fair: most of the reorganization efforts of the last 15 years have probably had more positive than negative effects.

The current proposals, which may be decided upon soon, have generated mixed support among NCI staff, advisors and cancer program constituents. Least controversial is the proposed move of the Cancer Centers Program, probably also along with community, construction and training programs, from the Div. of Cancer Prevention & Control to Director Vincent DeVita's office. None of the advisors (NCAB, boards of scientific counselors) have objected in any degree to that move, which would better position those programs to deal across division lines, and give them direct access to DeVita and the NCI Executive Committee.

That move, however, would strip DCPC of the lion's share of its budget and activities, leaving only the pure cancer control activities. DeVita has suggested moving the entire

Epidemiology Program from the Div. of Cancer Etiology to DCPC, strengthening the latter and getting the epidemiologists closer to those who apply the results of their research.

That is not one of DeVita's more inspired ideas, opponents of the plan have suggested. Those opponents include most of the epidemiologists involved, DCE Director Richard Adamson, the entire DCE Board of Scientific Counselors and the National Cancer Advisory Board's Carcinogenesis Committee, among others.

DeVita went prepared to the recent meeting of the DCE board; he had received a letter drafted at the previous meeting, strongly opposing the move of epidemiology out of the division. He went into the subject immediately.

"One of the issues is that (the move) would separate epidemiology from the laboratories. I agree that it would not be productive if in fact it would impair collaboration of epidemiologists and basic scientists. I have known Joe Fraumini (director of the program) for 20 years. He is an absolute genius in fostering collaboration. . . Our Epidemiology Program is the finest in the world."

DeVita pointed out that DCPC is the entity with responsibility for application of prevention research. "We're going to try the best we can to place the program where it will be most advantageous."

Second Epidemiology Program?

He also noted that the Epidemiology Program has for years been located in the Landow Building, in downtown Bethesda, a mile from the DCE labs with which they have collaborated. DCE staff at Landow has moved to the new quarters in the Executive Plaza Building, in Rockville, where DCPC offices soon will relocate from the Blair Building. When that happens, the epidemiologists and DCPC will be no more than 100 feet from each other.

An alternative would be to establish a second epidemiology program within DCPC, with Fraumini's group remaining in DCE. "That is a good idea, and in the best possible worlds is what we would do," DeVita said. "But with our FTE (staff positions) crunch, that is not possible."

Another alternative, DeVita said, "is that at some time in the future, we will decide that cause and prevention belong in the same place. My guess is that it will, some time down the road. In the past (when DCE was the Div. of Cancer Cause & Prevention) it was all cause, no prevention. Now the program has been built in DCPC for implementation of prevention."

"Etiology is the most important part of prevention," board member Allan Conney responded. "Once you understand the cause, the high risk groups can be identified, and then you can do prevention. Moving them away would be risky."

"The Epidemiology Program does brilliantly," DeVita said. "But they are not in a position to determine when to stop studying and start practical application. The division lines are artificial barriers, like separate countries. The application of prevention is where we're taking the most criticism."

"I understand both concerns," board member Alice Whittemore said. She suggested a compromise: "The epidemiologists most concerned with application go to DCPC, and those with one foot in the laboratory stay in DCE."

"I haven't heard a good argument that suggests we are breaking a link," DeVita said.

"It would turn the organization upside down," board member Moyses Szklo said. "If it is so easy to have links, why move? They can stay in DCE and link with DCPC."

"Links are everywhere, that is true," DeVita said. "But where they are not is in application. It's not there."

Moving epidemiologists into prevention means that attempts would be made "to reprogram them to use their expertise in prevention trials," board member Roy Shore said. "They've been trained to do epidemiology research, not prevention. They have built their careers on it. It would result in a severe morale problem, if they have to do a late career switch."

"You need to help us," DeVita said. "There are things we can do in prevention. That is part of our mission. You have to share with us the responsibility."

"We're saying something that's not coming through clearly," board member Anna Barker said. "It's not so much the links as the timing. It has only been a short while since molecular biology started taking off. It's not ready for application."

"There are many ways to prevent cancer," Conney said.

"We don't have unlimited resources," DeVita said. "Some shift is necessary. We have to give prevention and control some resources."

Board member Thomas London noted that epidemiology/laboratory collaboration also has a positive effect on the labs. "It works both ways."

"There is strong cross fertilization between laboratories and epidemiologists," board member Dietrich Hoffmann said. "But you don't see strong cross fertilization between behavior modification and epidemiology."

Szklo suggested that outside pressures for prevention trials is premature; "the science is not there."

"We're not doing this because of pressures," DeVita said. "If we did, we would have funded the Women's Health Trial. I do think that epidemiologists sometimes go on too long. They need to have a sense of knowing when to stop studying and start applying."

When board member Maureen O'Berg noted that there were three epidemiologists on the board, DeVita joked, "I should have asked for a show of hands. Will I have to back out of the room?"

Board Chairman Hilary Koprowski said that "being under the same roof (epidemiologists and DCPC) may help. I suggest we wait and see. We don't know much about the problems of the other division."

"I get the sense of the board," DeVita said. "I feel the sensitivity. This is a very effective board. If we can't persuade you that we're doing the right thing, I would hesitate to do it."

Shapiro, Strax, Knudson, Nishizuka Winners of 1988 General Motors Prizes

Four scientists who made breakthroughs in the diagnosis of cancer, prevention of cancer deaths, and understanding how cancer develops are the 1988 winners of the General Motors Cancer Research Foundation Prizes, the largest awards in the field of cancer research.

The $390,000 in awards were announced this week by Foundation President Joseph Fortner.

Sam Shapiro and **Philip Strax** will receive the Charles F. Kettering Price for the first and still most definitive study proving that breast cancer screening can save lives. Their work established the importance of early detection of breast cancer through screening. Ten to 15,000 American women's lives--and many more worldwide--could be saved with widespread use of regular breast cancer screening. Shapiro is professor emeritus of health policy and management at Johns Hopkins. Strax is clinical professor of oncology and radiology at the Univ. of Miami.

Alfred Knudson was named winner of the Charles S. Mott Prize for developing one of the most important theories in cancer research, which spurred much of today's genetic research. Long before anticancer genes were detected, Knudson predicted that they exist. He showed how their destruction or damage could result in certain rare hereditary childhood cancers and, probably, common cancers in adults. Knudson is senior member of the Institute for Cancer Research at Fox Chase Cancer Center.

Yasutomi Nishizuka was awarded the Alfred P. Sloan Jr. Prize for his discovery of one important way signals promoting cancer are transmitted to cells. His studies also uncovered one of the main ways virtually all cells talk to each other and coordinate their activities. Nishizuka discovered a hitherto unknown protein in cells that plays a critical role in the transfer of cellular messages, and showed that tumor promoters act directly on this protein. He is professor and chairman of biochemistry at Kobe Univ.

Each prize includes an award of $100,000 and $30,000 to cover expenses for a scientific conference or workshop. Shapiro and Strax will share the Kettering Prize.

Kushner Forms BreastPac To Raise Money For Political Contributions

Rose Kushner, fresh from victory in the long fight to get Medicare to pay for mammography screening, has formed a political action committee to finance a continuing fight "to find political solutions" in the search for new methods to reduce the toll from breast cancer.

Kushner, author and women's health activist, established the Breast Cancer Advisory Center several years ago to provide information to women concerned about the disease. The new BreastPac will raise money to contribute to campaigns of politicians who support breast cancer programs. "I ask every woman in the U.S. who has ever found a lump in her breasts to contribute $1 to BreastPac," Kushner said. The address is 9607 Kingston Rd., Kensington, MD 20895.

The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams

Published forty-eight times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter.