THE CANCER LETTER

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CCIRC OKAYS NEW EFFORT TO RATE DISEASE COMMITTEES, MODALITIES IN GROUPS, EFFECTIVE WITH NEXT ROUND

A major "change in the way we do business" was approved by the Cancer Clinical Investigation Review Committee at its meeting this month to be implemented with the next round of review at the committee's meeting in February.

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In Brief

NCAB GOES ALONG WITH NCI STAFF IN FUNDING EORTC STATISTICAL CENTER GRANT OUT OF PRIORITY SEQUENCE

NATIONAL CANCER Advisory Board agreed with NCI staff's recommendation to pay out of priority sequence a grant to the EORTC for partial support of a statistical center required for the group's clinical trials. The Cancer Clinical Investigation Review Committee had approved the grant on a split vote but at a score which left funding in doubt. "The committee should remember that a split vote permits others to fool around with what we do," committee member Clara Bloomfield said. A split vote earlier this year allowed the NCAB to add a year to the committee's decision to "phase out" the Northern California Oncology Group, thus giving NCOG a better shot at being renewed when it will be reviewed by the new study section organized to review regional and site specific cooperative groups. . . . **JOHN BATSAKIS** has been appointed head of the Dept. of Pathology at M.D. Anderson Hospital. He replaces **FREDERICK BECKER**, now vice president for research. Batsakis has been pathology chairman at Maine Medical Center. . . . **FOUR PHYSICIANS** and scientists were honored by M.D. Anderson at last week's "Cancer 1981/Cancer 2001" symposium—**JOHN FOWLER**, director of Gray Laboratory, U.K., who received the 16th annual Heath Memorial Award; **EMIL FREIREICH**, head of M.D. Anderson's Dept. of Developmental Therapeutics, who received the sixth annual Jeffrey A. Gottlieb Memorial Award; **ALLAN CORMACK**, physics professor at Tufts Univ. who delivered the 1981 Mike Hogg Lecture; and **ROBERT SCULLY**, pathology professor at Harvard, who received the fifth annual Joanne Vandenberge Hill Award. . . . **CASEIN IMPORT** restrictions would severely impair the quality of medical nutritionals, Susan Calvert of Ross Laboratories testified last week at an International Trade Commission hearing on limiting casein imports. She said casein is an essential ingredient in medical nutritionals because of its high quality protein. . . . **AMERICAN CANCER** Society outgoing President Edward Scanlon said at the Society's annual meeting that its program started in 1976 to reduce the number of adult smokers in the country by 25 percent and number of teenage smokers by 50 percent is slightly more than half way toward those goals. "We've built a momentum that will carry us the rest of the way," Scanlon said.

NEW CCIRC PROCEDURE TO RATE DISEASE COMMITTEES, MODALITIES IN GROUPS

(Continued from page 1)

The change will require the CCIRC to rate each disease committee and modality within a cooperative group as "strong," "average," or "weak." This will be in addition to the overall rating of the group.

"A lot of us have been frustrated, both staff and reviewers, by going through this elaborate review and then in the end the only decision we can make is go or no go on a group as a whole," CCIRC Executive Secretary Dorothy Macfarlane said. "We hope to ease that frustration a little, and give you the feeling that you can be a little more specific."

The ratings by disease committee and modality "will allow some comparative evaluation of the scientific efforts of committees within a group and across group lines," Macfarlane said.

"By doing so, can we cut out some portions of groups and reshape their nature?" asked CCIRC member Clara Bloomfield.

"That will be for program staff (Div. of Cancer Treatment Clinical Investigations Branch) to consider," Macfarlane answered.

"Instead of having staff do scientific review, we retain the prerogative of doing scientific review," CCIRC Chairman Joseph Simone added.

"This will have broad ramifications, and we have to be careful how we use it," Bloomfield said. "I can see how easy it would be to choose two people for a site visit who are real bastards, who would be excessively critical of the job being done in one area because it does not suit their biases. This should be applied only to future reviews, when it can be known in advance, and you can structure review teams accordingly. . . . This will be okay, prospectively. It would be very dangerous, retrospectively. This makes a difference in writing the grants."

"You will be forced to look at each disease committee and say if it is weak or strong," Macfarlane said.

"This will require the CCIRC as a whole to become familiar with the protocols of each group," member Roy Weiner said. "Therein lies the science."

Weiner added that "in order to make any sort of judgment that can be translated to funding, we have to know the percentage of funds allocated to each committee. It doesn't affect funding as we sit on this committee, but turn it over to staff and they make the funding decisions."

"I would get violent about using this retrospectively," Bloomfield insisted. "This would be changing the rules after the fact. That's something you could take to court."

Edwin Jacobs, associate chief of the Clinical Investigations Branch, said that the new policy would not affect the total funding of a group. "What happens now is, one or two people on a site visit write statements about a disease committee. Not one word is changed when that goes onto the pink sheet. We would like to see some deliberations about the disease committee, and a consensus of the study section."

CCIRC member Harvey Preisler said, "It is inconceivable that this information would not be used to determine funding. This system will force groups to improve or drop inadequate committees, and not let them slip through on the overall strength of the groups. This is a good approach and should start when we get the information."

"It should start with the next site visit," CCIRC member Robert Lindberg said.

"What you are saying is that groups no longer should be all things to all people," Weiner said. "That's a big improvement."

CIB Chief William DeWys said, "If we get a big percentage cut in the Institute's budget from Congress, as it now stands, we would have to make cuts across the board. This new procedure will permit some qualitative analysis. What we want is simply some quantitative assessment of the science."

"Bill's point is my greatest fear," Weiner said. "If we do make a semiquantitative assessment, staff will start making funding decisions based on patient accrual."

CCIRC member Joseph Eggleston tried to summarize the discussion. "What we are saying is, site visitors are now giving their opinions. This goes all the way to staff without modification by the CCIRC. Staff is asking that, if budget cuts come, will this committee take responsibility for (applying the cuts to the groups). If cuts are made, staff needs guidelines and is asking this committee to help."

"Cuts have been made anyway," Bloomfield said.

"And you have been the most outspoken against them," Eggleston responded.

"That's right," Bloomfield said. "You have to have the information at the site visit level. That information needs to be assessed. But this is not a process for something that is already done. I would rather see cuts across the board than changes now which could substantially change the nature of the groups."

"There is a reality factor," CCIRC member Harold Maurer said. "The folks who are making budget decisions need input from this group. If we don't provide it, others will make the decisions. Decisions will be made with or without our help."

"It should be obvious," committee member Laurence Baker said. "We're really talking about how we'll review CALGB. That's a major component of this discussion. Let's put it out there."

[Cancer & Leukemia Group B was one of four groups up for review at that meeting of the CCIRC, along with the Pediatric Oncology Group, Wilm's Tumor Study Group, and Ewing's Intergroup Study.]

"We're facing a difficult situation," DeWys said. "In the past, budgets were increasing. Now we're facing a possible budget cut. . . . Yes, CALGB is on the line at this meeting."

Simone attempted to wrap up the discussion. "The sense of the committee is that this has been sprung on us in too short a time, that we not institute it with this meeting but do so with the next meeting. In the meantime, we will inform the groups of the new rules. We will do the best we can with those being reviewed at this meeting. In case this does have influence on how grant applications are put together and how site visits will be conducted, we have to bend over backwards to be fair. . . . If we institute this procedure, semiquantitative judgments would be made on disease committees and modalities by this group."

After a discussion on asking for budget breakdowns in grant applications, Simone said, "I hear the group saying we would like for justification for, quote, scientific input and patient accrual. We should inform grant writers it is important to justify along those lines."

"Staff is asking for greater literal input, ammunition on which to base judgments. The better the information, the better the judgments will be," Dennis Cain, chief of the Grants Review Branch, said.

ORGAN SITE PROGRAM FATE ON LINE, REVIEW SCHEDULED FOR NEXT WEEK

Two scientists have been added to the ad hoc committee which will conduct the comparative review next week of the four organ site projects which make up the Organ Site Program.

Harry Grabstold, professor and chief of oncology, Div. of Urology, at the Univ. of Florida; and John Bailar, epidemiologist, former editor of the *Journal of NCI,* and presently senior science adviser in the Epidemiology Branch of the Environmental Protection Agency, were appointed after the original list of committee members was criticized because it did not include an epidemiologist or a urologist.

The review, all in closed meetings, will start Nov. 22 and conclude Nov. 25. Edward Copeland, chairman of the Large Bowel Cancer Project, and Gerald Murphy, chairman of the Prostate Cancer Project, will make their presentations Nov. 23. Gilbert Friedell, chairman of the Bladder Cancer Project, and Isadore Cohn, chairman of the Pancreas Cancer Project, will present Nov. 24. Executive sessions will be conducted each day and the reviewers will write up their recommendations Nov. 25.

Robert Handschumacher, Yale professor, is chairman of the committee. Other members are Stewart Sell, professor of Pathology at the Univ. of California (San Diego); Edward Bresnick, professor of biochemistry and carcinogenesis at the Univ. of Vermont; Anna Barker, senior research immunologist at Battelle Columbus; Albert Owens, director of the Johns Hopkins Oncology Center; Ralph Scott, director of the Radiotherapy Heath Science Center at the Univ. of Louisville; and Jerome DeCosse, chief of surgery at Memorial Sloan-Kettering Cancer Center.

The comparative review of the four projects was requested by the National Cancer Advisory Board after NCI Director Vincent DeVita suggested that some or all of the projects might be reduced or phased out for one of three reasons: Budget cuts which might make it necessary to eliminate some ongoing programs; achievement of project objectives; lack of progress or high quality science.

The NCAB has resisted previous efforts to drop the Organ Site Program, has staunchly defended it, and has suggested that consideration be given to adding new projects, including one for lung cancer.

This time, the Board's Organ Site Subcommittee recommended that a comparative review be done, by a group of scientists not presently NCAB members and without any present or prior affiliation with one of the projects.

Subcommittee Chairman William Powers said at the group's last meeting that the reviewers would be asked to assess the scientific merit of the activities in each project, including their broad communication activities to convey findings, coordinate studies and eliminate duplication.

Subcommittee members immediately questioned the lack of a urologist or an epidemiologist on the review group.

"There are three clinicians, and I assume they are knowledgeable," Mary Fink, who will be executive secretary of the review group, said.

"The problem is that if we get people who know something about it, they're already involved," NCAB Chairman Henry Pitot commented.

"This is set up for a catastrophe," NCAB member Harold Amos said. "We have to have people who know something about the organ sites."

Board member Philippe Shubik suggested questions the review group should ask. "Are objectives of these programs being achieved? Are those objectives additive to something being achieved through the regular study sections? Are they doing something not being done before?"

"Do we have to have experts?" Fink asked. "Can't objective, intelligent scientists provide those answers without being experts in those fields?"

"No," Shubik answered.

Amos asked Powers what was meant by comparative review.

"Is one better than the other," Powers answered.

Barbara Bynum, director of the Div. of Extramural Activities, asked if subcommittee members "feel this could better be done if the panel were augmented to include more people more in touch with these programs?"

Amos and Shubik both replied in the affirmative,

and Shubik insisted that an epidemiologist be included.

"That may be getting away from objectivity," Fink said. "If we include people who are experts in these fields. Experts in bladder cancer or colon cancer are going to argue for those programs."

Board member Robert Hickey said, "I feel strongly these four projects should have as peer reviewers people knowledgeable in those fields."

Fink and DEA Deputy Director William Walters asked for a restatement of the review group's charge. Amos responded, "First, we are asking the committee to critique objectives of each project. To what extent are those objectives still viable? To what extent have those objectives been met? Second, to what extent have they attracted investigators into their fields. Third, has the overall science been unique to the Organ Site Program, or would it have been done in other mechanisms? Could it be done better now in other mechanisms?"

The review group will present its answers to those questions to the subcommittee, which will develop recommendations to the Board. The fate of some of the groups, or the entire Organ Site Program, is on the line.

HEARINGS FIND DIFFERENCES AT FDA BETWEEN EXECUTIVES, MIDLEVEL STAFF

The sharp division between senior executives of the Food & Drug Administration and a few midlevel staff members surfaced during the hearings conducted by Sen. Paula Hawkins (R.-Fla) on NCI's Drug Development Program.

The dissenters, headed by Robert S.K. Young, charged that NCI is violating various regulations and has not been cooperating with FDA. The agency's senior executives—namely Commissioner Arthur Hayes and Bureau of Drugs Director Richard Crout—deny serious violations have occurred and contend that the two agencies are working well together.

Young and his friends deal with situations which arise any time a regulator leans on a regulatee. Hayes and Crout see the broader picture, in which NCI and FDA have worked out a series of agreements dealing with policy matters.

Those determined to find fault with NCI choose to believe Young and his friends despite the fact that many of their complaints were unfounded, others have resulted in corrective action, and still others fly in the face of the best scientific advice offered to the two agencies.

FDA career scientists, medical officers and investigators consider themselves dedicated to the ideal of protecting the public from unsafe and ineffective drugs while at the same time helping to guide the development of new, safe, and effective medicines. But is idealism a front for job security? Many of those, in and outside the Cancer Program, who have to deal with FDA, feel that the agency's staff members will do anything to avoid sticking their necks out and approve a new drug.

Rebecca Wood, an FDA supervisory chemist, was one of the midlevel staff members subpoened by Hawkins to testify.

"We are finding it difficult to get the best quality of scientific review of data submitted," Wood said. "There is an effort to compromise review."

"By whom?" Sen. Edward Kennedy asked.

"By FDA management under the guise of speeding up the drug development process. We'll lose our scientific staff if this continues."

Hawkins asked if FDA "upper management" overrules decisions of the agency's scientists, but Wood said she had not heard of that happening. Wood did describe an incident in which NCI had complained to Crout about too much interference from FDA. "We did not stop any studies. We just wanted more information to help them," she said.

"Have you ever been accused of overregulation by industry?" Hawkins asked.

"Yes. That's a chronic complaint," Wood said.

FDA has the same number of chemists it had eight years ago despite a huge increase in the workload, Wood said. "It would be tolerable if at the same time we were not subjected to pressure to compromise reviews and approve everything as fast as we can without thorough review."

That testimony was given Nov. 3. Crout was not present then, but he was on the panel testifying Nov. 6. Hawkins asked him about the pressures on Wood.

"It is true, she's under pressure because of delays on reviews. She has a bigger backlog than any other chemist. Her supervisors feel her group is not performing very well. She would be hard pressed to document that science is being compromised."

Hawkins said that Wood had phoned one of the committee staff members the previous night, describing a conference she had had with Crout that day concerning her testimony, and contending that Crout had "intimidated" her.

"Were you critical of her yesterday?" Hawkins asked.

"I was critical of her point of view as it was reported in the newspaper," Crout answered.

"Was she intimidated after meeting with you?"

"She may have felt that way," Crout answered. "That testimony does not represent my point of view."

Kennedy took Crout to task for criticizing an employee on the basis of newspaper reports rather than the transcript. Crout said he had not had the opportunity to get a transcript and that he felt he had to be prepared for his own testimony. "She had given that report and I had to deal with it today. It was not an unfriendly meeting."

"She does feel intimidated," Hawkins said. "We

have her affidavit saying she does."

"What do you think is a reasonable approach?" Crout asked. "These are people I work with every day, I know on a first name basis. I sat down with someone and discussed what went on."

"Your talking to her had an intimidating effect and I don't appreciate it," Hawkins insisted.

"I've faced that accusation before," Crout said. "I must tell you I've tried to maintain communications with my staff. I don't believe you don't want a man to deal effectively with his employees. Dr. Wood gave an impression in her testimony that she is under pressure to compromise science. She is under pressure to get the work done. I had to discuss that with her. It's not I who needs a lecture from you."

FDA pharmacologist David Richman denied in a statement prepared for the hearing that the agency's staff is unreasonable in regulating development of new anticancer drugs.

Richman contended that FDA has been flexible in accepting NCI guidelines and that reports "in certain elements of the press" on the new toxicity guidelines debate were "distortions of FDA positions." He insisted he is "an ardent supporter of NCI, its programs and its goals."

Richman said he would "rethink my position regarding preclinical requirements should hard data, rather than rhetoric, be forthcoming" regarding the therapeutic value of phase 1 trials. If 9.5 percent, "or any percentage near that amount of phase 1 patients are substantially benefitting from chemotherapy . . . then I would be here urging the most minimal animal studies prior to clinical trial."

NCI Director Vincent DeVita said at the recent President's Cancer Panel meeting and again at the Waxman/Gore hearing that a survey of phase 1 studies conducted over the past 18 months had revealed that of more than 1,400 patients involved, drug related deaths were reported in 43, about three percent, and that responses had been observed in 9.5 percent.

Charles Young, chief of developmental chemotherapy at Memorial Sloan-Kettering Cancer Center, told Hawkins that in the center's phase 1 studies involving 929 nonleukemic adults since 1976, objective antitumor effect was seen in 11.4 percent, including 30 complete or partial remissions, with only .97 percent drug related deaths.

SCIENTISTS DEFEND NCI, BLAST POST SERIES AS INACCURATE, DISTORTED

The Hawkins hearings provided an opportunity for several scientists to not only defend NCI and the Drug Development Program but also to express displeasure over the *Washington Post* series which painted a distorted and inaccurate picture of clinical tests of new drugs.

John Durant, director of the Univ. of Alabama Comprehensive Cancer Center, addressed two contentions in the Post articles, that phase 1 tests produce too few responses and too much toxicity.

"Because of FDA rules, these drugs must be started at doses so low that responses cannot be expected and toxicity is rare. Thus response rates in these studies are always lower than would be expected if all patients were treated with full doses. Many of us would like to start with higher but still safe doses that might produce more responses. . . . The toxicity of treatment is acute, dramatic, and usually transient. The benefit is substantial, enduring, and continues to increase as noted in the recent *Newsweek* article of Nov. 2. It is this substantial benefit which clearly supports the current process."

Durant submitted a letter to the subcommittee from his wife, Marlene, who received adriamycin, cytoxan and radiation following mastectomy last year. She described "the terribly hard" side effects but said "they were worth the chance of living."

John Speer, Penrose Cancer Hospital, Colorado Springs, said, "The recent series of articles in the Washington Post were seriously damaging to our efforts. They were grossly inadequate in covering the present status of cancer therapeutic research with new chemotherapy drugs. They were inaccurate in meaning, inaccurate in context and significant "factual" information was inaccurate. Nonetheless, many patients will believe what they have read possibly resulting in a decision not to seek treatment. It will certainly require much additional time and effort on my part and on the part of all other cancer specialists to dispel this new wave of suspicion which is not needed among those patients who do decide to come to us. Instead of dwelling on 620 patients who died of "toxicity" it should have been pointed out that somewhere in the neighborhood of 50,000 patients have probably been cured as a result of receiving chemotherapy."

Charles Young of Memorial Sloan-Kettering disputed the Post's contention that phase 1 trials have no therapeutic intent. "I find that proposition unacceptable and unrealistic. I could not offer or administer a drug to a patient if I had no hope that that specific individual could benefit thereby. I believe that the vast majority of my colleagues . . . are of this opinion and act in this manner. . . . Those new drugs with strong laboratory credentials for therapeutic benefit and promising results in clinical trials outside the United States are highly sought after by multiple centers. Protocol design that minimizes the likelihood of individual patient benefit is scrupulously avoided. Observations with regard to possible therapeutic effects are pursued assiduously in all phases of drug study."

Young said that NCI "has played and continues to play an absolutely vital role (in drug development). It provides the vast majority of research funds; it pro-

vides the majority of new drugs; it provides essential leadership and guidance. It provdes the means and mechanisms by which we have formed ourselves into a research community. At the level of clinical trials the staff of NCI are effective colleagues. Without being restrictive to our creativity they have greatly enhanced the precision and the research quality of our protocol design. . . . I have found them prompt to report possible unexpected drug toxicity."

Charles LeMaistre, president of the Univ. of Texas System Cancer Center, advised the senators to read the Newsweek article. "In contrast to a number of distorted explanations of how new anticancer drugs are developed, (that article) does a superb job of summarizing progress made in recent years in the field of cancer chemotherapy."

Newsweek, incidentally, is published by the Washington Post Co.

Durant's prepared testimony included a copy of a letter to the Post from Charles Vogel, clinical director of the Florida Comprehensive Cancer Center. Vogel and some of the patients at the center were featured in one of the Post articles.

The letter, which details a number of serious inaccuracies in the article, has never been published by the Post. Excerpts follow:

The Washington Post story dealing with patients treated at the Comprehensive Cancer Center for the State of Florida, while largely factual, is written with considerable negative bias and omission of critical points which alter circumstances as they actually occurred. The statements and facts were taken out of context and crucial words omitted so that misinformation was conveyed to your readers.

Before addressing individual inconsistencies, the obvious negative bias of the reporters is deserving of comment. This issue has been adequately addressed by Dr. DeVita in his letters to you and by Tom Brokaw in his recent television interview with the reporters. Additional emphasis on this unfortunate negative bias deserves repetition. Although it is true that no patient in the IMPY phase 1 study done at the Univ. of Miami had an objective antitumor response as rigidly defined in the protocol, our publication in *Cancer Treatment Reports,* Vol. 64: page 1153, 1980, clearly states that two patients had clinically useful improvements. One patient with lung cancer had an improved appetite and a 16 pound weight gain with a period of disease control lasting for six and one half months, directly attributable to treatment with IMPY. A second patient with a surgically unresectable cancer in the head and neck region had enough improvement and shrinkage in his tumor to allow for surgical excision that improved his performance status and quality of life for many months. While the authors commented on some of the patients receiving another investigational drug, ICRF-187, who had appeared to benefit little from the drug, no mention at all is made of another patient with malignant melanoma who did have an objective response to treatment and, indeed, has been maintained on treatment with continuing disease control for almost one year, with minimal drug-induced toxicity. Since the authors have chosen to include aminoglutethimide and provera as investigational drugs (although they have been widely used for two years) one might wonder why they focus on two patients (one of whom may have had a toxic reaction to these drugs) when the literature is replete with scores of patients who have had objective antitumor responses, prolongation of life, and relief of symptoms from these drugs when used in the managements of breast cancer.

In almost all of the clinical histories related by the authors, major omissions of information have probably already led to inappropriate bias. Because consent for the use of patient names was approved by the patient or family members and because your reporters have already mentioned them, I shall refer to the case histories by name. In the case of Jerry McClennan, the authors refer to a symptom complex occurring on Jan. 22, in vivid and graphic detail. What they fail to make note of is the fact that no such reaction occurred on his two previous doses of drug and none occurred during his last dose of drug on Jan. 29. The principal investigator of study was informed of the reaction and during the next administration the patient was watched closely for any signs of acute toxicity and there were none. It is possible that this reaction was related to the rate of drug infusion; however, this type of reaction has never been seen in any other patient treated with this drug at our institution, and, as previously stated, was encountered only once in Mr. McClennan's use. It is also of interest to note, that in spite of Mr. McClennan's apparently adverse reaction to this investigational drug he subsequently elected to receive still another investigational drug, mitoxantrone, at a later date.

In the case of Harvey Mottaz the investigational drug had indeed caused an objective antitumor response and with no nausea, vomiting, or bone marrow suppression. The patient had a very large tumor on the side of his face causing severe pain. After only one dose of drug the tumor size dramatically decreased and the pain virtually disappeared. This response, although impressive was of short duration and he was considered to have had progressive disease after a total of 69 days. The patient's attending physician, Dr. Mario Eisenberger, clearly recalls the objective and subjective benefits to the patient even though it was for a brief period of time. What the reporters stress, however, is their first visit to Mr. Mottaz on Jan. 15, 1981, where they state that "the day before he had been given more chemotherapy" (possibly implying some other investigational drug). At that time Mr. Mottaz had progressive disease and was starting to recover from acute toxicity of cisplatin, a standard drug in the management of head and neck cancer, and not an investigational drug. It is indeed ironic that just the preceeding day the authors had commented on cisplatin as a "success story," yet it was this standard drug and not an investigational drug that had caused the toxicity that the reporters decry. The quotations attributed to the patient's wife are also misleading because they do not refer specifically to the investigational drug. Our medical records clearly show that Mr. Mottaz developed no significant toxicity from the drug other than the hair loss and specifically no nausea or vomiting. The comment by the intern, Dr. Feldman, unfortunately is typical of the reaction of many young physicians and lay people alike about chemotherapy in general. His comments were fittingly dramatic and graphic for inclusion in an article with the very bias the authors were trying graphically to emphasize.

In discussing Margaretha Gaylord the authors once again neglected to mention the fact that while the drug did not stop the inexorable down hill course of her cancer it also did not cause any significant toxicity to the patient. Her death was clearly related to disease progression in the brain and not to any toxicities attributable to the drug.

In the case of Annie Laurie the extent of bone disease secondary to breast cancer was one of the most severe I had ever seen. In a telephone conversation with the patient's son, Mark, on Oct. 23, 1981, he recalls that she had already been told by her oncologist in West Palm Beach that he had nothing more to offer. The patient had a zest for life, a fear of death, and a desire to try anything that could stem the course of her

cancer. She had been suffering from severe bone pain and had received so much x-ray therapy to relieve that pain that further chemotherapy was out of the question because of compromised bone marrow function. Although the patient had not had a definite response to several previous forms of hormonal therapy she had had transient improvement of pain on estrogens, suggesting some possibility of hormonal sensitivity of the tumor. Aminoglutethimide was a logical treatment to try. This drug was considered by many oncologists, even at that time, more as a "standard" therapy, although it had not yet officially been released for commercial use. It is now available commercially, testifying to its widespread efficacy in the management of breast cancer. The quotation "But I never considered going off it. This went on for four months.... Why? Because the doctor said it takes that long to find out if it works" implies that we were keeping her on an investigational drug to gain scientific information perhaps at the expense of the patient's well being. In fact, we were the only people in Florida with ready access to this investigational drug which we were making available to qualified oncologists more as a humanitarian gesture than any scientific study. An informed consent form had to be signed because the drug was "investigational," however, she was not part of any cancer center study aimed at future publication or scientific aggrandizement of the center. As for her and her daughter's recollection of the side effects of the drug the medical record has a somewhat different account. The patient was begun on the drug on Aug. 21, 1980, and over the next four months traveled with her family to Acapulco, the Bahamas, and Jamaica. Medical records document that she benefitted by having decreased bone pain although she was suffering from depression. At a six week evaluation x-rays were also found to be stable. In the face of stable disease on x-ray and decreasing bone pain, a further six week trial was recommended and accepted by the patient. It was we who told the patient that some of her symptoms of depression might have been due to the drug. Yet it remains equally possible, as her son Mark now relates, that she was becoming depressed because she sensed the end was near and that she was going to die. . . .

On reading the authors' statements about Annie Laurie's recollections of her treatments I personally was hurt and my staff was deeply concerned because the article implies an impersonal rendering of investigational treatment. What she actually received was a very personal brand of medicine with drugs of considerable promise given in a humanitarian and not truly investigative setting. Having concerns about our doctor-patient relationship, I called Mark Laurie and asked him for his impressions of his mother's feeling about the care rendered at the center. His quotation was "she loved you guys down there." Does the casual reader carry that away from your author's version?

In the section on "The Director," two studied omissions have potentially dangerous implications. First [the article quoting Vogel as saying] "I would kill myself" leaves out all of the provisos. . . . far advanced disease, intractable pain, or other incapacitating symptoms in addition to the stated proviso of "lack of effective standard therapies," it it my recollection that I said, "I might consider suicide" in such a setting. In the paragraph stating "Vogel said" the omission of the phrase "Phase 1 drugs" leads the reader to the erroneous conclusion that Dr. Vogel feels that all drugs have a very low chance of success which is clearly not the case since chemotherapy is curative for a number of cancers as attested to by Dr. DeVita's previous comments.

Finally, several paragraphs on protocol conformity and recording errors imply widespread and frequent inconsistencies. A review of those allegations is underway and to date a few inconsistencies have been found, but these are isolated and sporadic. In the ICRF-187 study, which is being carefully monitored by NCI and G.H. Besselaar Associates, the compliance rating of the center with protocol requirements stands among the highest of all centers being monitored (third out of 50 monitored). I believe that the IMPY data have the same degree of protocol conformity and that the conclusions drawn were justified by the data and methods used.

The authors Ted Gup and Jonathan Neumann came to our center as wolves in sheeps' clothing. They questioned me and my staff about the pressures in the emotionally trying profession we had chosen. They were "sympathetic" with "burnout" among nursing personnel dealing day in and day out with cancer patients. They saw at first hand the loving care that was given to our patients whether they were on investigational drugs or standard therapies. Yet, none of this was dealt with except in the very briefest passing statements leaving the overall impression in the minds of most readers who have contacted me, of a heartless, soullesss group of diabolical "investigators."

Ted Gup and Jonathan Neumann have done cancer research and the dedicated people involved in it considerable harm and have put me and my already physically and emotionally depleted staff under dramatically increased stress. We feel deceived and disappointed that they could write such a story with such a negative bias after seeing clinical cancer research at first hand, essentially censoring most of its positive features.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs to the individual named, the Blair Building room number shown, National Cancer Institute, 8300 Colesville Rd., Silver Spring, Md. 20910. RFP announcements from other agencies reported here will include the complete mailing address at the end of each.

RFP NCI-CP-FS-21019-65

Title: *Tracing individuals for environmental epidemiologic studies on cancer*

Deadline: *Dec. 23*

Under the Field Studies & Statistics Program, Div. of Cancer Cause & Prevention, NCI, studies are conducted to define the distribution and determinants of cancer in man. Study data have been obtained from hospitals, clinics, unions, and federal, state, local, and other institutions. Subjects may have had suspect carcinogenic chemical, drug, food, or radiation exposures. Many studies require locating subjects to determine current vital status (dead or alive), and last known or current address if living, with accompanying date. It is crucial to locate a maximum number of persons (at least 90 percent) originally identified for study.

NCI plans to award master agreements to multiple organizations whose past experience and success in tracing individuals would be advantageous in locating persons identified in epidemiologic studies

The general objective of these support contracts is to locate study subjects by application of specific tracing tasks sequentially. The subjects may be (a) those whose vital status is not presently known, i.e.,

whether they are alive or dead, in which case vital status should be determined, or (b) those living for whom addresses are to be determined. If the subject has died, the contractor must provide the exact date of death and town or city and state where death occurred. There will be various categories of positive tracing results, such as "definite finds," or "possible finds," or only a new address, but all efforts should be targeted to "definite finds." The NCI project officers will follow up the subjects found.

This RFP will solicit a pool of organizations with pertinent successful experience and capabilities to car carry out certain tracing tasks. A master agreement will be signed with each selected organization, which will then compete for task orders to follow.

Respondents may be located anywhere in the United States. There will be five distinct categories of tracing tasks and separate costs for each. Eligible respondents may apply to use one or more of these tasks in connection with particular study cohorts to be described in the task orders. The five tracing tasks are: (1) tracing by use of credit bureaus, (2) tracing by use of motor vehicle bureaus, (3) tracing by use of vital statistics records, (4) tracing by use of publicly available directories and lists, and (5) tracing by use of other resources, after all the other tasks have yielded negative results. Respondents may reply to one or more of these tasks, but separate proposals must be submitted for each.

No government personnel may be contacted in connection with this announcement except for the individual named below.

Contracting Officer: Sydney Jones
RCB, Blair Bldg. Rm. 128A
301-427-8888

RFP N01-CP-15810-72

Title: *Biochemical pharmacological and tumorigenic studies on a composite of drinking water carcinogens and mutagens utilizing aquatic animals as a bioassay animal*

Deadline: *Jan. 14, 1982*

The Office of Environmental Cancer of NCI is interested in receiving four year proposals in conjunction with a project on collaboration with the Environmental Protection Agency to investigate experimentally the carcinogenic activity of a mixture of organic contaminants in the municipal drinking water supplies.

The primary goal specifies the use of fish (finfish) as a bioassay model to test for the response of small or aquarium type fish to a mixture of at least six organic biorefractories (contaminants) in drinking water and comparing the biological response (carcinogenicity) to aquatic animals in contaminant free purified water.

The type of fish envisioned are cyprinodon, guppies, zebra, rivulus rivulus, medaka and fundulus. Large numbers of test animals are contemplated and several dose levels are anticipated for long term exposure and testing. Evaluation for carcinogenicity will be conducted using statistical procedures based on test groups and a control or reference group of animals not challenged with water contaminants.

Histopathological confirmation of neoplastic and nonneoplastic lesions will be made.

The project has three goals as follows: 1) establishment of carcinogenic properties of drinking water contaminants, 2) demonstration of the fish as a suitable carcinogenic bioassay animal model, and 3) implementation of a bioassay project where significant chemical mixtures can be tested expeditiously and relatively economically.

Contract Specialist: Jackie Matthews
RCB, Blair Bldg. Rm. 2A07
301-427-8771

SOURCES SOUGHT

Title: *Specific physician referral letter mailing services*

Deadline for statement of qualifications: *Nov. 27*

The contractor shall be responsible for periodically mailing letters to physicians across the country in an effort for NCI to successfully solicit referral of patients with specific types of cancer. In order to successfully perform the required services, the contractor must: 1. Secure and maintain the most current American Medical Assn. (AMA) listing of practicing physicians, by specialty, throughout the United States. 2. Have the capability to mail (first class) 20-25,000 referral letters per order within 10 calendar days after receipt. 3. Obtain a license which will grant authority to imprint government envelopes with company permit number.

Responses should not include cost or pricing information. Concise responses directed specifically to the requirements mentioned above are requested. Send an original and two copies of responses to address below.

National Institutes of Health
Procurement Branch, Negotiated Contracts Sec.
Attn: Jody Crowley, Bldg. 31, Rm. 3C25
Bethesda, Md. 20205
301-496-4281

The Cancer Letter _Editor Jerry D. Boyd

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