THE CANCER LETTER

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ACCC SEEKS GREATER ROLE IN CLINICAL RESEARCH PRIORITIES; SUGGESTS UP TO 400 CANCER PROGRAMS

Members of the Assn. of Community Cancer Centers feel they should have a greater role in determining clinical research priorities and are marshalling their growing political strength to help them get it.

"The development of new treatment interventions that can only be applied in the comprehensive cancer center setting fails to address the needs of 85% of all cancer patients," said a summary of recommenda-

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In Brief

CANCER PROGRAM A "NOBLE VENTURE," KENNEDY SAYS; $937 MILLION NOT ENOUGH, UPTON SAYS

SEN. EDWARD KENNEDY, opening a hearing of his Health Subcommittee on the Cancer Program: "Americans are an impatient people. When the Cancer Program was launched in 1971, some advocates made exaggerated claims for what the effort could accomplish. Though others were more cautious in their predictions, we are now entering a period of rising debate over whether the billions of dollars spent by NCI have been spent wisely. It is clear that we have not turned the corner on the battle against cancer, and the American people are asking why. . . . However, I want to make one point very clear. I, personally, believe that our expanded effort to control cancer is one of the nation's most noble ventures. Its successes can and will benefit people in every country on this globe. No federal initiative better expresses the humanitarian instincts, the generosity and basic good sense of the American public." . . . **BOARD OF SCIENTIFIC** Counselors of NCI's Div. of Cancer Cause & Prevention will meet April 26-27, NIH Bldg 31 Rm 9. It will be closed for review of intramural programs April 26, open April 27, 9 a.m.–5 p.m. . . . **NATIONAL SURVEY** conducted by Gallup last October for NCI has found that 62% of adult Americans are aware of asbestos hazards, compared with 50% in a survey taken last June. . . . **ARTHUR UPTON**, answering House HEW Appropriations Subcommittee Chairman William Natcher's question on whether the $937 million budget request for NCI is enough: "Without question, investment in the Cancer Program has advanced the field immensely. At the same time, by opening up avenues, we have attracted new people, some of the best minds. The percentage of research proposals we will be able to support is not as large as we would like. In that sense, it is not enough. But if you ask will it suffice, it is adequate." . . . **ROLAND WUSSOW**, former deputy director of the Colorado Regional Cancer Center and former NCI staff member, is the new director of communications for Miami Valley Hospital in Dayton. . . . **JOHN KALBERER**, former chief of program planning in NCI's Div. of Cancer Research Resources & Centers, has been appointed assistant director of the NIH office for Medical Applications of Research.

ACCC URGED TO BE MORE AGGRESSIVE, FIGHT FOR TREATMENT RESEARCH FUNDS

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tions by the ACCC Policy Committee which was presented to the membership at the organization's annual meeting.

ACCC lobbied successfully for an amendment to the Cancer Act which requires that at least two members of the National Cancer Advisory Board be practicing physicians who treat cancer patients. Several existing Board members meet that requirement, but

gram. That program is institutionally oriented. This program would be community oriented and would not be an accreditation program."

ACCC has from its inception encouraged its members to assume the lead in developing cancer programs. NCI's Div. of Cancer Control & Rehabilitation has provided further stimulus with its Community Oncology Programs. In general, the community programs involve development and organization of multidisciplinary teams, tumor registry, multidisciplinary cancer conferences, consultation services, support services, physician and allied health education,

independent accrediting system. "But now might be an opportune time to set up liaison with ACOS, help them review the criteria and bring them up to date on oncology practice in the community."

"• ACCC's legislative effort should be more aggressive. We represent 85% of all cancer patients and should consider drafting cancer legislation. This has become extremely critical because of the competition for funding from the environmentalists."

Solomon Garb, director of the AMC Cancer Research Center in Denver and longtime Cancer Program advocate, suggested that ACCC "defend the entire Cancer Program more vigorously. I sat in on the Kennedy hearings and heard a coordinated attack on the Cancer Program and on physicians who treat cancer patients. The critics said that the treatment program is a failure, that radiation causes more cancer than it cures, and that money should be taken out of treatment research and given to prevention. They exaggerate, they don't tell the truth, but they have had an impact.

"I have the feeling that this organization has been far too modest, too low key, and set its sights too low," Garb continued. "One of Kennedy's aides asked me who ACCC represents. I said we represent cancer patients in community hospitals, 85% of all cancer patients, and that they're too sick to come here themselves so we're talking for them. It will not suffice to ask for 1-2% of the budget. We should take the lead, draw up a bill that places the emphasis where those who treat 85% of cancer patients think it should be."

"Congress thinks prevention is a cheap way out," Durant said. "Legitimate epidemiologists can't figure out where 20% of cancer is occupationally related. Congressman (Andrew) Maguire is misinformed, and we should help educate him. There's lots of good reasons to clean up the environment, but cancer isn't one of them."

Garb said the critics who are advocating increased emphasis on prevention "are a small group of political activists, and it's my guess there are no more than two dozen in the country. But congressional aides are very much impressed by them. A handful of political activists are pushing their program at the expense of hundreds of thousands of cancer victims. They're out to get enormous amounts of money for their own research, and to change the entire fabric of American Society."

"• The problem of inadequate reimbursement by third party payers needs to be addressed. Better coverage is needed for outpatient treatment and home care.

"• ACCC should support the National Hospice Assn.'s legislative efforts."

ACCC took no action on the Policy Committee recommendations at its general meeting. They were referred to the Board of Trustees.

Outgoing President John Nelson reported that delegate and general membership had more than doubled during the previous 12 months, "which clearly makes us the major spokesman for the community at NCI and Congress."

Nelson reported that ACCC will sponsor three regional meetings in 1979, in San Francisco, Indianapolis and somewhere in New York State. The organization has undertaken the task of developing a long range plan for improvement of cancer care in the community, Nelson said. With the membership growth, ACCC is on a sound financial basis. "It is clear that the Association has become a vital and effective voice, one respected by other organizations," Nelson said.

In addition to the election of Cobau as president and Robert Frelick of Wilmington, Del., as president-elect, the members elected Robert Clarke, Indianapolis, as treasurer, and Charles Van Allen, Modesto, Calif., as secretary. Elected to the Board of Trustees were William Dugan, Indianapolis; Kerman; David Johnson, Evansville, Ind.; John Yarbro, Columbia, Mo.; and Robert Wroblewski, Akron.

Clarine Porter, executive director of the Scandia County unit of the American Cancer Society in Pensacola, was presented with the annual ACCC award for outstanding service to cancer patients.

The Div. of Cancer Treatment hopes to have a committee of practicing oncologists organized by early summer.

The committee would not be an officially chartered advisory group; it is almost impossible now to get new charters approved by HEW. Instead, the group would be an unofficial body which would be encouraged to submit a grant application to support a series of meetings at which problems of practicing oncologists regarding clinical research efforts would be considered.

DCT is in the process of identifying individuals who would be interested in serving on such a committee.

CARBONE SAYS INVESTIGATOR INITIATED CLINICAL RESEARCH GETS MORE FOR LESS

Paul Carbone, chairman of the Eastern Cooperative Oncology Group and current chairman of the Cooperative Group Chairmen's Committee, contended that "investigator initiated clinical research, like the investigator initiated basic laboratory program, will provide the most answers at the lowest cost" in his overview of the Cooperative Group Program presented to the NCI Div. of Cancer Treatment Board of Scientific Counselors.

Carbone's statement pointed out some of the areas of impact the Cooperative Groups have had since the program began 25 years ago; described the stringent ongoing internal review conducted by the groups; suggested that efforts to reorganize the groups along geographical lines would be disruptive;

and called for "a more varied mechanism to do clinical research and not reshuffle the current ones."

Carbone is also director of the Univ. of Wisconsin Comprehensive Cancer Center. His statement (with some editing to conserve space):

The Cooperative Groups were initiated in 1954 as multi-institution study groups to develop concepts and test chemical agents in the therapy of acute leukemias and solid tumors. This involved the development of specific methodology, forms, definitions, and procedures. Not only were clinicians, pharmacologists, surgeons, and radiotherapists involved, but the initial efforts also included statisticians and biometricians who were equal members. In addition to research, the mission included cancer education to attract young people into this new field of research. The effort involved the development of standards of optimal cancer care including the application of staging and supportive care. Thus, over the years the groups have had three major purposes—research, cancer care, and education.

The group concept has become attractive to more and more hospitals, universities, and centers. The groups quickly became involved in multimodal trials in the late 1960s. Currently, specific specialty groups, such as the Gynecology Oncology Group, and the Lymphoma Pathology Review Panel are included in group activities.

The growth of the Cooperative Groups has been evolutionary and modulated by peer groups. Over the past 25 years, 31 groups have been formed; yet many of these have either gone out of existence and/or been remodeled, so that in 1979 we have only 14 active groups. The molding and reshaping of the Cooperative Groups has been the result of peer-review. The CCIRC has approved new groups and members as well as disapproved or denied funding to individual institutions and groups. Not only has the emphasis been on quantitative estimates of patient numbers entered on study, but it has consistently involved quality of the records and promptness of the data. More recently the CCIRC has made a practice of evaluating multimodality input into group activities by individual institutions.

To participate in group funding one must demonstrate not only an ability to provide a sufficient volume and high quality data, but also significant contributions from other than medical oncologists.

Not only are the investigator initiated trial programs of the Cooperative Groups modulated by outside review bodies on a regular basis, but they also have stringent internal review mechanisms to assure high quality performance. Most groups have strict membership requirements which usually include a site visit. Each member is also reviewed annually for quality and productivity. This aspect of review is truly a peer review system that is unique to Cooperative Group activities. In other clinical trials mechanisms no clear cut ongoing peer review occurs except when the grant or contract comes up for renewal.

For example, ECOG has an annual review of each member by the executive committee consisting of elected as well as ex officio members representing surgery, radiotherapy, cancer control, and the statistical office. Reviews are conducted emphasizing patient accession, quality, and promptness of records, completeness of followup as well as intellectual contribution to group protocol and paper writing. Moreover, each member must have a significant element of multimodality involvement in its membership as well as patient accrual. Each member, whether funded or unfunded, is reviewed. The committee may approve, warn, or put an institution on probation. Deficiencies resulting in probation must be corrected within two years or the membership is dropped. This activity is taken seriously and has resulted in the expulsion of several members and the voluntary withdrawals of others.

Impact of Groups

The impact of Cooperative Groups is usually measured in terms of scientific output, namely through the clinical and/or biological importance of its trials activities. Previous speakers have described these scientific efforts. My task will be to summarize other possible importances of the Cooperative Groups. Of major importance is the large number of clinical trials in the groups. As many as 38,000 patients directly participate in the clinical trials programs. Not all of these patients have far-advanced, incurable cancers; there are over 130 projects involving surgery and/or surgical adjuvant trials, 200 involving radiotherapy, and 160 involving immunotherapy. As we become involved with more early disease studies and develop more effective treatments, our active patient base becomes larger. We are currently following an estimated 64,000 patients. In ECOG alone we have over 15,000 patients in our active followup files.

I stressed earlier the idea of direct patient impact through clinical trials, but there is an indeterminable number of patients being treated at Cooperative Group institutions who were considered for group studies but were not entered. There are an equally large number of patients whose treatments may have been influenced by Cooperative Group protocols. Many major institutions, engaged in Cooperative Group clinical trials research, are also doing early or pilot projects as well as secondary protocols that are done preliminary to group protocols. At the Univ. of Wisconsin we have as many patients on pilot or institutional projects as we do on group protocols. Thus, the total number of patients on whom group activities impact may be two or three times the actual number of patients put on group studies, or close to 200,000.

Another important area is that of the impact on training and utilization of health personnel. (Carbone estimated participants by specialty at 1,600 medical oncologists, 400 pathologists, 290 pediatric oncologists, 50 statisticians, and 710 surgeons.) Unfortunately, this estimate is very likely imprecise since there is no uniform way to list members across groups or to determine the actual involvement of individuals at every institution. In addition to the health professionals we know about, there are countless others who are students, residents, and fellows who are exposed to clinical trial activities at the teaching institutions. These individuals are involved in rounds, conferences, case discussions about patients and/or studies. Finally, new specialists, oncology nurses and data managers, have come onto the scene with major responsibilities to collect data and treat patients on protocol studies. These individuals know the protocols and interact with the patients and other physicians explaining the side effects and practical aspects of the treatments as well as collecting the necessary data.

What kind of impact do the Cooperative Groups have on all these participating health personnel? The individuals are exposed to the concepts of clinical trials and its requirements in a first hand way. In the past the laboratory was considered the prime disciplinary modality to develop rigid scientific approaches to medicine. Currently, clinical trials have become the oncologist's training ground to develop the neces-

sary skills and discipline to do good clinical research. Bringing order to the chaos of the delivery of medical care is a major achievement and attraction of clinical trials. Further evidence is the fact that many trainees of oncology programs are keen to continue the association with clinical trials when they relocate to other hospitals. These young individuals seek and continue their association with the group. This aspect mushroomed into a large natural resource for cancer control activities in community hospitals.

Another impact of the groups can be estimated by counting the numbers of primary and affiliate member institutions. Over 1,000 hospitals are listed as participants in group efforts. Unfortunately, we know very little about the characteristics of these hospitals except that 18 of the 21 comprehensive centers participate. Almost all of the 110 medical schools are associated with one or more of the Cooperative Groups. Likewise, most Veterans Administration hospitals are affiliated with group activities. An interesting statistic is that 41 different countries have one or more affiliations with groups. These individuals are rarely funded to participate but find it important and necessary to do so.

In attempting to describe the impact of these institutions' participation in group studies there are other indirect attributes that can be cited. With the new federal regulations requiring institutional review boards for clinical trials, my own personal experience verifies that, in general, the group trials proposed and reviewed at these institutional review boards are readily accepted and serve as models for other clinical trials groups at the university. (Moreover, the numbers of cancer clinical trials at the Univ. of Wisconsin represent more than half of all clinical trials reviewed by the Univ. of Wisconsin Institutional Review Board.) Since many of the other trials are merely interviews or specimen obtaining studies, the cancer clinical trials probably represent most of the therapeutic trials at most major universities. There has never been a single ECOG trial that has been turned down by a significant fraction of institutional review boards.

Another indirect impact has been the fact that Cooperative Group standards in areas like response, toxicity, and performance status have become the international standards and reference points for many other clinical trials. The design of clinical trials in cancer evolved from efforts to understand the biology of cancer in the human and development of new research methodology. The basic concepts of remission, induction, and maintenance were first defined in the early leukemia protocols. Moreover, important principles of patient selection, multivariant analyses, stratification, and randomization parameters have come from group trials. In fact, the concept of phase I, II and III trials in cancer have evolved from the initial studies.

The groups have emphasized pathology review in clinical trials for many years dating back to the origins of the NSABP as well as the Veterans Administration lung groups. While disappointment exists in the treatment of lung, pancreas and colorectal neoplasms, much has been learned in a quantitative way about the impact of histology and natural history on survival and response.

Any research effort can be easily measured in terms of improved cure rate. This has occurred in certain diseases, particularly lymphomas, childhood cancers, testicular tumors, and more recently in breast cancer. However, little is mentioned about the impact of therapy that occurs when proposed "cures" of unctrolled observations are subjected to repetition using controlled clinical trials. Numerous studies that have disproven the uncontrolled benefits of specific therapies in myeloma, adjuvant therapy of colorectal and lung cancers, certain combinations in colon and lung cancers, as well as immunotherapy in a variety of tumors.

In addition the group studies have clarified the relative role of surgery and radiotherapy in several neoplastic diseases, disavowing the standard dictum from certain centers. The clinical studies have confirmed and shown the value of experimental therapies in acute leukemia, myeloma, and osteosarcomas, as well as multimodal efforts in others. These studies done as part of Cooperative Group efforts have eliminated ineffective treatments and defined more effective nontoxic therapies. Since these studies are carried out using the best of statistical design with input from a wide variety of specialists as well as at multiple institutions, the results are not easily misinterpreted or biased by investigator selection or enthusiasm. There are some benefits that are hard to quantitate but do provide real benefits to the understanding of cancer as well as the improvement in morbidity and mortality.

Similar observations can be made relative to the studies of immunotherapy. In the not too distant past enthusiasm abounded and results were highly encouraging. Yet in melanoma no group study has confirmed the benefit of nonspecific immunostimulation in these patients. On the other hand some preliminary positive results appear to be seen in adult acute leukemia by the SEG in ovarian cancer.

In the early 1970s the concept of adjuvant therapy appeared to be a promising way to overcome drug resistance inherent to treatment of bulky advanced disease. There were many contracts initiated with the feeling that the Cooperative Groups were not able to do these studies. In fact, surgery or surgery plus other modality trials have been in the groups for years dating back to the 1960s for lung and breast cancer and the early 1970s for most other tumors. Likewise, radiotherapy trials either alone or in combination have been done since the 1960s in several diseases. There are some group pathology efforts that will undoubtedly provide important answers to cancer biology.

A comment needs to be made at this point relative to the administrative control of group efforts. Like the evolution of the modern groups, the administrative responsibility in NCI of the groups has vacillated under six administrative units dating back to the CCNSC. In addition, at least two major reviews of groups have been held in the past. Currently the groups are undergoing another shift with the CCIRC, the major review group located in the Div. of Extramural Activities, while the administrative aspects are in DCT and the Clinical Investigation Branch. What changes the next few years will bring can not be divined. However, the Cooperative Group mechanism has been responsive to changes in the direction of science as well as the administration of NCI.

There is an academic tradition among group members that creates a "university without walls." Cooperation among university hospitals occurs because each unit retains its identity. Throughout the years, group members have developed a way of interacting with each other that is nonthreatening. I have heard comments that money enforces this type of behavior. In fact, the cooperation exists even when grant monies are not available to all participants. We need to be cognizant and supportive of this kind of association. The relationships have been built up over many years and the individuals feel that they lose very little of their autonomy but have the advantages of the larger cooperative effort. To merely shift the

monies to new managers and alliances will undoubtedly be disruptive, expensive, and forced. Rarely will the resultant relationships be any better than what we have now—more likely they will not be as good. To set up consortium memberships from geographical areas likewise submerges the individual member behind an organization that could result in difficulties in evaluation and review for NCI.

My firm belief is that we need to foster a more varied mechanism to do clinical research and not reshuffle the current ones because of administrative pressures. Obviously more monies need to be found, but we are in a situation where large amounts of monies are being spent in administrative mechanisms, state of the art demonstrations, NCI-directed studies as well as Congress-delineated mandates. The result may be to foster easy, quick answers to the various pressures rather than to carefully define priorities and possibilities.

I believe that the investigator initiated clinical research effort, like the investigator initiated basic laboratory program, will provide the most answers at the lowest cost. Investigator initiated clinical research, whether in the centers or the Cooperative Groups, has in general provided most of the answers to date. The future is likely to be a repeat of the past. The Cooperative Group mechanism has proven to be flexible and responsive. The administrative pressures for reorganization on NCI and from NCI must be carefully considered before acting. The Board of Scientific Counselors as well as NCI staff must be ready to defend investigator initiated research in the clinic as well as the laboratory.

Bernard Fisher, as chairman of the National Surgical Adjuvant Project for Breast & Bowel Cancers (formerly the National Surgical Adjuvant Breast Project), has had the somewhat unique experience of being funded simultaneously by grant and contract for the same project.

In his presentation to the Board, Fisher had little patience for the unending controversy over which mechanism is best:

My comments are related to the NSABP experience employing both mechanisms of funding, i.e., grants and contracts. Both mechanisms are far from perfect for all endeavors. I have no brief concerning either—in fact, the entire issue of grant vs. contract produces in me, as an investigator, a sense of uneasiness for, in my opinion, sufficient creative energies are already being sapped in a confusing and time consuming search for financing without creating additional conflicts for the investigator by taking away his options.

If the director of NCI favors grants and is going to make less money available for contract funding, if the scientific community attaches an unsavory stigma to contracts, if all of my colleagues—the group chairmen—become exercised at the slightest mention of the word "contract," if the investigator initiated research cannot be carried out via a contract, if contracts have no flexibility, if contracts lack "security" for long term research, and if in contracts more time is spent in complying with the paper work than carrying out the investigation, logic would dictate that a Cooperative Group should plan its future funding relative to grants.

Unfortunately, the matter cannot be so simply resolved. While the term "contract" may evoke an undesirable connotation, that is not the fault of the word. In that regard I am reminded of what Mayor Frank Rizzo of Philadelphia is reported to have said: "The center-city streets are safe enough at night. It's only the people who aren't." If certain undesirable aspects of the mechanism can be corrected it may be that for certain purposes, such as Cooperative Group funding, contracts have greater worth than do grants.

For example, if a contract insures the same degree of stability as does a grant by being awarded for more than one year, e.g., five years, if there is assurance that with a contract there is the same opportunity as in grants for investigator initiated research and if flexibility in subcontracting continues, then it is possible that the objectives of a Cooperative Group may be more expeditiously, and at the same time, more economically accomplished by such a mechanism.

Since 1970 the NSABP has been funded in part by grant and in part by contract. It is fair to say that the accomplishments of the group would have not been achieved without such combined funding and the contract component was a major element responsible for our success to date.

Let me explain why, at least for a Cooperative Group such as ours, keying in on a single disease—breast cancer—and limiting ourselves to early disease, the contract mechanism has been successful. The following points are relevant to my thesis:

1. A Cooperative Group is an entrepreneurial administrative mechanism established to obtain information that can be obtained in no other way which will answer questions relative to the biology of the disease under consideration or the worth of treatment modalities prior to their implementation by the medical community at large. Such a group is neither a club nor a power structure. Form is and should not be as important as accomplishment.

2. The idea must be emphatically dispelled that "institutions" participate in Cooperative Group programs. Nothing is further from the truth. Some individuals within an institution may do so while others do not. The leadership within an institution, its interpersonal dynamics and harmony, its political and economic structure, the "comings and goings" of key personnel all determine who and how many of its staff participate in which clinical trials sponsored by what Cooperative Group. Patterns of referral, competition for patients and varying levels of competence (relative to clinical trial participation) within a medical community add to the factors which involve individuals and not institutions. Consequently, it is individuals, or groups of individuals within an institution or a community who must be recruited and sometimes trained to participate in clinical trials if we wish to accomplish our primary goals, i.e., completing patient accrual in trials as rapidly as possible. It is our distinct impression that major medical centers in this country have almost never as institutions made contributions to the clinical trial program; individuals from such centers yes, but total institutions rarely. This at least has been the experience within the NSABP. Moreover, even if there were total institutional commitment there are few if any who have sufficient patients to merit meaningful clinical trials and obtain results within a reasonable time period.

3. Because of the myriad of factors which affect individual participation in a Cooperative Group we have come to realize that there is more often than not an "investigator half-life" which determines his/her contribution. The surgeon with the large large cancer practice who one morning finds that the medical oncologist participating with him in an adjuvant trial of the NSABP has departed and the new oncologist does not care to do so or prefers some other trial with another Co-

operative Group is now effete insofar as the NSABP is concerned. Conversely, the surgeon may lose his patient referrals, enthusiasm or both and the medical oncologist formerly so valuable to the NSABP is no longer able to make a contribution since he no longer gets patients referred to him by that surgeon. Societal mobility has been the subject of numerous essays. We have anticipated that a certain proportion of patients would change addresses and be difficult to find. We have not been prepared for the physician mobility–both physical and mental–which we have had to contend with. Protocol No. B-04 which has just entered the eighth year since its inception points up such problems. In many instances, the principal investigator who was responsible for conducting the trial at an institution has either moved, has retired, has changed his/her area of interest, etc. The person entrusted to carry on has also departed. There may be nobody available who is remotely interested or knowledgeable about the trial and continuing patient followup. When one compounds this situation with the transient population of radiation oncologists, pathologists, surgeons, medical oncologists, endocrinologists, nurses, secretaries, etc., one is faced with a chaotic situation which far and above exceeds patient transiency. How does one accomplish quality followup on such patients under such conditions?

4. Just as it is fanciful to believe that "institutions" participate in clinical trials so is it naive not to believe that in any Cooperative Group there is likely to be a relatively small core of people from whom the scientific input is generated and who assumes the burden of responsibility for the group's success or failure. Those are individuals who are willing to tolerate the distaste of the entrepreneurial and promotional efforts which are required to make a group function because they believe that the scientific and clinical end results justify the endeavor. Most of the membership may be likened to the "infantry." None of the battles can be won without them. They supply the "ammunition" (patients and investigative material) and without them, all of the most elegantly devised strategies by the "generals" are useless. Their participation must be nurtured by rewarding them in some fashion for their contribution. For some, the intellectual stimulation engendered by group meetings is recompense enough. Others receive satisfaction by participating in the planning of new protocols and not a few participate so that they have access to the most up to date information. Practically all expect to receive funding to defray the costs of patient accrual, data collection, patient studies unique to the protocol and travel to group meetings.

I shall now relate those considerations to my subject, "contracts." Before doing so, however, let me make it absolutely clear that I am not espousing an argument against grants. Moreover, let me make it clear that I am not opposed to the CCIRC as a group or to any individual comprising it or to its overall function. That would be foolish since we are three weeks away from CCIRC review of our Cooperative Group. There are several aspects of the review process which I have found difficult to comprehend. I have been unable to understand why the CCIRC should, can, or want to apply priority ratings to "institutions" which apply for grants in a Cooperative Group program. Such an activity has no relevance to the quality of the science espoused by the group. Unfortunately, priorities of the CCIRC do not necessarily conform with those of the individuals responsible for accomplishing the scientific goals and rapidly completing patient entry in protocols. For example, a surgeon from a small community hospital who has many breast cancer patients which he is willing to put on a specific protocol and submit all followup information is of great value despite the fact that he may never "3.–participate in group committees or group administration or both" or will never "4.–participate in study design." (The Cancer Letter, March 3, 1978, page 2), or have the "right societies" in his C.V. In order to complete the protocol evaluating segmental mastectomy, it is necessary to recruit surgeons who operate on such patients and are willing to participate in the trial. Within reason, other factors such as their university affiliation, willingness to participate in other protocols, whether their staff has a clinical immunologist, whether they have a staff oncologist who belongs to ASCO, etc., and other factors which would preclude their getting a grant award are of secondary importance.

Those of use who are desperately trying to fulfill our goals should have greater opportunity to do so by putting together the team for the purpose of contributing patients, others for their scientific input, some for their administrative talents or others for combinations thereof. Recently five NSABP institutions (four in December and one in February) applied for grants and the only one receiving a high enough priority rating by the CCIRC to be funded was that institution which was fourth in our priority rating.

There is clearly a dichotomy of purpose which is frustrating, demoralizing and antithetical to our group interests. There are many compelling factors which influence a decision regarding who sould participate in a group, when they should be terminated and what their disposition should be. If such decisions cannot be a prerogative of those entrusted with the operation of the group then how can responsibility for a group's failure of performance be attributed to them? Individual institutions should be reviewed relative to their contribution to the group. This seems more appropriately to be a function of the group itself. If the group is successful in achieving its goals, clearly a judgment within the perview of the CCIRC, then the members of the team are adequate. If not, then new leadership of the group may be in order so that a more effective team may be developed.

The accomplishments of the NSABP during this decade have been due to the availability to us of a contract which gave us considerable flexibility in:

1. Recruiting and financing investigators in a timeframe that would be impossible under a total grant program.
2. Rapidly eliminating investigators who fail to contribute patients, supply data, comply with protocol or make no contribution to the NSABP.
3. Targeting resources according to needs as we perceive them.
4. Making available funds for long term followup or providing funds for the implementation of contingency mechanisms for obtaining data.

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. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Address requests to the contract officer or specialist named, NCI Research Contracts Branch, the appropriate section, as follows:

Biology & Diagnosis Section and Viral Oncology & Field Studies Section–Landow Building, Bethesda, Md. 20014; Control & Rehabilitation Section, Carcinogenesis Section,

Treatment Section, Office of the Director Section—Blair Building, Silver Spring, Md. 20910.
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NO1-CP-95618-59

Title: *Pathology support for Carcinogenesis Testing Program*
Deadline: *June 19*

The objective of this project is to provide professional and technical pathology support to the Carcinogenesis Testing Program. This project involves three tasks which include the following:

1. Diagnostic Pathology Support—this task includes tissue processing, slide preparation and staining, histopathologic diagnoses and for pathologists to serve as consultants to the Tumor Pathology Branch through participation in advisory panels, workshops, seminars and site visits.

2. Quality Assurance Report Production—this task includes validation of data in computer tables, validation of tissue counts, histopathologic review and validation of diagnoses of all tumors, target sites and compound related lesions from rodent bioassays, review and validation of diagnoses from all tissues from a statistically suitable sample of the animals in the bioassay, and formulation of detailed reports on the findings of the review.

3. Pathology Repository and Archives—this task includes providing storage facilities for at least 3,000,000 microscopic slides, a storage area for wet tissues, paraffin blocks, pathology narratives, computer tables and forms and other tabular data; provide transportation for the movement of materials from the repository to NCI and other NCI contractors in a timely fashion; provide the capability to retrieve specific tissues and lesions from the repository slide, block and wet tissue collection.

Contract Specialist: J. Roland Castle
Carcinogenesis
301-427-7914

RFP NO1-CM-97293-14

Title: *Synthesis of nucleosides as potential anticancer agents*
Deadline: *June 1 (approximately)*

The Drug Synthesis & Chemistry Branch of NCI is seeking organizations having capabilities, resources and facilities for the synthesis of unique nucleosides as potential anticancer agents. The objective of this project is the rational design and synthesis of potential inhibitors of key enzymes involved in the salvage pathway and deo novo biosynthetic pathways to nucleic acids. Samples, greater than one gram, fully characterized, will be prepared and submitted to NCI for antitumor evaluation.

The principal investigator should be trained in organic/medicinal chemistry at the PhD level, from accredited schools and experienced in the synthesis of nucleosides of potential antitumor activity. He must be named and available to the project a minimum of 50% of his time. All other technical supporting personnel are required to be trained chemists. They must devote at least 50% and preferably 100% of their time to the project.

It is necessary to maintain collaborative studies in the nucleoside area between the synthesis group and established groups of biologists interested in cancer chemotherapy. Laboratories are to be equipped with modern equipment and facilities for synthesis and characterization of compounds. Library resources must be adequate.

It is anticipated that one contract of two and a half technical man-years per year will be awarded for a period of three years.

Contract Specialist: Susan Hoffman
Cancer Treatment
301-427-8125

RFP NCI-CP-VO-91020-79

Title: *Induction and control of MuMTV expression in mouse mammary preneoplastic tissues.*
Deadline: *May 11*

Proposals are being requested to develop a model system for techniques, reagents and concepts applicable to the search for a putative breast cancer virus in precancerous human mammary tissues.

Contract Specialist: James Doyle
Viral Oncology & Field Studies
301-496-1781

RFP NO1-CP-95616

Title: *Carcinogenicity studies in rodents*
Deadline: *June 6*

The Carcinogenesis Testing Program of NCI is interested in receiving proposals to obtain toxicological and biochemical data in chemicals, in addition to carcinogenicity data, which would aid in the prediction of the potential carcinogenic risk of chemicals to man from carcinogenicity studies in rodents.

The experimental protocol will involve two major tasks: Task I – subchronic phase and Task II – chronic phase. Responders may propose in both or separately.

Contract Specialist: Dorothy Britton
Carcinogenesis
301-427-7914

The Cancer Letter _Editor Jerry D. Boyd
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