THE CANCER LETTER

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

Vol. 16 No. 7
Feb. 16, 1990

Price $195 Per Year US, Canada.
$220 Per Year Elsewhere

NCAB Considering Concept Review Of Large, Expensive Investigator Initiated Proposals

The National Cancer Advisory Board is considering establishing a policy that would require large investigator initiated research proposals (RO1s) to go through a concept review by the board before submission to peer review. The board asked NCI staff to write a policy based on one

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In Brief

Couple Gives $1.1 Mil. To NCI Intramural Research; Kuller Replaces Grufferman At PCI

NCI'S INTRAMURAL research effort has received a gift of $1.1 million from Mr. and Mrs. Gerhard Andlinger of Vero Beach to aid in the development of innovative therapies for the lymphomas. The money will go to Thomas Waldmann's laboratory for studies of anti-TAC antibodies in B and T cell lymphomas; Tito Fojo, Susan Bates, Michael Gottesman, Wyndham Wilson, and Jane Treppel, who have initiated trials of reversal of drug resistance in non-Hodgkin's lymphoma; Dan Longo and the Biological Response Modifiers Program for studies of lymphoma cell death in response to CD-3 antibodies and for investigations of new approaches to autologous bone marrow transplantation; and to Maria Zajac-Kaye and Mary Stetler-Stevenson for work on molecular aspects in diagnosis and detection of residual disease in the lymphomas. . . . **LEWIS KULLER** has been named associate director for the epidemiology and preventive oncology division at Pittsburgh Cancer Institute. Kuller succeeds Seymour Grufferman, who was recently selected professor and chairman of clinical epiidemiology and preventive medicine at the Univ. of Pittsburgh. Kuller is a former member of the Div. of Cancer Prevention & Control Board of Scientific Counselors. . . . **CATHERINE LYONS,** acting director of nursing at Roswell Park Cancer Instititue, has been named director of nursing, ending an extensive national search for "the most qualified person to fill the position," according to Thomas Tomasi, director of Roswell Park. Lyons began her career at Roswell Park in 1975 as staff nurse on the Medical Oncology Service. . . . **GREGORY BURKE** has been named acting director of FDA's reorganized Div. of Oncologic & Pulmonary Drug Products. Radiopharmaceuticals has been moved to another division. Burke has been a medical officer in the division for six and a half years. . . . **JOHN LESHNEY** has been named vice president for development at Hipple Cancer Research Center, a new position in which he will head the center's new development department, responsible for fundraising, community relations, community grant writing, and planned giving programs.

NCAB Considering 'Concept Review' For Large, Costly RO1 Proposals

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in force at the National Heart, Lung & Blood Institute. The policy is to be presented for the board's approval at its May meeting.

NCI Director Samuel Broder introduced the idea at the December board meeting. He asked the board whether NCI should institute an upper funding limit for RO1s. NCI does not have a limit, but any RO1 proposal greater than $1 million a year is brought to the Executive Committee for consideration before the application is sent out for review.

Board members were wary about setting a specific dollar limit over which applications would have to seek concept review. "It's hard to know what is the right number," said Board Chairman David Korn.

However, the large, multicenter trials tend to be costly and long, resulting in a major commitment of funding over many years. "This would give you an early look at those proposals, rather than going through the whole review process and coming up to the board. It would be happier for everyone," Korn said.

Board members indicated that the impetus for such a concept review was the Diet FIT proposal for a large, multicenter trial of the relationship of dietary fat to cancer, lasting 10 years. The proposal went through peer review successfully, but was voted down by the board. On that proposal, "the board acted well within its authority, but whether it could have acted more gracefully is another question," said Korn.

"When we get these very large proposals, they make an initial impact on the RO1 pool and also have an outlay cost," Broder said.

"They may be worth it. But you are decreasing the amount available for other applications for 10 years."

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ISSN 096-3917. Published 48 times a year by The Cancer Letter Inc., also publisher of The Clinical Cancer Letter and AIDS Update.

NCAB member John Durant said that when an investigator-initiated research proposal involves many investigators and many institutions, "it should be a cooperative agreement instead of an RO1."

A policy allowing the board to consider such proposals before peer review would enable NCI to advise the investigator to consider another funding mechanisms, such as the cooperative agreement, or to rewrite the proposal to make it more acceptable, said Div. of Extramural Activities Director Barbara Bynum.

The HLBI policy that the board asked NCI staff to rewrite follows:

"Effective immediately any application for an investigator initiated clinical trial, a demonstration and education research project or a large community based study, expected to be submitted for review under the auspices of the National Heart, Lung & Blood Institute, will undergo concept review prior to initial peer review. The goal of this review is to assess the consonance of the proposed study with the program and fiscal priorities of the Institute. New, renewal, or amended applications requesting less than $400,000 in direct costs (calculated individually or as the total of separate applications participating in the study) in each year, and supplemental applications requesting less than $100,000 in direct costs in each year are exempt from this policy. In addition, NHLBI will routinely consider the need for involvement by the Institute scientific staff in the cited type of projects and therefore the use of the cooperative agreement as the mechanism of support."

Other Institutes within NIH have similar policies, Bynum said. The National Institute of Allergy & Infectious Diseases requires applicants requesting a budget over $1 million in direct costs in any year to have prior written permission from NIAID to submit the application.

In other action at the recent board meeting, Acting NIH Director William Raub discussed the $15 million that Congress appropriated, to be taken out of each of the Institutes, for biomedical construction. After sequestration, the amount is actually $14.8 million, Raub said. He indicated that cancer centers may have a shot at some of the money.

NIH soon will release two RFPs, one for construction of an experimental animal facility, and the other dealing with other types of construction. The main impetus for the funding was the fire last year at the Jackson Laboratory that destroyed the world's premier mouse production facility. However, Congress stipulated that funding for a replacement facility were to be awarded competitively.

The second RFP will be awarded for "other types of

construction such as those identified in the Senate report," Raub said. He was referring to language in the Senate Appropriations Committee report on the needs of cancer centers. He told the NCAB he was aware of the many construction projects NCI had already peer reviewed and approved that were waiting for funding.

"We reported in our recommendations that while one can't make argument that competition for the $14.8 million ought to be a unitary event, and that no allocations should be made until all solicited applications are available, there is a rather strong counterargument that there are some high quality, high performance aircraft already on the runway lacking only fuel," Raub said.

Raub said "it's NIH's decision" on how to split up the $14.8 million between the animal facility and other construction. The Jackson Laboratory has said it needs $25 million to rebuild its facility, and Congressional leaders have said $10 million is the minimum needed for an animal facility. "The way to resolve this is through solicitation of grant applications and let the process determine the amount," Raub said. He noted that Congress wanted the funds to go to areas of "national urgency."

"I can assure you we think funding of cancer centers is over that threshold in terms of national urgency," he said.

Raub also discussed the recent withdrawal of conflict of interest guidelines proposed for NIH grantees. HHS ultimately expects to issue regulation through a notice of proposed rulemaking, but publication of such a notice "still seems premature" until NIH completes its analysis of the more than 700 comments sent in response to the guidelines, he said. NIH may hold another conference on the subject and is considering a series of smaller regional meetings.

Raub defended the need for clear rules covering potential conflicts. "When a privately owned commercial product is the subject of publicly financed research and development, conflicts of interest can arise readily, at least in appearance if not in fact. For example, the principal investigator of an NIH funded clinical trial of a privately owned drug or device most likely would be considered to be in conflict of interest if he or she had a principal financial interest in the organization that manufactures the product.

"The prospect of monetary reward flowing from successful commercialization in that instance could lead to biased interpretation of data, selective reporting of some research results and nondisclosure of others, or falsification or fabrication of records."

Broder as well as several NCAB members noted that the proposed guidelines may have taken too drastic an approach to the problem.

Centers Urged To Apply Soon For Comprehensive Status

NCI is urging cancer centers who plan to apply for comprehensive status to submit applications by June 1 in order to go through peer review in August. In a letter sent this week to cancer center directors, NCI Director Samuel Broder outlined the process for the August review and a second route for review.

Enclosed with the letter were the new guidelines for comprehensive status. "It is important to provide an orderly process of transition" for centers designated as comprehensive during the "previous era," Broder wrote. He outlined that process as follows:

"During the two-year period hat began Jan. 1, 1990, there will be two procedures by which institutions with currently funded Cancer Center Support Grants (CCSG) or with pending CCSG applications, might submit requests for comprehensive designation:

"1. All cancer centers with active or pending CCSGs may submit a request for comprehensive designation through the peer review process according to the guidelines. In order to maintain an equitable separation of the CCSG (P30) review from the review for comprehensiveness, a special meeting of the Cancer Center Support Grant Review Committee (CCS) will be held during August 1990. The deadline for receipt of applications for review at this special meeting of the CCS will be June 1, 1990. If disapproved by the CCS, the center will be asked to cease using the comprehensive designation even if it has had this designation in the past. If approved by the CCS, comprehensive status would be retained for a five year period as long as peer reviewed support of the parent P30 grant remains continuous during that period.

"At least one center has already formally asked for peer review of its request for comprehensive designation under the new criteria, and NCI strongly encourages other centers to take advantage of this peer review opportunity. NCI prefers that institutions seeking comprehensive status utilize this route.

"2. Alternatively, cancer centers with currently funded CCSGs have a one-time opportunity to make a request for an interim designation of comprehensiveness following the instructions in sections 6.2.1. and 6.2.2. of the guidelines. This procedure involves an administrative review as outlined in section 7.3. If the administrative review is

unfavorable, the center director may ask that the request be considered by the CCS. If the subsequent peer review of comprehensiveness is also unfavorable, the center will be asked to cease immediately using the comprehensive designation even if it has had this status in the past. The option for administrative review will end on Dec. 31, 1991. Centers which request and receive an interim designation of comprehensiveness must agree to apply for full peer review under the newly implemented guidelines at the time that the parent P30 grant undergoes recompetition. If renewal application is not successful, a center will not be permitted to use the comprehensive designation in its title or public materials thereafter.

"Please note that after Dec. 31, 1991, NCI will expect that no NCI funded center will use the term 'comprehensive' in its official designation indicating NCI sponsorship unless it has received this through one of the processes described above. Thus, centers which were accorded the comprehensive designation before these new guidelines were issued will be expected to qualify under the guidelines or discontinue using the comprehensive designation.

For assistance in the preparation of the request for comprehensiveness designation, center directors or staff may call Brian Kimes in the Div. of Cancer Biology, Diagnosis & Centers, 301/496-8537, according to the letter.

For further information about the application and review process, centers may call John Meyer in the Div. of Extramural Activities, 301/496-7721. Meyer will be responsible for peer review of the requests.

Center Core Grants Could Face Downward Negotiations Of 20%

Cancer centers whose core grants are being competed this year "face serious downward negotiations," NCI Director Samuel Broder told the Div. of Cancer Treatment Board of Scientific Counselors this week.

Center directors thought the situation was serious last year, when "downward negotiations" (the euphemism for reductions from the peer review approved budget) slashed 15 percent from their grants. This year, the cut "may be as high as 20 percent," Broder said.

That will be for new and competing renewal grants. Noncompeting awards will be cut by 4 percent, Broder said. Those cuts will be in line with the estimates for research project grants (RO1s, PO1s).

"Downward negotiations," Broder said, "is when you ask an investigator how he would like to take a 20 percent cut. He eventually says he would like that, when he learns what the alternative is."

The alternative, if there are no downward negotiations this year and all grants are funded at their recommended levels, would be a reduction of about 200 in the number of grants NCI would award.

These dire predictions assume that Congress will not add anything to NCI's budget, a reasonable assumption given that Congress has not increased NCI's budget over the President's request for the last two years. With deficit reduction sequestration and various taps on the budget, NCI actually received less than the President's request for FY 1990.

Broder will go to the congressional hearings (Feb. 20 in the Senate, March 13 in the House) and defend the President's budget, knowing full well the disaster that would be. If he did not, he would be looking for a new job Feb. 21 or March 14.

It will be up to Cancer Program constituents and supporters to make the case to Congress for a healthy share of the "peace dividend."

In another budget cutting maneuver, Broder announced that NCI had terminated the contract for basic science Cancergrams, the monthly compilation of current literature abstracts NCI has been publishing for more than 10 years. The clinical Cancergrams will be continued.

Broder said that the Cancer Information Service "has been renewed and strengthened." The new contract awards are scheduled to be made this week. Seventeen contracts will be awarded at a cost of $8.8 million a year.

Boyd Steps Down As DTP Director To Return To Full-Time Research

Michael Boyd, who has headed NCI's cancer and AIDS drug development program for the last six years, is giving up his position as director of the Developmental Therapeutics Program to return to full time research.

Boyd and Div. of Cancer Treatment Director Bruce Chabner announced the change at this week's meeting of the DCT Board of Scientific Counselors. Chabner said that DCT Deputy Director Michael Grever would serve as acting director of DTP while a national search for Boyd's replacement is carried out. Chabner said it could take as long as nine months to fill the Senior Executive Service position.

"Mike has done an extraordinary job of setting the course and mustering the resources for the screening program and the natural products effort," Chabner

said. "Without his tenacity and single minded commitment," the new in vitro disease oriented human tumor panel screening system "would not be there. In 1985, he accepted the challenge to set the screening experiments in motion and accomplished this. He was also responsible for a major shift in DTP resources into the National Cooperative Drug Discovery Groups. This program has been accomplished despite a multimillion dollar reduction in the DTP contract budget over the past five years, a credit to his management ability."

Boyd, who said he had intended when he took the job to return to research after one or two years, will concentrate on natural products in DTP's Natural Products Branch at Frederick Cancer Research Facility. "I'm going to enjoy working on implementation of the system we've put together. This last six years has been an incredible challenge."

In addition to overseeing the wrenching, almost revolutionary changes in the program, Boyd had to manage the additional burden of AIDS drug development imposed on DTP. Part of that burden was eventually shifted to the National Institute of Allergy & Infectious Diseases, but NCI retained the anti-HIV screening and preclinical development.

DeVita, Moertel Engage In Debate Over Release Of Levamisole Results

Key participants in NCI's decision last year to release a clinical update on 5-FU/levamisole in the treatment of Dukes C colon cancer entered an at times heated discussion of the chronology of events of that decision in a recent meeting on clinical updates.

The participants were brought together by National Cancer Advisory Board Chairman David Korn to discuss the controversy over NCI's issuance of two clinical updates in the past two years and to attempt to set some ground rules for future communication of research results. The consensus of the meeting was that discussions of whether to issue an update should be initiated and controlled by the principal investigator and that the NCAB should set some general guidelines for those discussions (**The Cancer Letter**, Feb. 9, 1990).

Some of the most heated discussion at the all-day meeting centered around the decision to issue a clinical update on 5-FU/levamisole, based on the results of an intergroup colon cancer adjuvant therapy trial, led by Charles Moertel, chairman of the North Central Cancer Treatment Group. The intergroup study, INT0035, confirmed the results of an earlier NCCTG trial.

Vincent DeVita, physician in chief at Memorial Sloan-Kettering Cancer Center and former NCI director, engaged Moertel and Michael Friedman, associate director of NCI's Cancer Therapy Evaluation Program, in a series of debates throughout the day about when the results of the trials should have been released. NCI Director Samuel Broder, whose final decision it was to issue a clinical update, attended the meeting at the beginning and end of the day, but was not present during the DeVita-Moertel debates.

DeVita began by questioning why the levamisole update was not reviewed by the full NCAB in a public session, as the 1988 clinical alert on adjuvant therapy for node negative breast cancer, which DeVita had issued, had been. The levamisole update was reviewed by Korn, Div. of Cancer Treatment Board of Scientific Counselors Chairman John Niederhuber, as well as the leadership of the American College of Surgeons, the PDQ Editorial Board, the American Society of Clinical Oncology, and principal investigators of the NCCTG INT0035 studies, Friedman said.

Data 'Solid' In 1988, DeVita Asserts

"Those (reviews) are done in private. I'm curious why the process was changed from review by the full board to review by board chairman in private?" DeVita asked.

DeVita also said that in May of 1988, when the breast cancer alert was released, "Chuck Moertel came to my room with a number of other investigators with cooperative groups and reviewed the colon data with me, which was positive at that time. The first study was positive for disease free survival and survival and (the confirmatory study) was tracking exactly on the first study, but not for survival. We talked about whether or not this could be an alert. Certainly the data were very solidly in hand by July of 1988 or September of 1988. We're talking about the issue of what you do in September of 1989. What happened to that entire year of 1988, when you might have been in the position to say you had a positive study, the first one?"

Friedman responded that when an interim analysis of the intergroup study was completed in September of 1989, "that was the first time that the previously agreed to statistical levels were reached. The time from that analysis to the public announcement was one month, and during that one month none of the boards met. It wasn't possible to publicly discuss this. We did the next best thing, which was to show it to representatives of the board, sharing your desire to have this information disseminated as quickly as possible. There simply wasn't a board meeting."

DeVita noted that some data on the colon cancer trials were discussed at a closed session of the NCAB last May. Friedman said the reason for the closed session was "at the time it had potentially important

implications having to do with a company and a product. I had the lawyers look at it because I was concerned about it as well."

"I have no doubt that if you go to a lawyer and try to find a reason for holding a closed session he can give you one," DeVita responded. Throughout the meeting, he pressed for open discussion of whether to issue a clinical update, even if it meant that the press covering the meeting would write about the data. He argued that clinical updates are not meant to inform the public about research results, but to inform physicians that NCI is preparing to inform the public about such results.

During the development of the protocol for the colon trial, Moertel said, investigators recognized that a positive study would result in the need to release data earlier than usual. NCI and the investigators agreed on statistical rules for ending the study early. He noted that DeVita, who was NCI director at the time, agreed to those rules. "Everyone had the opportunity before the fact to have input into these decisions. They were planned for early release in the protocol. Rightfully, Dr. DeVita initiated these types of joint reviews."

Moertel said the investigators notified each patient on the untreated control arm of the study results by phone "long before" the update was issued.

Untreated Control Arms

DeVita brought up the fact that a few months before the NCCTG colon trial results were released, an unrelated intergroup trial of 5-FU plus leucovorin vs. no treatment was just beginning. He asked whether it was ethical to allow the no treatment arm on the leucovorin trial when it was becoming clear that the no treatment arm on the levamisole study would have to be closed.

"My point is you can't split Mike Friedman two ways" (in that the CTEP director knew about both trials), DeVita said.

Friedman said that if he could do it over again, he might have made a different decision. "We did not feel that confident then about the (levamisole) data," he said.

"I felt the data were sufficient, but there was no forum for discussion," DeVita said.

Bernard Fisher, chairman of the National Surgical Adjuvant Breast & Bowel Project, noted that an NSABP protocol for colon cancer comparing MOPP vs. 5-FU/leucovorin eliminated the control arm. "This was selected and approved by NCI and was also made a high priority trial before the other trial--the levamisole study--became known. And yet the levamisole trial was being done using untreated control. This just doesn't add up."

"I don't what doesn't add up," Friedman replied. "If there's imprecise information, if there are multiple 'legitimate' points of view, some investigators feel the answer's in and other investigators looking at exactly the same body of information are unconvinced. All we're saying is that for NCI to take a position when there are legitimate differences in interpretation of the data, (while) waiting for more definitive information to become available, I think you should permit trials of different sorts to proceed, as long as the investigators and the patients understand what the options are."

Moertel 'Wanted To Wait'

DCT Director Bruce Chabner said the question of precisely when to release results is an area in which "the investigator's rights come in conflict with what are perceived to be the rights of the public to know."

"We engaged in a long dialogue with Dr. Moertel about the time for release of the data from his colon trials," Chabner said. He said that in both the breast cancer and the levamisole updates, "we felt in both instances that we should release this information as soon as we and whatever expert advisors we had were sure that the trials had reached an important conclusion. We shouldn't wait for publication. In the most recent instance, Dr. Moertel wanted to wait until the time of publication of the paper."

The actual data from the confirmatory trial "was missing" in the levamisole alert, Chabner said. "You should have all the data available at time of the update," he said.

DeVita said that at the time of the breast cancer alert, "JNCI" offered to publish Fisher's paper in less than two months as an alternative to the alert. Fisher declined the offer and sent the paper to the "New England Journal of Medicine." Had Fisher accepted publication in "JNCI" there would have been no clinical alert, DeVita said.

DeVita said he called "New England Journal" editor Arnold Relman to ask whether a clinical alert would harm publication of the article. "He said his job was to decide whether something was appropriate for publication in the 'New England Journal,' not to decide whether it is an issue of public health. He did not see himself selecting information and expediting publication because it's a public health issue. He said, 'If that's what your advisors think, then you do it and we'll go about our business.'"

DeVita noted some "mistakes" made is issuing the breast cancer alert were corrected in the levamisole update: the breast cancer alert was sent to only 13,000 physicians on PDQ's list, was not sent to

surgeons, and NCI did not hold a press conference to announce the alert because "we wanted to underplay it." Instead, DeVita and others discussed the alert at the ASCO meeting that year.

DeVita offered some advice on issuing an update: "Have the NCAB debate the issue of whether or not this is an issue which should be handled by clinical alert. It would have to be a common disease, probably for which we had no treatment, that would affect many, many people." He said it would have to be a large study with a confirmatory trial, although there could be a time for a disease for which no treatment exists that a single trial might be enough for issuing an update.

"When you do this aren't you in fact giving a clinical alert?" Moertel asked. "If something comes out with a positive result, even though it's debated, even though the debate might be won or lost by one side or another, there is going to be press coverage. You have immediately put it out on the table, physicians are immediately struggling with patients out there who read these news items, coming right from the citadel of cancer, and this has an enormous impact. I just wonder if discussions at a lower level before you hit that press coverage isn't a better way of handling it."

"This wouldn't happen without discussions at a lower level," DeVita responded. "You can't just walk into the NCAB and start a discussion. For example with the breast cancer alert we first went to the NCI Executive Committee, we went to the PDQ Editorial Board, we met with the investigators."

DeVita asserted that federal law requires public discussion in an instance such as this. "I think (press attending the meeting) would report that this was debated by the NCAB and they concluded it was too early for general use. So physicians would have the additional information in their hands. They can tell their patients this board said it wasn't ready yet. If they say it is, then we would assume their judgement was valid and they are intelligent people and it should be disseminated."

Moertel objected to "not telling physicians before it hits the front page of 'The Washington Post.'"

"That's life. We live in this kind of a world," DeVita said.

Moertel's 'Conversion'

When the conference participants began to develop some preliminary guidelines to send to the NCAB (see last week's issue), those opposed to clinical updates launched a last-ditch effort to argue that updates interfere with peer review. Moertel jumped into the discussion to defend clinical updates.

"There is a need for this," he said. "I didn't think I'd ever speak in favor of clinical alerts. I think the question is how are we going to meet the public demand in a careful, cautious, scientific, carefully planned way, or are we going to meet it helter skelter. I was very pleased with the way the last alert was developed. We got this published when we were thoroughly convinced (of the results). We brought this to the public when we were sure. Second, we had planned carefully. I was thoroughly involved, the versions of (the update) went back and forth time after time."

NCAB member John Durant, noting that Moertel had been opposed to releasing the data, asked Moertel, "When did your conversion occur?"

"In our protocol we had written down the criteria for early release was that the p value for survival must be less than .0058," Moertel said. "That was a rule that was set down. When we hit that I said, 'Hey, this is true,' my statisticians said it was true, we collected all the outlying data, there weren't any changes, and I said, 'Yeah, ok, I've got to believe this.'"

Korn noted that with the levamisole update, the investigators made the decision to release the information and found a way to release the alert close to the time of publication. Korn wondered what would have happened if the paper had still been in peer review.

"Chuck's process was great, but there was a lot of serendipity," he said.

'Why Couldn't The Alert Have Come Out Earlier?'

DeVita argued against "hanging with bated breath on peer review. There was no question this article was going to be published. There was no way it was going to be rejected by that journal."

Moertel said the article on the first study was accepted before positive results on the second study began to come in. He noted that preliminary data from the first study were released at the 1986 ASCO meeting.

Then DeVita and Moertel engaged in their most heated exchange.

DeVita: The alert was held up until the article could be published. By what rationale?

Moertel: Because we wished to use this as a vehicle for the alert, so that physicians would have something to read and look at and avoid the previous criticisms where they had nothing to look at. So it was a fortuitous event that in fact this was coming up for publication, because I agreed and we all agreed that we wanted to get that information out there, because it appeared that we were going to have such striking results.

DeVita: Why couldn't the alert have come out earlier?

Moertel: Because we didn't have the information from the confirmatory study earlier.

DeVita: You had that information months before.

Moertel: We did not have it, Vince. We had recurrence data. The protocol that you had approved demanded a certain standard of survival improvement, we had not met that standard and I'll be damned if I was going to approve anything until we met the standard that you had approved, that we had negotiated, for early release of that protocol information.

DeVita: The point is, does one investigator have the right to hold up release of information when a large number of people feel that it is appropriate to release that information? What you're saying is, your desires are overriding in reference to a public health issue.

Moertel: I was not the only investigator, there were representatives from every major cooperative group as well as your statistician, as well as your (NCI's) representative. Your representative as a matter of fact said, 'What the hell is Moertel getting so excited about?' So this was not a single investigator's decision. You had the leading gastrointestinal oncologists in the country sitting on that panel as well as your chosen representative. My individual decision? No, sir. This was a decision made by very thoughtful people, including your representative.

Moertel's 'Moral Force'

After that exchange, Niederhuber concluded that any guideline on clinical updates "ought to say we're not willing to take the initiation of this process out of the hands and the control of the investigator. If we could agree on that, that would be a major accomplishment. While not all investigators are of the stature and caliber of Dr. Moertel, I think Dr. Moertel has demonstrated a moral force. And I'm unwilling to deviate from that."

Chabner said he agreed that the "way things worked out" in the levamisole update were the better than the breast cancer alert. He did not agree that a study must have a survival impact in order to put out an update. Quality of life, or less costly procedures also could merit updates, he said.

In any event, when the decision is made to issue an update, NCI and the investigators should seek expedited publication, and the update should be issued in accordance with the time of publication, Chabner said. However, he wondered what should be done in the case in which an article has been submitted but its publication date is uncertain. Moertel said data from a study could be released "as soon as you have scientifically credible information."

Moertel said he hoped the NCAB's guidelines are "more a message of philosophy" rather than specific rules.

Whatever guidelines the NCAB eventually comes up with, there is no doubt the levamisole update had an effect. When the drug was approved for Group C status last May, there were few requests for the drug, but more requests for information, Friedman said. After the update was issued in October, requests for the drug soared, he said.

Between last May and mid-January, there were 6,966 physician inquiries about levamisole, 937 protocol requests, and 1,495 patients registered on the Group C protocol, Friedman said.

"We're probably capturing 25 to 30 percent of all Dukes C patients available in the U.S., which is rather remarkable," he said.

The treatment is recommended for patients whose tumors were removed within five weeks of seeking adjuvant therapy, but NCI made exceptions for 635 patients who had surgery seven or eight weeks before seeking adjuvant treatment, allowing those patients to receive levamisole.

RFPs Available

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

NCI-CO-03879

Title: Booklet printing

Deadline: Approximately March 26

Single award for a fixed price contract for delivery 60 days after award of contract. Production area, assumed 125 mile radius of zero milestone, Washington, D.C. Bidders outside area must furnish documentation of their ability to meet schedule. Inspection of source materials will be from March 8-9, 8 a.m.-5 p.m., at NIH Bldg 31 Room 10A30, 9000 Rockville Pike, Bethesda, MD. For an appointment contact Erin Lange one week prior to source review. Booklet, 202,700 copies of 12 pages with separate wraparound cover. Printed in four color process and black ink or additional color ink. Operations include saddle stitch, trim, printing, folding, negatives, packaging, mailing and f.o.b. destination to Columbia, MD. Contractor will furnish paper. Quality attributes level 1 for printing and level 2 for finishing. Bid request on standard form 26. Telephone, telegraph, fax request not acceptable.

Contract Specialist: Erin Lange
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301/496-8628