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THE CANCER LETTER

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DCT BOARD APPROVES PROPOSALS FOR INCREASED EFFORTS WITH BIOLOGICAL RESPONSE MODIFIERS, OKs CONTRACTS

The NCI Div. of Cancer Treatment Board of Scientific Counselors last week accepted the report of its Subcommittee on Biological Response Modifiers which outlined plans for the institute's only major new program this year. The Board also approved the concept of four new contracts in DCT's stepped up efforts to comply with the congressional mandate on biological response modifiers; the new contracts will

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In Brief

SENATE MARKUP OF CANCER ACT RENEWAL BILL DELAYED AGAIN; NEW MONEY LEVELS CONSIDERED STILL TOO LOW

TED KENNEDY put off indefinitely the markup of his bill (S. 988) to renew the National Cancer Act and other biomedical research programs. The markup by Kennedy's Senate Health Subcommittee had been scheduled for last week, but now his staff is saying they "hope" they can get it in before the end of the session. Present version of the bill adds $80 million to NCI's authorization for FY 1981 over the original bill; Cancer Program advocates think it is still too low. The authorized levels for 1981 would be $1.1 billion plus $113.3 million for control; 1982, $1,172,655,000 plus $124,630,000; and 1983, $1,348,-555,000 plus $137,093,000. The bill also would increase the maximum grant the NCI director could award from $35,000 to $50,000 in direct costs without concurrence of the National Cancer Advisory Board (a Board subcommittee was not aware this was in Kennedy's bill when the issue was discussed recently—***The Cancer Letter***, Nov. 2). The bill now also leaves NCI's budget bypass intact, leaves the NCI director as a Presidential appointee, but reduces NCAB appointments to the HEW secretary level. . . . **VIDEO TAPE**, "The Treatment of Primary Breast Cancer," recorded immediately after last June's NIH consensus conference on the subject, is available free to any professional audience from Ted Klein & Co., 118 E. 61st St., New York 10021, phone 212-935-1290. It features a discussion among Bernard Fisher, Joseph Allegra, Franco Muggia and Gerald Urban, conference panelists. . . . **MULTIDISCIPLINARY CONFERENCE** on head and neck oncology is planned for Sept. 8-10, 1980, at NIH by NCI's Div. of Cancer Treatment. Topics will include recent clinical trials, new diagnostic and therapeutic approaches employing surgery, radiation therapy, chemotherapy, immune modulation or other investigational modalities, and lab investigations in immunology, virology, cell cuture and animal tumor model development. Investigators interested in making presentations may contact Gregory Wolf, Special Assistant for Surgical Oncology, Landow Bldg 8C17, NCI, Bethesda, Md. 20205, no later than Jan. 31. . . . **COLORADO REGIONAL** Cancer Center has moved its offices to 234 Columbine St., Suite 200, Denver 80206.

DCT BOARD APPROVES CONCEPT OF FOUR NEW CONTRACT PROGRAMS WITH BRMs

(Continued from page 1)

spend about $3 million of the $13.5 million Congress earmarked for the program.

NCI had previously issued an RFP for the purchase of interferon. DCT Director Vincent DeVita told the Board that that contract was being negotiated and the award probably would be made soon.

The voluminous report of the subcommittee, chaired by Enrico Mihich, presented a detailed overview of "Clinical Aspects of Biological Response Modifiers—Current Status and Future Prospects." It included reviews of preclinical therapeutic evaluation, clinical model and phase 1-3 development schemes, and clinical trials in lung, breast, colon, gynecological, bladder, renal, and head and neck cancers, malignant melanoma, skin cancer, lymphomas and leukemia.

The two volume report (termed an interim report by the subcommittee) also included descriptions of program components, operations, administration and recommendations for initial implementation. Separate categories of implementation were outlined for interferons, thymosins and augmenting agents. Recommendations were made for confirmatory clinical therapeutic trials of augmenting agents in ovarian cancer, lymphoma and renal adenocarcinoma; further clinical development of chemoprevention; production of tumor necrosis factor; definition of distinctive cell surface antigens of human cancers and development of immunogenic antigen preparations; development of systems of BRM evaluation; and overall preclinical research program.

The Board agreed the four new contract programs presented for concept approval were compatible with the recommendations of the subcommittee. They were:

Phase 1-2 clinical evaluation of biological response modifiers for the treatment of cancer. Proposed first year award, $2 million, with multiple awards to clinical contractors as "Quick Reaction Task Order" contracts. The Investigational Drug Branch described the project:

"Quick reaction contracts are master contracts which are competitively negotiated and awarded to more than one contractor. This type of contract is designed to accomplish a specified piece of work as promptly as possible. The individual target dates will be determined for each project. These master contracts are unfunded, except for a minimum guaranteed amount (retainer fees) required to have the contractors maintain available capacity and capabilities regardless of whether or not a work order is issued.

"Cancer chemotherapeutic drug development has evolved because of early successes, along lines which have yielded cytocidal drugs. There has been at the same time, an accumulation of evidence that neoplastic cells may be responsive to, or dependent on, 'cell growth factors' or 'cell growth hormones'. In addition, there is evidence that agents might be identified that trigger phenotypic commitment of cancer cells to become differentiated cells or to assume regulated growth patterns. Still other evidence suggests that some agents may prevent the expression of genetic information in the first place and serve as prophylactic agents in high risk populations (chemoprevention).

"In addition, there has been an accumulation of evidence that the host cellular and humoral immune system can limit the growth of cancer cells. Concurrently, it has become increasingly clear that the host immune system may be favorably modulated by specific agents. All these and other similar kinds of agents have been referred to as Biological Response Modifying (BRM) agents.

"Work orders are individual competitively negotiated contracts for specific agents to be clinically evaluated and are awarded to those contractors listed as recipients of Master Quick Reaction Work Order Contracts. The specific work orders will be issued after competitive selection among a suitably qualified subgroup of the master contractors. The individual work orders will be issued on either a completion or level of effort basis, whichever is deemed appropriate by the contracting officer.

The contracts will provide NCI with a clinical protocol for the evaluation of a particular BRM which will have the following objectives:

"—To characterize and measure the magnitude of all relevant biological responses as a function of dose of the BRM agent.

"—To characterize and measure the magnitude of toxicological properties of the BRM agent at these doses.

"—To determine if the maximum dose of the BRM agent is characterized by (a) unacceptable toxicity or (b) the dose-response characteristics of the relevant biological responses.

"—When possible, to characterize the pharmacokinetics of the BRM agent.

"—To characterize or develop suitable end points appropriate for use in evaluating the BRM agent for efficacy.

"—When possible, to evaluate the BRM agent for efficacy in a relevant patient population."

Phase 2 new lead development. Proposed first year award, $500,000. The description:

"These contracts represent a new concept in clinical trials. New leads in cancer therapy frequently require high priority evaluation, but existing resources have not always been appropriate for the rapid response often necessary for these evaluations. If new therapies are contemplated which do not readily fit into the scope of work of existing contractors, separate competitions are required to respond to these needs.

"The purpose of these contracts is to assemble a

group of contractors with wide varieties of facilities and expertise. The contractors, having demonstrated an interest in participating in a broad range of studies, will be maintained on a minimal retainer fee. Whenever a new therapy has been identified by the program as being of high priority, and not within the workscope of other projects, the institution(s) capable of performing the appropriate studies will be designated.

"Since projects will be approved and funded individually, level of effort and expense can be identified for each task. Examples of the types of projects which contractors will be asked to participate in are the evaluation of new analyses, new specific and nonspecific therapies and other supportive therapies (e.g. marijuana and other antiemetic drugs). The contractors will have the responsibility for the design of a suitable protocol, for the accrual of an appropriate number of patients, for the proper followup of those patients, and for the analysis and publication of the results of the trial."

Chemoprevention of cervical cancer. Proposed first year award, $250,000. The description:

"Over the past few years there has been considerable clinical interest in the use of retinoids as preventive agents in persons at high risk of epithelial cancer. The prototype animal model for this phenomenon is the protective effect of 13 cis-retinoic acid in prevention of carcinogen-induced bladder cancer in the mouse. This example, plus observation of other vitamins with cancer-preventive activity, has stimulated a number of clinical trials in high risk groups.

"One potential clinical trial which has received strong advocacy from the gynecologic community is to treat women with moderate to severe cervical dysplasia, a group at high risk for progression to in situ or invasive squamous carcinoma of the uterine cervix. Several meetings at the NIH conducted by the Div. of Cancer Cause & Prevention addressed the logistics and feasibility of such a trial. The consensus of these meetings was to use topical retinyl acetate in a double-blind randomized controlled chemoprevention trial. Clinical experience with topical retinoids has been combined to the dermatologic disorders where the limits of human toxicity have been well-defined.

"It is envisioned that such a project will require a large number of patients be followed over many years. In order to accomplish this, a consortium or group effort is projected. The first year of such a project would involve a subcontract for the formulation and pilot study of the topical retinoid preparation. In addition, the awardee would standardize cervical cytologic, and histologic criteria, determine risk factors, and natural history of cervical dysplasia, coordinate participating institutions, and arrange for computerized support for the conduct of the trial. The design of the trial, including the dose, formulation, schedule and duration of application, would be a subject for the contractor to propose and consider. It is anticipated that approximately one year of topical retinyl acetate would be reasonable trial duration. The reversion or differentiation of abnormal cytology to normal would be taken as a positive therapeutic effect. Stability of the lesion would be interpreted as indeterminant, whereas progression of cervical cytologic abnormalities, or the development of in situ cancer despite the application of retinyl acetate would be interpreted as a trial failure. Careful consideration and participation by biostatisticians would be an integral part of such a study."

Chemoprevention of skin cancer in albino Africans. Proposed first year award, $75,000 (non-competitive—the contract will be negotiated with the Univ. of Dar Es Salaam in Tanzania). The description:

"Albino Africans living in the equatorial zone are subject to the most intense ultraviolet irradiation on the surface of the earth, and are subject to a virtually 100% incidence of skin cancer. Since they lack a pigmented layer of epithelium, their only defense against solar irradiation is hypertrophy of the stratum corneum. It is possible that the carcinogenic effect of ultraviolet light on hypertrophied epithelium results in the high incidence of skin cancer which afflicts this population. Squamous carcinoma has been noted in albino youngsters as young as five years old and occurs entirely in the sun-exposed areas of the skin. Aside from protective clothing, sun screens, and avoidance of mid-day sun, there is no preventive regimen which might avert the multiple squamous cancers in this patient group.

"This project proposes the use of oral 13-cis retinoic acid as a chemopreventive agent in albino Africans. An albino clinic exists at the Univ. of Dar Es Salaam in Tanzania, set up in 1978 by Prof. Ulrich Henschke, chairman of radiotherapy, Howard Univ., and sponsored by a grant from USAID. The clinic has registered over 300 albinos who are seen at weekly or monthly intervals and observed for the development of skin cancer. Suspicious lesions are then biopsied and treated either surgically or with radiation therapy as appropriate. The clinic also operates a protective education program in which patients are instructed on the use of sun screens, clothing, umbrellas, and sun avoidance. Despite these measures, over the past year, the frequency of skin cancer in these subjects is virtually 100%; very often these cancers are multiple and recurrent.

"It is anticipated that a double blind randomized clinical trial employing 13-cis retinoic acid would be conducted in this population. Patients would be stratified by risk factors and allocated to one year of oral 13 cis-retinoic acid, or a placebo. The daily oral dose would be in the range of 0.5 to 1.0 milligrams/kg as tolerated. It is felt that the dose level should be maintained in a range just under that which produces side effects, (cheilitis, headache, rash) and may vary from individual to individual. Patients will be followed

weekly, and later monthly for the development of skin cancer or suspicious lesions which will be photographed and biopsied. A trial of one year's duration is anticipated and the overall duration of the project will be three years."

Those projects and the contracts for purchase of biologicals, including interferon, will account for approximately half the $13.5 million earmarked by Congress. The Board asked the subcommittee and DCT staff to develop additional specific proposals for consideration at the Board's spring meeting.

The subcommittee suggested a number of grant and contract supported projects for implementation during the first year of the BRM Program:

—Phase 1-2 BRM Therapy Study Group.

—Production of interferons.

—Phase 1 study of interferon therapy.

—Phase 2 study of interferon therapy.

—Phase 1 study of thymosin fraction 5 immunotherapy.

—Phase 1 study of MVE-2 immunotherapy.

"Because of limitation related to the grant calendar, no grant in the BRMP can be funded before December 1980," the report said. "Thus, during the first year of its existence, the BRMP is likely to be funded primarily through contracts. The subcommittee wishes to be on record in strongly suggesting that an RFA (request for applications) and PA (program announcement) grant program be planned by DCT as soon as possible so that it can be funded in 1981 and that a ceiling of about $10 million be submitted to the DCT Board for approval for this purpose. The subcommittee plans to submit to DCT an additional list of priorities for RFA and PA as soon as possible after the October meeting of the DCT Board."

Details of the subcommittee's recommendations in each of the BRMP areas will appear in subsequent issues of The Cancer Letter.

DCT BOARD APPROVES CLINICAL TRIALS RECOMMENDATIONS—SOME CONTROVERSIAL

The massive review of large scale clinical trials conducted by the Board of Scientific Counselors of NCI's Div. of Cancer Treatment has resulted in recommendations by the Board that:

- NIH should establish a new study section to review individual investigator initiated clinical cancer research grant applications.
- Funding of the Cooperative Groups should be changed from the existing grant mechanism to the cooperative agreement, if and when HEW approves that new mechanism.
- DCT's phase 2 and 3 contract supported programs would be phased out and those studies would be conducted by the Cooperative Groups under the terms of cooperative agreements.
- The size of the Cooperative Groups would be scaled down, with multidisease groups not exceeding 12-15 member institutions plus a statistical office.
- Cooperative Group member institutions should be encouraged to work with geographically relevant satellite institutions.
- Member institutions should be permitted to belong to only one multidisease Cooperative Group.
- Three general classes of research protocols would be recognized with differing guidelines for approval by NCI—groupwide protocols, generally calling for greater than 100 cases, which could not be activated until NCI has approved; groupwide protocols requiring less than 100 case accrual, which would have to be filed with NCI but could be initiated without specific NCI approval except when a new drug IND is involved; and group pilot studies initiated by a limited number of institutions within the group, which also would have to be filed with NCI but NCI approval not required except when an IND is involved.
- Funds from the Cancer Control Program should be transferred to DCT to support groupwide phase 3 studies.
- Greater efforts should be made to exchange information among investigators, especially between the Cooperative Groups and clinical program projects.

Some of the recommendations most certainly will generate raging controversies as DCT moves toward implementing them, particularly transferring cancer control money to DCT and the limits on group membership and size.

Board member Sydney Salmon, who chaired the subcommittee which reviewed the clinical trials presentations made earlier this year to the Board, submitted the subcommittee's recommendations at last week's meeting.

John MacDonald, director of the Cancer Therapy Evaluation Program, said he had some question about whether the numbers should be so clearly defined. He pointed out that before NCI would agree to phase out the phase 2 and 3 contracts, the workability of cooperative agreements would have to be demonstrated.

Board member James Holland, who is chairman of Cancer and Leukemia Group B, said he was "uncomfortable" with some aspects of the recommendations. "What makes a Cooperative Group?" Holland asked. "It has nothing to do with geography but a state of mind. It depends on who one wants to work with."

Salmon commented that the recommendations "do not address group reorganization along geographic lines," but Holland insisted that they do in the sections referring to satellite members.

"I hope everyone realizes how far we've come," said DCT Director Vincent DeVita. "A lot of our problems have been worked out in the process of review. I hope we can put together a plan for the Clinical Trials Program which will carry us through the next decade."

DeVita said the "key to the whole process is the language in the cooperative agreements." Use of the task order mechanism along with cooperative agreements offers the prospect of a great degree of flexibility for NCI in supporting phase 1, 2 and 3 studies, permitting quicker starts and stops, DeVita said.

NCI has started using task orders. Guidelines for cooperative agreements are floating back and forth between NIH and HEW headquarters, with no major hangups but only some bureaucratic concern over language.

The Board approved the subcommittee recommendations, which follow:

1. We recommend that a new study section be established to review individual investigator initiated clinical cancer research.

This recommendation is made in light of evidence that individual investigator initiated clinical cancer treatment research proposals which are competitively submitted for grant funding have lacked an appropriate review body. While this function historically has been played by the CCIRC many years ago, this is no longer the case. Additionally, available evidence suggests that the enormous breadth of the task for which the experimental therapeutics study section is responsible (which includes both preclinical and clinical R01's) can interfere with review, priority ranking and funding of innovative clinical investigations. The subcommittee believes that the current mechanism for review of P01's and R10 cooperative group grants are satisfactory as are those for preclinical R01's.

2. In accord with federal guidelines [not yet finalized], a cooperative agreement should be negotiated between the Div. of Cancer Treatment and the Cooperative Groups.

The cooperative agreement will provide DCT with additional mechanisms for review and consent on group protocols, and to prevent unneeded duplication while providing the groups with increased flexibility and latitude for funding promising new clinical research and cancer control activities. By intent, the cooperative agreement would also progressively eliminate DCT's need for a separate set of phase 2 and 3 clinical trials groups supported primarily by contract. With time and increasing expertise and referral into multidisease, multimodal cooperative groups, and increasing intergroup studies, the need for specialty groups or task forces conducting separate phase 2-3 studies, would also diminish. Proposed guidelines for the cooperative agreement would include the following:

A. Cooperative group member institutions and the group biostatistical office will be part of an R10 grant supported clinical trials program. Each institution grant must be capable of successfully passing peer review by the CCIRC.

B. The size of any individual Cooperative Group will be set to be a size no larger than that which is considered optimal for the specific clinical trials program which it undertakes. Funding is determined by patient volume of its member institutions and NCI requirements for clinical trials research. In general, multidisease groups should not exceed 12-15 member institutions plus a statistical office. For rare tumors, and areas of low case accrual, the intergroup mechanism established by NCI is to be encouraged.

C. Group statistical offices will, in general, be decentralized (as opposed to being centralized at NCI) to facilitate interaction between the statistician and his staff and the various investigators.

D. Adequate pathology support should be made available for studies wherein pathology review is required for signal tumors wherein responses are observed and subgroups need to be identified.

E. Cancer centers with NCI support (core grant and/or clinical program projects) will comprise the majority of the funded institutions. The membership of a given Cooperative Group will be comprised by those investigators whose institutions form natural links in relation to scientific activities, education and referral patterns. Each funded institution should have evidence of recognized scientific leadership among its principal investigator and co-investigators, and not merely case contributions. The only exceptions to this guideline would be in a minority of institutions with a vary high case volume and an outstanding record of protocol compliance. Institutions in the latter category should comprise no more than 10-15% of group membership. At any one time, an additional one or two institutions which are not NCI funded via the R10 mechanism will also be permitted. All member institutions whether R10 funded or not should meet minimum group guidelines for case contribution. For adult multidisease groups this number would be at least 75 evaluable cases annually.

F. Institutions within Cooperative Groups may have "satellite institutions" which have skilled oncology specialists associated with them in the various disciplines. Satellites must be geographically relevant also to the member institution and provide a natural line for case referral and educational activities. Thus, satellite and case recruitment from large geographical distances are both to be discouraged because of problems in protocol compliance with such cases.

G. Member institutions of any given multidisease Cooperative Group should not be permitted to belong to or participate in other multidisciplinary cooperative groups, and funding to the institution should be limited to a single multidisease group. This same proviso should hold for investigators associated with satellite institutions who must also be committed both to a given institutional principal investigator, and a given Cooperative Group, whether the satellite receives funding or not. This guideline is intended to minimize intrainstitutional competition as well as "picking and choosing" among protocols of different groups by clinicians associated with centers or satellite institutions.

H. Investigators associated either with member institutions or satellites of a Cooperative Group must be highly experienced oncologists who submit an adequate number of cases annually in their specialty area in addition to having specialty competence. For example, for a surgical oncologist to contribute cases, at least 10 evaluable cases in that disease category should be submitted. We believe that it is critical that the surgeon perform an adequate number of specific operations per year which are subjected to pathology review. Guidelines for anatomic adequacy of the surgery will be established and the various surgical participants reviewed for protocol compliance. This would be analogous to the type of quality control that is currently achieved in radiation therapy, through radiation physics monitoring and review of port films, and in medical oncology by review of flow sheets and toxicity data. Specific guidelines for compliance in surgical subspecialties and immunotherapy will also be required. Such quality control is essential for excellence in combined modality studies.

I. With approval of NCI, and the availability of contract funds from DCT, the group chairman may contract to fund additional institutions, case contributions, pathology review, specialized tests or assays, etc., when these appear necessary. A maximum of 10% of such contract funds could be applied by the group chairman on a descretionary basis to these various activities without prior approval by NCI. the remaining 90% of such contract funds would be applied in relation to previously agreed upon specialized activities. Not all institutions would necessarily receive specialized funding. Specialized funding would normally be available only for a few years until the time of the next formal grant review by the CCIRC. Other DCT contracts (except for phase 1 study) would be phased out once the groups are competent in any given area for phase 2-3 studies.

J. Three general classes of research protocols will be recog-

nized with differing guidelines for approval by NCI:

1) Groupwide protocol requiring large case accrual (generally greater than 100 cases) must be filed with NCI and cannot be activated until approval is granted. This is to assure that major scientific questions have been broached in such expensive trials and to avoid excessive duplication of specific therapeutic programs in the various cooperative groups. For purposes of definition after more than three protocols involving a very similar treatment for any given disease are initiated, additional protocols will be considered excessive unless new major scientific objectives are sought. An appeals mechanism will be established to deal with disagreements between respective groups and NCI for adjudicating disputes wherein NCI acts negatively on proposed groupwide protocols. A permanent subcommittee consisting of three members of the CCIRC will serve as the appeal board for adjudication in such disagreements on specifically appealed protocols. The appeal board recommendations will be considered as binding to NCI with respect to scientific soundness and the question of duplication. If an approved protocol has accrued significantly in excess of the required number of the evaluable cases (e.g., 150%), the group chairman has an obligation to communicate with NCI and indicate the reasons that the group has chosen to keep the study open. NCI may request that case entry be discontinued if the protocol objectives have been met satisfactorily and any disputes may again be referred to the appeal board if required.

2) Groupwide protocols requiring case accrual of less than 100 must also be filed with NCI, but can be initiated by the group without specific NCI approval unless the treatment involved a new drug under IND regulations. In that circumstance, NCI approval must also be obtained. Typical phase 2 new agent trials which might require 25 evaluable cases for a given disease category must thus be referred for approval before the drug will be shipped. Appeal mechanisms will be as described above for Class 1 protocols.

3) Group pilot studies initiated by a limited number of institutions within the group (e.g., 1-4) must also be filed with NCI for informational purposes, but specific approval will not be required unless a new drug under IND with NCI is involved in the trial. Pilot trials from a single institution will generally not have over 25 cases enrolled, and maximum enrollment for group pilot studies will be 50-75 cases for any given disease category. Protocols involving specific laboratory testing which may not prove feasible in all patients will be judged on the total number of evaluable cases that had the necessary laboratory procedure (e.g., in vitro drug testing) carried out successfully. Broadening of a group pilot to a groupwide study will require specific NCI approval. In general, individual institutions will have no greater than 25% of the total group effort devoted to pilot studies. However, the importance of pilot studies as a wellspring for innovative groupwide studies cannot be overemphasized, and the group chairman should encourage such activities. When possible, the chariman might be able to provide, for example, specific contract support for group pilot studies that involve more than one institution should this appear warranted based on the scientific originality and the requirements of the research protocol.

3. We recommend that funds from the Cancer Control Program be transferred to DCT for cooperative group activities in support of groupwide phase 3 protocols.

Phase 3 as conducted in both the satellites and the centers represents one of the leading approaches to cancer control through the delivery of effective standardized treatment and the related referral and educational processes. It is essential that the peer review process for award of cancer control funds be the same as that applied to the groups as a whole. This will assure that the same criteria apply to case entry and quality control at satellites as applies to the group members. We believe that the current process of direct awards from Cancer Control to Cooperative Groups should be discontinued and replaced by transfer of funds for this purpose to DCT.

4. We recommend that DCT continue and increase its efforts toward information exchange on cancer therapy evaluation. It should be extended so that it includes more input and return to participants in clinical program projects as well as to the Cooperative Groups.

The program of specialized seminars on specific diseases, modalities, drugs and other components relevant to the clinical trials program and staffing of group meetings has been an important and effective DCT program and expansion of this effort is warranted. Annual multigroup review of major ongoing trials might also have additional value in relation to communications in the clinical trials program. Thus, individual groups might have two intragroup meetings per year and one plenary intergroup meeting

For informational purposes, DCT staff members should also be represented in ex officio fashion at clinical program project and core support grant site visits at which time the overall impact of a given center's local clinical trials program can be reviewed in perspective. While DCT staff members would not participate in the site team's deliberations, they would read the progress report and attend the various presentations. The subcommittee recognizes that expansion of the Cancer Therapy Evaluation Program as we recommend will require additional staffing and **we recommend that additional government positions be created in DCT to permit expansion of the Cancer Therapy Evaluation Program.** This would facilitate future evaluations of all the major components of the cancer clinical trials program supported by NCI.

The preamble to the report included the comment that "the subcommittee recognizes that the details of interrelationship between DCT and the Cooperative Groups are of crucial importance as is the relationship of both DCT and the groups to the numerous well trained oncologists who now practice in many communities and play an important role in lines of referral not only for routine clinical care, but in relation to investigation. Applications of new and effective treatments under development and in various stages of testing, confirmation and extrapolation to standard patient care through the vehicle of phase 3 clinical trials can benefit from participation of skilled oncologists at defined satellite locations. While some of these areas may constitute problems, they also may provide important new opportunities for major thrusts in clinical cancer research in the future.

"We also must make note of the fact that thus far, a complete review of clinical trials research that has been sponsored under R01 or P01 grants has not been possible. As DCT increases its capabilities to review ongoing cancer treatment research, it will be very important to analyze these programs in detail as well. The P01 clinical program projects constitute a particularly valuable resource for large scale multidisciplinary institutional cancer treatment research."

NEW PUBLICATIONS

"Hospital Days–Treatment Ways," a coloring book designed for young children with cancer to provide them with an introduction to hospital experience and treatment procedures. By Jenene Warmbier and Ellen Vassy; published by Ohio State Univ. Comprehensive Cancer Center and Children's Hospital of Columbus. Free from Office of Cancer Communica-

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tions, NCI, Bethesda, Md. 20205, or OSU Comprehensive Cancer Center, 357 McCampbell Hall, 1580 Cannon Dr., Columbus 43210.

"Malignant Lymphoma," edited by R. Levy and H.S. Kaplan. Proceedings of a workshop on the biology of human cancer. UICC, 3 rue du Conseil-General, CH 1205, Geneva, Switzerland, 25 Swiss Francs including postage.

"Cancer Screening: When Is It Worthwhile?" Edited by Deborah Hall and Martha Wood, a guide for primary care physicians. Published by Sidney Farber Cancer Institute, 44 Binney St., Boston 02115. Free copies are available from Farber's Communications Office.

"Living in a Strange World," by Elaine Shimberg with illustrations by Jeanne Kennedy. Published by the Florida Div. of the American Cancer Society for parents of children with cancer. Available free to Florida residents at the 28 ACS information centers in the state; $1.50 postpaid outside the state. Write to ACS Florida Div. Inc., 1001 S. MacDill, Tampa 33609.

"Breast Cancer Digest, A Guide to Medical Care, Emotional Support and Educational Programs," A handbook for health communicators, planners and professionals organizing breast cancer education programs. "Progress Against Breast Cancer," a 17-minute slide/tape show. Produced for the general public covering important information on breast cancer, with emphasis on early detection and prompt treatment. Available as a package of slides, cassette tape, script, checklist, poster and pamphlets. "Breast Self Examination" (also available in Spanish). Provides step by step instructions. "What You Need to Know About Cancer of the Breast," a pamphlet designed for patients which discusses cancer symptoms, diagnosis, rehabilitation, emotional issues, and glossary of terms. All above are published by NCI's Office of Cancer Communications, available free except for a charge of $23.50 for the slide/tape show.

"Innovations in Cancer Risk Assessment." Edited by Jeffery Staffa and Myron Mehlman. Symposium proceedings. Published by Pathotox Publishers, 2405 Bond St., Park Forest South, Ill. 60466. $29, plus $2.80 for countries outside continental U.S.

"Modifiers of Chemical Carcinogenesis." Edited by Thomas Slaga. Raven Press, 1140 Ave. of the Americas, New York 10036. $30.

"Cancer Mortality: Environmental and Ethnic Factors," by Dorothy Wellington, Eleanor MacDonald and Patricia Wolf. Academic Press, 111 Fifth Ave., New York 10003. $16.

NIH PUSHING FOR MORE WOMEN, MINORITY SCIENTISTS ON ADVISORY COMMITTEES

HEW Secretary Patricia Harris is insisting that the department's advisory committees must increase their representation of women and minorities and has warned that proposed slates will be rejected "if there is no evidence of adequate participation" of those groups.

Harris said in a memo to committee management staff:

"Although individual agencies have increased the number of women and minorities, the total representation of women and minorities among HEW's 272 advisory committees is inadequate. Women constitute only 24% of that group and all minorities have only 15% representation. (These figures are virtually identical to those in effect when this Administration took office.) The President is committed to see that HEW provides an example for the Federal government.

"Until further notice, all proposed advisory committee slates forwarded for my approval will be reviewed by the special assistant in charge of advisory committees to insure they meet affirmative action objectives. Each nominee must be qualified for the appointment; each committee must meet the objective of increasing the number of women and minority group members. If there is no evidence of adequate participation of women and minorities, the slate will be rejected.

"In addition, I have asked the special assistant in charge of advisory committees to review the performance of components where the authority to appoint committee members has been delegated and to recommend any action that is needed to meet affirmative action objectives.

"There are many competent women and minority group members who are eligible for appointment to HEW advisory committees. I ask that you seek them out."

NIH Deputy Director Thomas Malone has asked the executive secretary of each NIH advisory group to solicit from active committee members recommendations on women and minority scientists "who might serve as potential reviewers or participate in related activities." Malone asked that names be sent to George Bowden, Div. of Research Analysis, OPPE, Bldg 31 Rm 1B62, NIH, Bethesda, Md. 20205.

Malone said that a special initiative by NIH to identify qualified women and minority scientists through appropriate professional organizations has produced 3,300 names, of which 900 have expressed willingness to serve.

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 Biological Carcinogenesis & Field Studies Section—Landow Building, Bethesda, Md.

20205; Control & Rehabilitation Section, Chemical & Physical 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 NCI-CM-07347

Title: *Provision of tissues and cells, and conduct routine tests in support of tumor cell biology and virology*

Deadline: *Approximately Jan. 19*

The Laboratory of Tumor Cell Biology, Developmental Therapeutics Program, DCT, NCI is interested in the qualified organization to supply NCI with tissues, cells, and small quantities of fresh type C RNA tumor viruses, and to conduct routine tests and immunoassays for viral antigens in support of ongoing studies in tumor cell biology and virology. The government will provide necessary nucleic acid template primers and radioisotopes for the required work.

The contractor must have adequate biohazard containment facilities (levels P-2 – P-3) to handle tissue culture cells and type C RNA tumor viruses. The organization must be located in close proximity to the NIH (35 mile radius) so that daily deliveries and pickup of fresh samples are possible within one hour limit to protect viability of cells and biological and biochemical activities of RNA tumor viruses.

Contract Specialist: Helen Lee
Cancer Treatment
301-427-8737

RFP N01-CO-05475-69

Title: *Programming and data entry services in support of the NCI contracts management system (NCI-CMS)*

Deadline: *Dec. 7*

NCI is seeking an organization to provide programming, data entry and analysis, and other related data processing services in support of the NCI contract management system. The contractor must possess a thorough knowledge of automated procurement systems, as well as extensive experience with the IBM 370/168 computer, JCL, WYLBUR (text editor), and MVS (multiple virtual storage). Experience in the use of inquiry and reporting system (IRS) and Cobol is mandatory.

All contract management system report programs are written in the IRS language; update programs and file maintenance are written in Cobol. It is anticipated that the great majority of programs to be written and systems to be documented will require a thorough knowledge of Cobol as well as the IRS language and programming techniques, as they relate to the NCI contract management system.

This procurement is 100% set aside for small business concerns.

Specific tasks include the following: (1) Perform data entry and file maintenance for the CMS; (2) Perform the operation and maintenance activities of all contract managements programs and subsystems; (3) Modification, execution, and distribution of monthly recurring report programs; (4) Design and implementation of new recurring report programs; (5) Modify/develop, test, document and execute report programs to meet unscheduled requests for information; (6) Assist in coordination and dissemination of information, documentation and program changes necessary to maintain the contract management system's interface with various subsystems, management information systems, components and external systems; (7) Maintain and update all systems' documentation and users' guides for all operational systems and subsystems of the CMS; and (8) Perform other tasks as required for training, documentation and status reporting.

Offerors will be limited to those firms having operating facilities within a 35-mile radius of Bethesda, Md., as daily person-to-person contact is often necessary.

Contracting Officer: Linda Waring
Office of Director Section
301-427-8747

RFP CI-80-0011

Title: *In vitro and in vivo mutagenicity testing of EPA generated samples*

Deadline: *To be determined*

EPA shall be generating environmental samples at irregular intervals for testing by the contractor in one or more of the following systems: Ames test, in vitro Sister chromatid exchange (SEC), unscheduled DNA synthesis in rodent hepatocyte cultures, rodent cytogenetics, rodent micronucleus test, rodent sperm abnormalities, SEC in rabbit lymphocytes following in vivo exposure. These samples may be defined chemical species or they may be complex samples such as drinking water concentrates. In addition, the following biological samples will be supplied: Rodent sperm slides for sperm abnormality evaluations, urine samples for Ames testing and human lymphocyte slides for cytogenetic evaluations.

This procurement shall be screened for a possible small business set-aside. Further screening shall be done for a possible labor surplus area set-aside.

Negotiated Contracts Branch
Contracts Management Div., EPA
Cincinnati, OH 45268

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