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DCPC BOARD APPROVES $40 MILLION IN NEW CONCEPTS, INCLUDING THREE IN BREAST CANCER, ONE IN MELANOMA

The Board of Scientific Counselors of NCI's Div. of Cancer Prevention & Control approved concepts for seven new research programs and additional funding for a controversial project previously approved, all with a total estimated cost for up to five years of nearly $40 million, at the Board's meeting last week. The Board deferred action on two other concept proposals. Concepts approved:

*A study of nutrition and genetics in breast cancer, to include support of 28 screening centers; five or more contracts for studies on how to increase utilization of early breast cancer detection technologies; and expansion of the low fat diet breast cancer study to add 15 additional clinical centers and 3,000 more patients at an

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In Brief

HAWAII STUDY FINDS NO INCREASE RISK FOR LARGE BOWEL CANCER FROM HIGH INTAKE OF SATURATED FAT

ANOTHER THEORY on the etiology of cancer shot down? The current issue of "Cancer Research" includes report of the 15 year followup study of 7,074 men of Japanese ancestry, ages 45-68, living in Hawaii. Grant Stemmermann and colleagues found that a high intake of of saturated fat did not significantly increase the risk of large bowel cancer. This held true whether the intake was expressed in terms of grams of fat per day or as a proportion of the total caloric intake. During the period of the study, 165 men were diagnosed as having large bowel cancer. In the detailed analysis of the data, there was a hint of a positive association between high saturated fat intake and rectal cancer risk, but the association was not an impressive one. There was also a suggestion that the highest consumers of saturated fat had a decreased rate of cancer of the colon, but there was a lack of a clear dose response relationship. The risk of colon cancer did not progressively decrease as the intake of saturated fat progressively increased. The article cautioned that the level of dietary fat should remain of concern since other adverse effects of high fat diets, such as coronary heart disease, are evident. The study did find a relationship between fat intake and heart disease.... **MARY LASKER** has done more for biomedical research than any other person in the world, NCI Director Vincent DeVita said in reporting on dedication ceremonies of the Mary Woodard Lasker Center for Health Research & Education at NIH. . . . **NEXT WEEK'S** meeting of the Board of Scientific Counselors of NCI's Div. of Cancer Etiology will be closed on the first day, Oct. 18, from 9 a.m.-noon, contrary to the schedule in The Cancer Letter's listing of meetings Sept. 28. It will be open 1 p.m.-adjournment Oct. 18 and 9 a.m.-adjournment Oct. 19.

DCPC BOARD APPROVES PDQ EVALUATION, ARGUES DEVITA'S OFFICE SHOULD PAY

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estimated total cost of nearly $14 million.

*A five year, $6 million evaluation of strategies for early detection of malignant melanoma.

*An evaluation of the PDQ system for providing clinical information to physicians, somewhat controversial because the half million dollar cost of the evaluation would come out of the DCPC budget rather than that of the NCI Office of Director, where PDQ is located.

*Primary prevention studies within defined small business occupational settings.

*A double blind evaluation trial of slit-scan flow cytometer.

*Support services for development of a "program tracking data base."

The Board delayed final action on a proposal to extend phase 3 randomized clinical trials of chemoprevention of cervical cancer for an additional five years, and on a proposal for assessment of occupational nursing practices and educational needs in the primary prevention of cancer.

The approved concepts, with staff description and justification, follow:

Title: Nutrition and genetics in breast cancer. Estimated 28 contracts for screening centers at a cost of $105,000 each per year for two years; one contract for a data collection and monitoring center at a cost of $600,000 a year for four years; a specimen repository to cost a total of $1.3 million; and pilot studies to cost $50,000. Staff narrative:

We propose to study the relation of nutritional variables, nutrition mediated variables, nutrition related variables, and genetics to the incidence and survival of breast cancer. Specifically, the hypotheses that will be tested include:

*Nutritional variables--high caloric, high fat and high protein intake; low carotenoid; and low selenium are associated with an increased incidence and reduced survival for breast cancer.

*Nutrition mediated variables—enduring anthropometric indicators of increased growth during adolescence as measured by adult body size (height, frame size, lean body mass) are associated with increased incidence and decreased survival for breast cancer in women. In postmenopausal women, high per cent body fat, excess total body fat and high estrogen levels are associated with increased incidence and decreased survival for breast cancer.

*Nutrition related variables--constipation and increased breast secretory activity are associated with increased incidence and decreased survival for breast cancer.

*Genetic characteristics—dermatoglyphic patterns (increased whorl count), cerumen type (wet), and lipoprotein patterns (low HDL 2) are associated with increased incidence and decreased survival for breast cancer. Other established risk factors for breast cancer will also be studied, as will other cancers besides breast (e.g. colon).

Each of the objectives outlined is designed to increase understanding of factors associated with breast cancer incidence and survival. Identification of such factors is critical for future cancer control efforts. Information obtained in pursuit of these objectives can reasonably be expected to help identify factors associated with increased risk of cancer onset or recurrence, and inhibitors of cancer or cancer recurrence. Ultimately, the goal is the manipulation of these factors to improve morbidity and mortality.

To test the stated hypotheses, four established subcohorts will be utilized from the Breast Cancer Detection Demonstration Project followup. The screening phase of the BCDDP was operational between 1973 and 1981 and enrolled about 280,000 women from 29 centers who were offered annual breast cancer screening exams for five years. Followup of the BCDDP cohort started in 1979 and will not be completed in all centers until 1986. Followup is limited to four subcohorts of the original cohort and totals 64,185 women, including all new breast cancer cases (n=4,275), all benign breast disease patients (n=25,066), a sample of normals (n=25,163), and all women with an identified screening abnormality resulting in a biopsy recommendation who, for whatever reason, did not have a biopsy performed (n=9,681).

Women in these four subsets are being tracked for the five years following their initial five year screening period to ascertain cancer and vital status. We propose a five year prospective design which will combine additional data and sample collection in Year 1 followed by four years of observation on all 64,185 women.

Data on possible determinants of incidence and survival will be obtained in several ways. Dietary calories, fat, and protein will be estimated using a semiquantitative food frequency questionnaire; carotenoid and B-carotene values will be determined by analysis of serum; and selenium will be measured by analysis of toenails. Stature and weight will be directly measured while per cent body fat and total body fat will be estimated by a series of skinfold thicknesses and impedance measurements. Various estrogens will be measured in blood, urine, and breast fluid. Breast secretory activity will be studied by characterizing breast fluid obtained. Bowel function will be assessed by questionnaires. Dermatoglyphic patterns will be determined from fingerprints; cerumen type from otoscopic examination; and lipoprotein pattern from blood analysis.

It is anticipated that a case referent sampling scheme will be used in the analysis of the laboratory specimens and in analysis of these data. Specifically, measurements of the determinants under study actually used in the analysis will be limited to all cases and a random sample of reference subjects selected to be some numeric multiple of the number of cases. Collaborative laboratory arrangements with the National Bureau of Standards and U.S. Dept. of Agriculture already

exist and could potentially be utilized for certain of the analyses anticipated.

The present age range is 45 to more than 80 with the median falling in the 55-59 year old group. The anticipated 254 incident breast cancers over the five year study period (51 annually) will provide adequate power to discriminate the various hypotheses proposed from the null.

A pilot study is planned for the first six months of the project during which the details of recruitment, data and specimen collection and management, and other measurements to be taken, will be refined.

Collaboration with the Div. of Cancer Etiology and with the National Heart, Lung & Blood Institute and National Institute on Aging is anticipated.

The project will involve the following tasks:

1. The existing 28 screening centers will contact the subjects in year one to establish cancer and vital status; administer a questionnaire capturing data on demographics, dietary intake, and detailed family history of cancer by site; collect and ship to a central repository biologic specimens including blood, breast fluid, urine and toenails; perform otoscopic examination and obtain anthropometric measurements; and obtain fingerprints.

2. A central data collection center will be established to continue monitoring cancer and vital status annually by mail contact and use of vital statistics registries in years 2-5; provide a mechanism for capturing additional information from members of these cohorts as needed; and manage the data.

3. A repository of biologic samples will be established.

4. Completion of a pilot study prior to initiation of the full study.

Richard Costlow, chief of the Cancer Detection Branch, and Philip Taylor are the project officers.

Title: Increasing the utilization of effective early breast cancer detection technologies. An estimated five or more awards will be made at a total cost of $1.75 million in FY 1986, $2.5 million in 1987, and $2.5 million in 1988.

To increase and sustain utilization of state of science mammography and breast palpation within geographically defined population areas are the goals and major objectives. Within selected geographic communities, this research will develop, implement, and pilot test interventions to (1) stimulate and sustain increased utilization of mammography and breast palpation among women 50 years of age and older and their health care providers; and (2) upgrade the quality of these detection technologies. Data from a baseline survey will establish the initial frequency and quality of mammography and breast palpation, and it will also provide a validity assessment of barriers to utilization and competency in that particular focal community.

Endpoints of the intervention studies will include process measures (such as changes in the quality and cost of mammography and breast palpation) and impact measures (such as changes in the utilization rates of these technologies among patients and their health care providers). The objective of the research should be to effect substantial increases in utilization patterns, not simply statistically significant changes. A variety of experimental and quasi-experimental designs may be employed in testing the pilot interventions, including the use of control communities.

During the second year of the contract, NCI staff will evaluate the interim success of the pilot interventions in increasing the use of state of science mammography and breast palpation. If the early results look promising, staff will begin to develop a research initiative aimed at enlarging the scope and scale of the intervention studies. Completion of this initiative will await the final evaluation of the full array of pilot interventions being tested, so that the most efficacious can be incorporated into the next research phase. Any decision to enlarge the program will be made by the Board of Scientific Counselors with input from appropriate external consultants.

The Health Insurance Plan of Greater New York demonstrated a 30 per cent 10 year reduction in breast cancer mortality among women screened by mammography and physician examination. This controlled trial is the strongest available scientific evidence to justify extending the screening approach to relevant women in the population at large. There is general agreement that HIP showed an unequivocal screening benefit for women 50 years of age and older. For younger women, the benefit/risk ratio is still the subject of scientific discussion.

The early case finding in the BCDDP supports the thesis that mammography combined with breast palpation reduces the likelihood of metastatic breast cancer at diagnosis and subsequent mortality. Although it was not a controlled intervention trial, BCDDP adds confirmatory evidence to the proposed concept. Further, it has been estimated that in the 1980s improvements to 40 per cent reduction in breast cancer mortality might be attained with the full application of quality mammography and competent breast palpation. Recent data from The Netherlands lend credence to the idea that modern screening technologies may result in larger mortality reductions than were found in the HIP study.

As a consequence of scientific evaluation, NCI recommends the routine use of state of science mammography and breast palpation for women 50 years of age and older. However, national data indicate that this position has not been accepted or adopted by the medical profession and its clientele. An increase in the utilization of these effective technologies for early breast cancer detection could contribute substantially to the Institute's goal to reduce cancer mortality in the U.S. by 50 per cent by the Year 2000.

Reported utilization of mammography by American women above the age of 50 suggests that between 15 and 43 per cent of them have had a mammogram at some time in their lives. The weight of evidence indicates that the utilization figure is much closer to 15 than 43 per cent, and at least some of these mammograms were

done for diagnostic rather than screening purposes. Very little is known about the frequency or periodicity of mammography, but studies report that only four to 14 per cent of women over age 50 are receiving annual mammography.

Breast palpation by a health professional is much more frequently used. According to national interview data, between 43 and 58 per cent of women aged 45 to 64 have had a breast examination within the last year. However, little is known about the quality of these examinations. It is also important to note that an inverse relationship exists between age and frequency of breast palpation, with older women reporting a lower proportion of breast examinations by health professionals than younger women report.

Among the preventive strategies available to physicians who treat chronic and infectious diseases, mammography appears to be regarded as least important. And in a recent California study, even those physicians who gave mammography a relatively high rating on importance tended not to recommend it. Yet, interviews with women suggest that the vast majority would be receptive to mammography if their doctors did in fact prescribe it.

Only two attempts to increase the utilization of mammography are reported in the literature. Both were conducted within residency programs. One used computer reminders and showed essentially no improvement in physician recommendations over a two year period (2% to 8%). The other used face sheet reminders with better success (4% to 32%) over a four month period. No intervention studies to increase the use of breast palpation by physicians have been found in literature review.

Census and/or survey data should permit the characterization of both the female population and their professional providers. The wide diversity of medical practice (prepaid health plans, fee for service, and welfare care) as well as the demographic heterogeneity of the American female population should be represented in the mix of selected communities. Moreover, the composite choice of communities and contractors should provide opportunities to test a variety of promotional strategies. Innovative approaches to the problem at hand should transcend more than one type of medical care setting, particularly when the women themselves are targets of the health promotion activity.

In developing the pilot interventions, researchers should identify and consider barriers to the utilization and competency of mammography and breast palpation among the target populations. The literature suggests that the economic costs of mammography for screening purposes and the potential radiation hazards are important impediments to its utilization by both patients and health providers. But a number of other obstacles have also been identified, such as doubt about the benefits of mammography and problems of access. Although breast palpation is a more frequently used procedure than mammography, there appear to be special barriers to examinations among the elderly.

With respect to quality issues, mammography varies appreciably from one laboratory or clinic to another, partly because of variations in case load and technical experience. In addition, concerns exist as to the competency of breast palpation by health care providers. Thus, it is important to design interventions that will upgrade the quality of these technologies to state of science levels.

The interventions that will be developed, implemented, and evaluated in this research initiative are expected to address and remedy the barriers to routine and competent use of these technologies. It is anticipated that separate, but complementary, interventions will be designed for the women and their health care providers. If subgroups of women do not have established sources of care, special attention should be given to expediting their access to mammography and breast palpation within the existing health care system or through creative outreach programs. It is expected that the development of appropriate economic incentives will make an important contribution to the improved utilization of mammography. No funds in this contract are to be used to offset the cost of screening procedures, but they can be used to stimulate plans for lowering cost.

To ensure a sustained reduction in breast cancer mortality, utilization of effective screening technologies must be sustained within the population. Therefore, interventions which are durable are needed to achieve the goal of this proposal. Over the period of the contract, some assessments of durability will be undertaken. And if the scope of the effort is later enlarged, further evaluations will be possible.

Costlow and J. Howard are the project officers.

Title: Additional funding for a phase 3 trial of a low fat diet in women at high risk for breast cancer. An additional 15 awards are anticipated for clinical centers at an estimated cost of $3 million in FY 1985, $3.3 million in 1986, $3.6 million in 1987, and $4 million in 1988.

Goals and objectives are to reduce the incidence of breast cancer in women who are at high risk of developing primary breast cancer, and to evaluate the impact of this diet on the incidence of other cancers and overall morbidity.

This project was presented initially to the Board

CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY: RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

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of Scientific Counselors in January, 1983, and approved in May, 1983. On the basis of the recommendations of the peer review committee, three clinical units have been funded for the feasibility trial and an additional 10 clinical units have been selected to be funded for the full scale trial. The patient accrual from these 13 clinics will be approximately 3,000. Another 3,000 patients will be required to meet the estimated power calculations. The complete protocol and manual of operations will be developed at the start of the feasibility trial. In order to accrue the additional patients, we propose to bring in additional clinical units at the conclusion of the feasibility trial to coincide with full scale implementation. We are aware of a number of investigators who did not apply to the original RFA but now are expressing an interest. In addition the applicants who were unsuccessful initially may be able to revise their proposals to compete successfully.

The previous budget estimates were based on assumption of use of group training sessions for this trial. However, the applicants have felt that more individualized instructions and attention to modification of individual behavior are necessary for the success of this trial. This approach obviously is more labor intensive and more expensive.

The project will be a randomized controlled clinical trial in which the study participants will be randomized either to receive a diet in which 15 per cent of calories are derived from fat or to continue their usual diet.

The results of the feasibility trial will be evaluated by a committee of the BSC before implementing the full scale trial. A report of the committee will be presented to the full Board at its September, 1985 meeting. The funding requested in this concept will not be awarded until after the completion of that review.

Ritva Butrum is the project officer.

Awards to the first 13 clinical centers were tentatively approved by the National Cancer Advisory Board at its recent meeting, with the stipulation that it review the feasibility study before the awards are made. The NCAB then will make a decision on whether to go ahead with the project.

BSC member Laurence Kolonel commented that the prospect that the project may not be funded if the feasibility study is negative "might discourage some good people from applying."

The motion to approve, offered by Jerome DeCosse, stipulated that the BSC participate along with the NCAB in the decision on whether to proceed with the project. It was approved, with four abstentions.

Title: Evaluation of strategies for early detection of malignant melanoma. Three cooperative agreement awards are anticipated, at a total estimated cost over five years of $6 million.

Goal of this study is to evaluate two strategies for early detection of malignant melanoma using prospective controlled study designs. Specific objectives include reduction of the incidence of advanced stages of melanoma in the study population (early endpoint); and reduction in mortality from malignant melanoma in the study population (later endpoint). Related objectives include assessment of acceptance of detection strategies by health professionals and the public; and assessment of any adverse effects generated by the strategies.

The proposed strategies are an invitation to examination to first degree relatives of melanoma probands; and an education program aimed at health professionals and the public in a defined population.

Malignant melanoma accounts for 5,000 deaths per year in the U.S. Because the majority of cases arise in the skin, this tumor should be amenable to early detection by inspection by trained observors. However, according to SEER data, at the time of diagnosis more than 60 per cent of the cases have invaded to or beyond Clark's Level III (interface of papillary and reticular dermis). Because of the low frequency of the disease, mass screening programs are generally thought to be not feasible. Two approaches may be considered for this dilemma: (1) identifying a higher risk subpopulation and focusing a screening program on this population; or (2) increasing the pool of trained observors so as to facilitate the screening of the general population.

Factors which may identify a high risk subpopulation include family history of melanoma, the dysplasia nevus syndrome and excessive actinic exposure. The observed to expected ratio for melanoma in first degree relatives of melanoma probands has been reported to be eight. The dysplastic nevus syndrome was the focus of a recent consensus development conference sponsored by NCI and NIH. The consensus included the recognition of the dysplastic nevus syndrome as a recognizable entity, the appreciation that DNS is associated with an increased risk of malignant melanoma especially if associated with a family history of melanoma and the recommendation that programs of early detection of melanoma should focus on the DNS.

Each of the two different intervention strategies will be tested in a separate, defined geographic area having an established population based cancer registry. Strategy #1 will have an internal control group, while the impact of strategy #2 will be assessed on the basis of population based cancer registry data. Any diffusion effect of strategy #1 will be assessed by the population based cancer registry data. Each intervention plan will include details as to criteria for biopsy and plans for participation in a central pathology review.

Strategy #1 will involve an invitition for examination extended to first degree relatives over age 20 of probands with malignant melanoma. The probands will be identified from pathology files. First degree relatives will be identified by interview or questionnaire of the proband or next of kin. The unit of randomization will be the family, to minimize contamination of the nonscreenees by the screening activity. The control or nonscreened population will be followed without screening, while the screened population will be screened periodically during the study. Applicants will be expected

to address the ethical issues of their proposed study design and also the issues of permission for implementation, including permission of physicians and patients.

Exclusion from randomization (and assignment to screening) may be considered for families with the dysplastic nevus syndrome and two or more family members with a previous melanoma confirmed by the pathology reference center. If this option is chosen the randomization would include families not having the dysplastic nevus syndrome, and families with the dysplastic nevus, but with only one family member with melanoma. The applicants will specify the details of examination, the use of lesion photographs and the frequency of examinations. The research plan must include plans for long term followup to be able to evaluate the impact on melanoma related mortality.

Strategy #2 will involve a health promotion strategy to include an education program, use of media, etc., aimed at health professionals, the general public, and persons who may have unique opportunities for inspection of the skin such as lifeguards, beauticians, barbers, and clothiers. Instructional content would include recognition of the characteristics of malignant melanoma and characteristics of DNS and recognition of changes in nevi which should prompt examination by a physician. The intervention would be delivered in a defined population area having a population based cancer registry and high actinic exposure, and the mortality compared to that in all other population based cancer registries including SEER (adjusted for differences in mortality prior to initiation of the study).

All pathology laboratories in the study areas must agree to submit in a timely manner representative slides on all cases of DNS and melanoma for review by the pathology reference center. The pathology reference center will verify diagnoses and will classify melanoma cases according to the Clark and Breslow classifications.

Funding for this project will include the costs of study coordination and data collection and analysis, but will not include the costs for medically indicated biopsies or therapy.

Dorothy Brodie and Lillian Gigliotti are the project officers.

Board member Robert Cooper said, "The first strategy appeals to me, the second does not. How can you make sure that barbers, clothiers, etc. follow through?"

"My inclination is to focus on doctors," DCPC Director Peter Greenwald said. "There are dermatologists who are pushing for strategy #2 without a cancer control research effort first."

"I have ethical problems with randomization," Board member Lewis Kuller said. "I would not want to be in a community sending out melanoma prone families and not offering a treatment that works."

"There is no evidence that periodic screening works," William DeWys, director of DCPC's Prevention Program, said.

Greenwald argued that scientific evidence is needed that the intervention works. "If there is some way to refine the studies, fine."

"Your study is to determine the best method of finding melanoma early enough to make it more treatable," Board Chairman Barbara Hulka commented. "Would you, in a cervical cancer test, take Pap smears and not read half of them?"

Board member Saxon Graham asked about the use of historical controls, and DeWys answered that "it has to do with sample size."

Greenwald suggested that the request for applications could state that the issues of ethics and study design are questions to be considered. Kuller offered a motion to approve, with the stipulation that the RFA leave out recommended strategies. Hulka added, "The basic thrust is that we want some activity in melanoma, but we want to reduce the amount of direction in study design."

"If we leave too much to the prerogative of the investigators, we might get a hybrid of design, with uninterpretable conclusions," DeWys said.

"We've got some smart investigators out there," Hulka answered.

"Peer review can deal with that problem," Kuller said. His motion was approved.

Title: Evaluation of the PDQ System: Implementation, awareness, adoption and utilization. One or two contract awards are anticipated, at a total two year cost of $467,000.

PDQ (for Physician Data Query) is an innovative and important cancer control mechanism, designed to facilitate progress toward NCI's Year 2000 goal by increasing the rate of clinical information transfer from the clinical research environment to physicians who encounter or treat cancer patients in the community. Physicians currently receive information on clinical innovations from a variety of formal and informal channels, each of which affects clinical decision making in a different way, and to a greater or lesser degree. In oncology, extant information channels are insufficient in their ability to diffuse clinical cancer innovations to all physicians who could benefit from the information. As an on line information system containing up to date staging, treatment, referral and protocol information for over 80 cancers, PDQ can greatly extend the capacity of the clinical cancer information diffusion system by making this information readily and easily available to all physicians.

Goal and objectives of this proposal is to monitor and evaluate PDQ's implementation and adoption by the medical community. Evaluation information will serve as a means to refine the PDQ System to improve its rate of adoption and utilization. Major objectives include an assessment of National Library of Medicine and vendor based PDQ systems; and a profile of PDQ users and nonusers, including patterns of use among the target audience.

The information content of PDQ will be reviewed to establish accuracy of information within the system and veracity of the process update. An expert panel will be assembled and a process of staff review will be used to assess information content of the system.

Characteristics of PDQ, its implementation by each vendor, and the user instruction materials will be assessed with one or several panels of users and through a series of controlled experiments. System characteristics of particular interest are ease of accession, speed of response, and degree of user cordiality. Initial user expectations will be determined with user questionnaires and through market research. User instruction/information materials will be pilot tested and assessed through expert panels.

The awareness and use of PDQ, characteristics of those aware of and/or using PDQ, attitudes of users and nonusers towards PDQ, frequency of use, and extent of use with reference to files accessed, circumstances or reasons for use, the specific question searched, and the specific decision that may be influenced will be assessed. A number of strategies may be employed including several varieties of user panels, user surveys, online questionnaires, and demographic and frequency information generated by NLM and vendor delivery systems.

Edward Sondik is the project officer.

"It's hard for me to believe, given all the discussion and concern about this, that an evaluation system was not built into the original funding," Cooper said. "Why has this been brought to this division? Why not (NCI Director Vincent) DeVita's office (where PDQ is housed)?"

"It was built in," Sondik answered. "Evaluation just needs a house, in my body, I guess."

"Why in heaven's name is your division being asked to pay for it, given the constraints on the cancer control budget that Vince has described to us?" Cooper persisted.

"Because this is treatment delivery," DCPC Associate Director for Centers & Community Oncology said.

"I can take the funding issue back to the (NCI) Executive Committee," Greenwald said. "The issue to me is whether this is cancer control."

"I'm for this," Cooper said. "I just want Vince to pay for it."

Sondik said that DeVita had made it clear the evaluation should be done by DCPC. DeVita later told **The Cancer Letter** that "I certainly don't want PDQ staff to evaluate it."

Sondik said that "it had been my understanding, money will be added to this division's budget to pay for this."

DeVita said that he is not committed to transferring additional money to the DCPC budget for the evaluation. "My view has always been that there is one NCI budget, and the money all comes out of the same pot," he said. "Part of the cancer control function is to evaluate. If money does become a problem, we can see about sending some over then to pay for evaluation."

DeVita said DCPC's budget situation depends on the responses to various program initiatives and how much will be needed to fund the high priority proposals they generate.

(The remaining DCPC concepts will appear in next week's issue of The Cancer Letter).

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-57714-26
Title: Neutron therapy clinical trials
Deadline: Approximately Jan. 19

The Radiation Research Program of NCI's Div. of Cancer Treatment is seeking contractors to be part of a collaborative effort to conduct phase 2 studies and prospective phase 3 randomized clinical trials of fast neutrons vs. photons for tumors which are not presently controlled by conventional radiotherapy in the major anatomical sites, to include the head and neck, thorax, abdomen, pelvis, extremities and extra-abdominal, extra thoracic trunk. Contractors are required, at the time of proposal submission, to have available an operational clinical neutron therapy facility and a modern, well equipped conventional radiation therapy facility. In addition, contractors must be able to document extensive experience in conducting photon and neutron prospective phase 3 clinical trials and must be able to treat no fewer than 150 neutron patients/year and place no fewer than 100 evaluable patients/year (neutron plus photon) on phase 3 clinical studies.

It is anticipated that multiyear, incrementally funded, completion type contracts will be awarded for a period of four years. Each increment will be for a 12 month period.

A preprosal conference will be held approximately four weeks after the RFP issuance date, expected to be on or about Nov. 9.

Contract Specialist: Carolyn Swift
RCB Blair Bldg Rm 228
301-427-8737

RFP NCI-CM-57715-21
Title: Evaluation of high energy external beam treatment planning
Deadline: Approximately Jan. 19

The Radiation Research Program of NCI is seeking contractors to be part of a collaborative effort to develop criteria, guidelines and methodology for the performance and evaluation of state of the art high energy electron external beam treatment planning. This will be accomplished by extensive treatment planning for actual patients using state of the art beam delivery, computerized treatment planning and imaging systems. Each contractor shall furnish all necessary personnel, labor, materials, equipment and

facilities not otherwise provided by the government. The results of this work will be described in a final report which will define state of the art treatment planning and provide criteria, guidelines and methodology for its application and evaluation.

It is anticipated that multiyear, incrementally funded, completion type contracts will be awarded for a period of three years. Each increment will be for a 12 month period.

A preproposal conference will be scheduled approximately four weeks after the RFP issuance date, expected to be Nov. 9.

Contract Specialist: Barbara Shadrick
RCB Blair Bldg Rm 228
301-427-8737

RFP NCI-CM-57693-16

Title: Novel drug formulation and delivery systems

Deadline: Approximately Dec. 15

NCI is interested in receiving contract proposals from offerors who have innovative research ideas regarding improvement of the intravenous delivery of antitumor agents. Accepted approaches for enhancing drug solubility include salt formation, water miscible solvents, micellar solubilization, complexation, emulsions, and prodrugs. In spite of these techniques, several compounds have not been successfully formulated. The magnitude of the difference between inherent and desired solubility is frequently about 10 to the fourth. These compounds frequently present inadequate stability, and approaches to resolve these problems are also needed. The successful contractor shall evaluate the suitability of these research approaches in biologic tests pertinent to the intravenous route of administration, i.e. compatibility with blood cells and plasma, and acute toxic effects of the vehicle system including an estimation of the LD50 in mice. These studies are designed to obtain preliminary information on the pharmacologic effects of the drug delivery system per se (not drug loaded). Therefore, these studies need not be carried out in facilities conforming to the Good Laboratory Practices Act.

Compunds to be investigated may be either some of the following compounds, or structurally related model compounds such as NSC 278214, carbamic acid, (1-methylethyo)-, (5-(3,4-dichlorophenyl)-2,3-dihydro-1H-pyrrolizine-6,7-diyl)bis(methylene)ester; the anthracycline derivative, AD 32(NSC 246131); and NSC 267213, (4-methoxyphenyl)sulfonyl hydrozono) acetic acid.

The government anticipates one or two awards. The RFP will require that offerors submit two separate proposals, one at the two staff year level of effort and one at the three staff year level of effort. It is anticipated that resulting contracts will be awarded on an incrementally funded basis for a three year period, beginning on or about June 30, 1985. Each increment will be for a one year period.

Contract Specialist: Patricia Shifflett
RCB Blair Bldg Rm 228
301-427-8737

SOURCES SOUGHT

Title: Fungal fermentation

Deadline for documentation of capability: Nov. 13

The Div. of Cancer Treatment is seeking sources with the capability to provide and operate a microbiological and small extraction laboratory to ferment various genera of the fungal world for use by NCI in the systematic evaluation of their ability to produce antineoplastic agents. The ultimate goal is to provide NCI with the potential antineoplastic agents of novel structural types from fungal origin for use in the treatment of cancer in man.

Objectives of this project are to (1) ferment approximately 1,500 fungal cultures under various conditions and/or using many different substrates; (2) optimize and scale up certain cultures in 10-20 liter volumes as may be required by NCI; (3) filter sterilize and lyophilize broths and concentrate mycelial extracts.

Interested sources must demonstrate the following: (1) experience in all phases of laboratory scale fermentation (shake flask and/or microfermentor); (2) expertise to accomplish fungal culture isolation, maintenance and preservation, fermentation optimization, laboratory scale up production, filter sterilization of broth cultures, extraction of mycelia and concentration of extracts; (3) a proposed team which consists of (a) a principal investigator, trained in microbiology or mycology, at the PhD level or equivalent, with at least five years experience in the proposed area, with knowledge of fermentation concepts, in particular those related to growing fungi, and who will be assigned to this project approximately 50 per cent of the time, and (b) at least one microbiologist trained in microbiology mycology, including fungal taxonomy, at the MS or PhD level, with at least one year experience in maintenance and preservation of fungal cultures. Experience in antibiotic research would be helpful; and (4) availability of adequate facilities and equipment: (a) microbiology laboratory facilities, including area for extraction and concentration of extracts, (b) facilities for lyophilization and sample preparation, and (c) library.

Submit 10 copies of complete documentation which demonstrates ability. Each of the above requirements should be addressed specifically. This is not an RFP; responses should not include budgetary information.

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