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DEVITA ASKS PANEL FOR HELP ON FILLING VACANCIES, OBJECTS TO "EFFORT TO GET US BACK TO 1970 LEVEL"

NCI Director Vincent DeVita criticized "the consistent trend of smaller percentage increases in our budget than for all other NIH institutes" when he met with the President's Cancer Panel last week.

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In Brief

KENNEDY, WAXMAN MAY AGREE ON SIMPLE EXTENSION OF BIOMEDICAL RESEARCH AUTHORITY, INCLUDING NCI

KENNEDY-WAXMAN agreement on a simple extension of biomedical research authorities has a better than 50-50 chance before the lame duck session of Congress ends. The Senate has passed Sen. Edward Kennedy's bill and the House has approved Congressman Henry Waxman's measure, but they are so far apart on several substantive issues that no compromise is possible (***The Cancer Letter***, Sept. 26). Instead, a bill which merely extends for two years existing authorities, with no changes except in dollar authorizations, probably will be reported back to each house. The new dollar limits will be the 1980 fiscal year authorization plus increases for FY 1981 and 1982 based on inflation. Changes sought (and opposed) by Cancer Program advocates in the Kennedy and Waxman bills will have to await action by the new Congress. . . . **MEANWHILE**, it appears likely that no HHS appropriations bill will be passed in the lame duck session; rather, an extension of the continuing resolution which will expire Dec. 15, will be made to carry interim financing into January when the new Congress can work its will. . . . **KEY SUBCOMMITTEE** chairmanships in the Senate probably will go to Republicans Orrin Hatch of Utah and Charles Mathias of Maryland. Hatch will take over Kennedy's Health Subcommittee as well as the parent Labor & Human Resources Committee, insiders predict. They also say Mathias will replace Warren Magnuson as chairman of the Labor-HHS Subcommittee, choosing that one over several subcommittees on which he is the ranking Republican. . . . **GOODWIN INSTITUTE** for Cancer Research has moved into new quarters in Plantation, Fla. Thirteen research labs occupy half the 26,000 square feet, with the other half containing a primary genetic center for rodents operated under contract with NCI's Div. of Cancer Treatment. . . . **NEW BROCHURE**, *NIH Extramural Programs*, is available from the Office of Grants Inquiries, Div. of Research Grants, NIH, Bethesda, Md. 20205, phone 301-496-7441. It is a compendium of the scientific programs at NIH which award grants and contracts. It indicates current areas of research emphasis, highlights the special interests of each awarding component, and identifies specific NIH offices which may be contacted for further information.

UNFAIR HIRING ALLOCATIONS PREVENT DEVITA FROM FILLING KEY VACANCIES

(Continued from page 1)

DeVita also appealed to the Panel for help in getting some relief from HHS policies which are hampering his effort to recruit a new executive officer, four new division directors and his own deputy.

DeVita pointed out that the average budget increase for NIH this year is 5.8 percent, while NCI's increase is .1 percent. "The rationale for that escapes me, except that it seems to be an effort to get us back to the 1970 level," in relation to other components of NIH.

Under terms of the continuing resolution passed by Congress which provides interim financing for agencies which do not yet have completed appropriations legislation for the current fiscal year, NCI is limited to spending at the $1 billion, 1 million rate in the House passed bill. At that level, DeVita told the Panel, NCI will be unable to fund at recommended budgets both program project and cancer center core grants competing for renewal.

Instead, those grants will be funded at their 1980 levels plus a 7 percent cost of living increase. Those approved for funding during the first grant cycle of the fiscal year are in fact being funded under that formula. "We hope to fund at recommended levels, as we did last year," DeVita said. NCI started the 1980 fiscal year with the assumption that funds would not be available to support competing program projects and center core grants at recommended levels, but DeVita eventually was able to channel more money into those areas.

The traditional investigator initiated (R01) grants will be funded at recommended levels "down to a reasonable estimate of what we think we can support," DeVita said. Determing what the payline will be is difficult right now because the November cycle had the largest number of grant applications in the history of NIH.

NCI's final appropriation could be substantially less than $1.001 billion, with Ronald Reagan's transition team and the more conservative Congress talking about a 2 percent across the board budget cut. If NCI ends up with the $965 million recommended by President Carter in his revised budget, R01 competing renewals may be held to cost of living increases only, DeVita said.

DeVita's problem with filling the key vacancies is rooted in the government wide policy prevailing since last March of permitting agencies to fill only one vacancy for every two that occur. HHS departmental policy has been that vacancies could be filled from within the department without regard to one for two policy. But those recruited from outside the department, and outside government, fall into the one for two category.

Even that would not be impossible for DeVita to live with if the one for two policy were applied fairly to NCI. The institute is now 124 positions under the ceiling imposed by the Office of Management & Budget and 221 under the budgeted ceiling authorized by Congress. DeVita would be delighted, at least for the moment, if he could fill half the 124 vacancies on the one for two formula.

The problem is that hiring authority periodically is passed down from HHS to NIH. In splitting up those authorities, NIH has not given NCI its proper share.

"The Cancer Institute has a unique problem," DeVita said. "We've been going through a number of changes," and he cited improvements in the contracting process as one. "This requires bringing in new people. . . . Having done things to make changes, with positions open, now we can't fill them. Why make changes if we lose the positions?"

Panel Chairman Joshua Lederberg said, "This is a serious problem. You need people to manage a large, complex program." Panel members Bernard Fisher and Harold Amos agreed.

"We need those people on board soon," DeVita continued. The process of recruiting a new executive officer has been completed; DeVita needs only the permission to fill the vacancy. "I dearly need the executive officer. Our next highest priority is to go over position in the institute. I can't do that myself. I need the executive officer for that, and my executive officer is off sitting somewhere downtown."

Lederberg said he and his fellow panelists "sense the gravity of the situation."

"If we have to live with a restricted budget, we need our management team in place," DeVita said. "Top flight people want to come here, to get involved, despite the (lower) salaries. It's an opportunity to bring in fresh people, and we're in danger of losing it."

"We're not trying to break ceilings," Lederberg said. "We're just trying to get the tools that are needed."

"If we didn't have the Panel, I would be speaking out of school," DeVita said. "We are expected to go through channels, which I do. I've been making a pest of myself at Building 1 (NIH headquarters) and at the department. The feeling in the department is that NCI is large enough, that we have everything we need."

"You're not talking about a major budgetary change, just a small bottleneck," Lederberg said.

"It's a major bottleneck," Fisher said. "Vince has presented us with a major problem. It doesn't make sense. The government did all it could to get the best person for director, and it did that. Now they have to let him go to work. It's up to us to help him resolve this problem."

"I have full confidence in your directorship,"

Lederberg said. "You need the tools to do the job. I hope we can remove the roadblocks."

The President's Cancer Panel was created by Congress in the National Cancer Act of 1971 specifically to handle situations such as this—to hear, in public meetings, of any significant problems NCI may be encountering, and to inform the President of them. In almost every other federal agency, going public with problems caused by superiors in the heirarchy can bring on reprimands and even dismissal.

The NCI director is a Presidential appointee and he is charged by law to report problems to the Panel. In the past, the Panel has helped overcome similar roadblocks, with former Chairman Benno Schmidt going straight to the White House.

President Carter defers most health matters to his HHS secretary, and Lederberg told ***The Cancer Letter*** he would start with Patricia Harris in attempting to resolve DeVita's personnel problems.

Other issues discussed by DeVita and the Panel:

• National Toxicology Program. In view of the level 1981 budget (at least as voted by the House), the proposed $20 million increase in NCI's contribution over the $45 million the institute gave the program in 1980 is too much, DeVita said. "We've argued that a $20 million increase is not appropriate. We've taken steps to transfer NTP entirely to NIEHS, but it will be in our budget at least through 1982. That amount was taken out of our budget without our concurrence. . . NTP supports the regulatory agencies, and the regulatory agencies should pay more of the cost. We pay most of the cost because of the image in the department that NCI is fat and needs to be trimmed." DeVita added that the problem is not with NTP Director David Rall or his staff. "They have been reasonable."

• Grants and study sections. Objecting to the fact that so many grants are three year awards (instead of five years or longer), Lederberg said that some people "spend 25 percent of their time on grantsmanship, preparing for reviews. It leads to stultification." He objected to voting procedures on study sections "where one person has veto power by giving it a low score. I would rather have one person make the decision, rather than have the rule of unanimity. One has to adjust one's thinking, objective, and approach. It kills creativity."

"I'm totally in agreement," Fisher said. "My great concern about the research process is that it's an adversary process. There is no opportunity (in review) for scientific interaction. It is totally impersonal interaction, and that is detrimental to science. There should be in the process an opportunity for discussion of scientific issues."

"Our Div. of Extramural Activities director should play a role in that process," DeVita said. "We hope to get someone with a fresh look, who can discuss this with the Div. of Research Grants. It will require a diplomatic approach."

"Just reading the summary sheets," Amos said, "there is no question that conformism has high merits. If the work is immunology and you do what the gurus say should be done, you get ones. If you come up with something different and one person disagrees, you are in trouble. We can help them to do better, namely by being more open to new ideas, not just bet on sure things."

"I would like our new DEA director to discuss this with the Panel, determine what we can do administratively," DeVita said.

• Organ site programs. "I've been bombarded with questions," Fisher began.

"Don't tell me," DeVita interjected. "The Breast Cancer Task Force. I've heard from every women's group in the country." His problem began when he cited the BCTF as an example of how an organ site program was developed to stimulate research in a field where an insufficient amount of work was being done. With the task force successful in stimulating a vast amount of work, DeVita has said that NCI should consider whether it and other similarly successful organ site programs should be reduced in scope or phased out.

"I used the Breast Cancer Task Force as an example. I'll keep using it as an example, and that flatters the program. . . . We have no intention of cutting out breast cancer research. It is our shining example. . . but people are overlooking one point. If the budget goes down, it will not be possible to keep everything."

GUIDELINES WORKING GROUP AGREES: NO MULTIPLE GRANTS, $750,000 BASE

Members of the Working Group on Guidelines of NCI's Div. of Resources, Centers & Community Activities Board of Scientific Counselors reached agreement on a number of issues in proposed revisions of guidelines for cancer center core grants, including tentative approval of a new plan to limit the size of the grants as reported in ***The Cancer Letter*** last week.

The group ran out of time before completing section by section consideration of the proposed changes, but they did agree on three changes recommended by Centers Program staff and concurred in previously by the National Cancer Advisory Board Subcommittee on Centers, with some modifications:

• No multiple core grant awards to a single institution. Three institutions presently have more than one core grant, and there is no reason to change them, DRCCA Acting Director William Terry said. But staff has feared that with the present guidelines, a small group of investigators within a center could put together an independent application for support, defeating one of the primary purposes of the core grant. The new guideline provision states:

"A cancer center support grant is designed to sup-

port those activities that will consolidate and focus cancer related research efforts in a single administrative and programmatic structure. Applications for additional separate CCSGs will not be accepted from groups, departments or other units of institutions funded with CCSGs. Increases in core support will be provided only through an existing funded center. CCSG support is intended to contribute to stability and development of the center and to facilitate administrative and programmatic control of center activities."

The proposal states that in the case of a statewide university system or similar organization, "institution" is defined as a major unit of such a system rather than the system as a whole.

Working Group Chairman Charles Moertel said he would favor the status quo, with general agreement that there would be no additional multiple grants. "However, if someone really had a persuasive case, he could approach this Board or the National Cancer Advisory Board, and attempt to justify it."

Working Group member Harry Eagle suggested that language be added to the provision that there will be no additional multiple core grants "except in unusual circumstances." The group accepted the provision with Eagle's modification.

• Qualifying criteria for a core grant. These were among the most controversial of the new proposals when they were first submitted by NCI staff. Subsequent modifications and discussion appear to have softened much of the opposition.

The first criterion is that a center must have "an adequate base of established programs of high quality in laboratory and/or clinical cancer research. The high quality of the programs should be evident from the fact that they have been awarded support through national peer reviewed competition, such as in the form of NCI grants and contracts. In order to apply for a CCSG, an institution must have a base of at least $750,000 direct costs in peer reviewed research and research training support. This requirement is not meant to imply that the center must control all of these supported programs."

When first submitted, the $750,000 base was limited to NCI grants and contracts. Center executives objected strenuously, and that has been broadened to include other support. Here is how the definition now stands:

NCI awards identified as R01, R10, R26, R23, P01 research grants; K04, T32 and F32 training grants; and N01-CB, N01-CP and N01-CM research contracts. Contracts that support primarily the production of materials in support of research will not be included. The base also may include research grants and awards from the American Cancer Society, and 25 percent of research grant and training support from other NIH institutes and the National Science Foundation. Contracts from sources other than NCI may not be included.

The NCAB subcommittee had agreed with the concept of a limit based on research support but deferred to the DRCCA Board on determining the amount and nature of the base.

Albert Owens, director of the Johns Hopkins Cancer Center and representing along with Timothy Talbot the Assn. of American Cancer Institutes at the meeting, said AACI had agreed that the amount of national peer review supported research was acceptable in defining the base.

Terry pointed out that NCI cancer control grants are not included in the base, and neither are clinical cancer education grants.

Moertel said that some cancer control supported projects are peer reviewed research. "Why should they be excluded?"

"Much of cancer control is not research and this core grant is for research support," Terry said. "There are other mechanisms for cancer control support."

Moertel said his center (Mayo Clinic) has a grant for study of the physics of joint replacement. "That has nothing to do with our cancer control support."

Terry said there are some centers where there is almost no research and where, if cancer control support were included in the base, it would put them over the limit. "We could ask the staff to review these on an individual basis, but that adds to the complexity."

"We could include only those cancer control grants with a major research component," Eagle said.

Moertel pointed out that some work at cancer centers is supported by foundations and which does not have a peer review requirement. "Why not include them? Much of it is high quality research."

"If it is not peer reviewed, how do we know if it is high quality?" Terry said. "It is difficult to measure."

Ray Morrison, program director in the Cancer Centers Branch, said that the $750,000 figure was not "entirely arbitrary." Only one of the 61 existing core grants would be borderline with that as the minimum base.

Owens said AACI members had a variety of opinions on what the amount should be, "but we had no alternate solution."

The Working Group voted to accept the $750,000 base, with the definition of the components it could include as proposed by staff, with Eagle's modification, that it also include cancer control grants with major research components.

The group accepted without change two other provisions:

—"There must be research activity in a variety of disciplines and there must be evidence of a high degree of interdisciplinary coordination, interaction and cooperation among center members. Scientists or clinicians, each pursuing his or her research effort independently so that interdisciplinary interactions are

limited or nonexistent, cannot be considered to be functioning collectively as a center. Such individuals are supported more suitably by other mechanisms such as individual project grants. A center's core support should facilitate creative interactive activities such that the whole is greater than the sum of its parts, and should increase efficiency by providing support for shared equipment and centralized multiuser facilities.

"Examples of suitable activities for a cancer center include, but are not limited to: collaborative, interdisciplinary laboratory research efforts; collaboration between laboratory and clinical investigators; publications resulting from such efforts; significant sharing of facilities and equipment; seminars involving all center members; multidisciplinary clinical research or trials."

—"The center must have appropriate and adequate organization and facilities for the conduct and evaluation of center activities. The facilities and organizational arrangements should facilitate collaboration among constituent programs."

Provisions still to be considered in the section on qualifying criteria are the center director's authority and institutional commitment.

Other provisions—some of which remain controversial—still to be considered by the Working Group include the requirement for submission of letters of intent, with details on what they should include and NCI staff authorized to disqualify those (and thus not permit submission of applications) which do not meet criteria in the guidelines.

Also still to be considered by the Working Group are:

—Qualifying requirements for salary support (in addition to the tricky problem of staff investigator salaries).

—Shared resources and services, and requirements for recovering some of the costs from individual grants.

—Eligibility of such costs as clinical research and hospitalization, alteration and renovation, for payment out of the core grant.

—Detailed instructions on how to prepare the core grant application.

Meanwhile, AACI's president-elect issued a statement making it clear that the organization has not endorsed the Working Group's proposal for limiting the size of core grant renewal budgets.

Richard Steckel, director of the UCLA Jonsson Comprehensive Cancer Center, referred to the proposal as a "freeze" and indicated there would be considerable opposition to it from AACI members.

"Dr. Owens and Dr. Talbot attended the recent Bethesda meeting of the Working Group on core guidelines as vitally interested center directors who are also AACI members," Steckel said in a statement to ***The Cancer Letter.*** "Their reported comments on the proposed plan to freeze upper limits of core grant renewals at this year's levels were not intended to reflect the views of the directorate or membership of AACI. The freeze is a new proposal which was first raised at the recent Bethesda Working Group meeting and accordingly has not been considered by the AACI directorate or its membership. Considerable opposition to this proposal might be anticipated."

The proposal would limit core grant renewal applications in total amount of funds requested to that amount they receive in the final year of their current grant plus a fixed percentage, to be determined based on NCI funds available. Budget requests would be subject to revision in peer review. "Bonuses" up to but not exceeding the fixed percentage increase could be awarded based on priority scores, with similar deductions possible for those with lesser scores.

KNUDSON NAMED PRESIDENT OF FOX CHASE, TALBOT BECOMES BOARD VICE CHAIRMAN

Alfred Knudson Jr. has been named president and chief executive officer of Fox Chase Cancer Center by the center's board of directors. Knudson will direct the affairs of the center's two component institutions, the American Oncologic Hospital and the Institue for Cancer Research. He will continue as director of the institute, a post he has held since 1977.

Former President Timothy Talbot Jr., who has headed the center since it was formed in 1974, becomes vice chairman of the board. Before he was the center's president, Talbot was director of the Institute for Cancer Research, a post he held for almost 20 years. It was during this time that the institute achieved recognition as one of the outstanding research institutions in the world. Talbot was responsible for bringing many of the senior scientists now on the staff, including five members of the National Academy of Sciences. One of these is Baruch Blumberg, who received the Nobel Prize for medicine in 1976.

Edward Roach, who has been president and chief executive officer of American Oncologic Hospital, will now be chairman of the hospital board. Paul Grotzinger will serve as interim medical director of the hospital and will continue as chief of surgery.

G. Morris Dorrance Jr., chairman of the center's board, said in making the announcement, "Our directors, without exception, believe that the measures which have been announced today will greatly strengthen the center. They will help to maintain its stature among cancer care institutions and in the fields of basic and clinical research. We are especially grateful that Dr. Talbot and Dr. Grotzinger will continue to play an active and important role in center affairs."

He said that the new organizational structure will permit a better exchange of ideas and programs, and insure a more effective use of physical and human resources.

Knudson, 58, is a physician and a scientist. His research has focused on the genetics of human cancer and of childhood cancers in particular. He came to Fox Chase from the Univ. of Texas Graduate School of Biomedical Sciences in Houston, where he was dean and professor of medical genetics and professor of pediatrics in its School of Medicine. He also served as professor of biology and pediatrics at the M.D. Anderson Hospital & Tumor Institute.

Contract Awards

PHASE 1-2 TASK ORDERS FOR BRMS AWARDED TO 12 INSTITUTIONS

Fourteen task orders totaling nearly $2.6 million have been awarded by NCI's Div. of Cancer Treatment to 12 institutions for phase 1 and 2 studies of biological response modifiers.

The awards were made after competition among 27 institutions which were selected to receive "master contracts" for phase 1 and 2 evaluation of biological response modifiers. Under the mast contractor-task order plan, institutions which wish to participate are peer reviewed and if found "technically acceptable" (that is, capable of doing the specified work) are placed in a pool. When NCI subsequently has a task which fits that category, the RFP is circulated among those master contractors. Competition is relatively simple and awards based on what NCI determines will be the best performance for the price.

Master contracts for phase 1 and 2 testing of biological response modifiers were awarded to Mayo Clinic, M.D. Anderson Hospital, Ontario Cancer Institute, Illinois Cancer Council, Wayne State Univ., Univ. of Pittsburgh, Univ. of Cincinnati, Univ. of Southern California, Univ. of Minnesota, Dartmouth College, Hahnemann Medical College, Roswell Park Memorial Institute, Fox Chase Cancer Center, Institute de Cancerologie, Temple Univ., Duke Univ., Georgetown Univ., Univ. of Wisconsin, Sidney Farber Cancer Institute, UCLA, Sloan-Kettering Institute, Northern California Cancer Program, Fred Hutchinson Cancer Research Center, George Washington Univ., Univ. of California (San Diego), Vanderbilt Univ., and Ohio State Univ.

Task order awards went to:

–Univ. of California (San Diego), thymosin, $223,422.

–George Washington Univ., thymosin, $183,258.

–Fred Hutchinson Cancer Research Center, thymosin, $183,258.

–Sloan-Kettering Institute, fibroblast interferon, $202,043.

–Northern California Cancer Program, leukocyte interferon, $125,463.

–Vanderbilt Univ., MVE-2, $94,038.

–Ohio State Univ., MVE-2, $98,635.

–Georgetown Univ., leukocyte interferon, $174,530.

–Sidney Farber Cancer Institute, leukocyte interferon, $246,078.

–Duke Univ., leukocyte interferon, $249,865.

–Univ. of Wisconsin, fibroblast interferon, $235,956.

–UCLA, leukocyte interferon, $249,963.

–Northern California Cancer Program, thymosin, $80,127.

–Sloan-Kettering Institute, thymosin, $160,000.

Four task orders for phase 1 evaluation of drugs with pediatric patients have been awarded by NCI to institutions selected from a master list of those approved previously for such tests with pediatric cancer patients. They are:

–M.D. Anderson, $69,519, for phase 1 studies of 6-diazo-5-oxo-L-norleucine (DON).

–Ohio State Univ. Children's Hospital Research Foundation, indicine-N-oxide, $69,537.

–Memorial Hospital-Memorial Sloan-Kettering Cancer Center, $61,446; and Childrens Hospital of Los Angeles, $44,977, both for testing AZQ-aziridynylbenzoquinone.

Other contract awards announced recently include:

Title: Chemoprevention of epithelial cancer by reinoids
Contractors: Middlesex Hospital Medical School, $776,239; Michigan State Univ., $299,363, and IIT Research Institute, $589,712.

Title: Study of the DuPont Chambers Works Bladder Cancer Screening Program
Contractor: E.I. DuPont & Co., Deepwater, N.J., $60,480.

Title: Production of antineoplastic compounds using fermentation, biotransformation and cometabolism techniques
Contractor: Bristol Laboratories, Syracuse, N.Y., $663,000.

ANNOUNCEMENT

Basic and clinical research studies on ocular melanoma

GRANT APPLICATIONS–National Eye Institute and National Cancer Institute

The Retinal and Choroidal Diseases Branch of NEI in conjunction with the Cancer Biology Branch and the Cancer Therapy Evaluation Program of NCI encourage submission of grant applications for research on ocular tumors. Specifically, the institutes would like to receive applications for research which have

potential for expanding knowledge of the biology, natural history, epidemiology, diagnosis, and treatment of ocular melanoma, as well as the natural history, management and biology of this disorder.

It is expected that such information will add to understanding of how to manage ocular melanoma patients appropriately. Research on the characteristics of tumor cells is expected to provide information on ocular melanomas as well as on other pigmented cells with abnormal growth properties.

Ocular melanoma is the most common primary intraocular malignancy in adults and comprises over 80 percent of all eye malignancies. In the U.S., the annual incidence of ocular melanoma is six cases per million people. Those tumors not only cause blindness, but can also cause death if metastasis occurs. Because of the importance of ocular melanoma, NEI upon recommendations of the National Advisory Eye Council, convened a task force in April 1980 to review critically the recent scientific literature on this subject and to recommend what research is most needed to solve some of the critical problems associated with this disease. (Proceedings from this meeting were published in the November 1980 issue of the *American Journal of Opthalmology.*)

Listed below are some examples of research areas which are expected to lead to better understanding of the biology of uveal melanomas and to determining how to manage this ocular disorder appropriately.

—Epidemiological studies to determine the risk factors associated with uveal melanoma.

—Natural history studies to determine the nature and progression of this disease.

—Development of techniques and biological assays to monitor tumor growth serially in vivo.

—Investigations to determine whether the histopathological features of the tumor can be correlated with the natural history of the disease or with prognosis.

—Development of methods to improve the cellular criteria for categorizing tumors by the Callender classification and to expand the Callender classification to an ultrastructural level.

—Randomized controlled clinical trial to determine the effect of enucleation on the natural history of primary ocular melanoma. Patients eligible for the study should be limited to those with a poor prognosis, such as patients with large melanomas or those having melanomas with extrascleral extensions.

—Studies to define the immunologic status of the individual in relation to efficacy of treatment of disease progression or regression.

—Investigations of the biological, biochemical, and immunologic properties of uveal melanomas utilizing established cell lines and appropriate animal models.

Applications for grants are invited from investigators in all relevant disciplines, as well as from investigators new to this problem area. Applications which propose collaborations between basic and clinical research scientists are particularly encouraged.

Applications will be received by the NIH Div. of Research Grants, referred to an appropriate initial review group for scientific merit review, and assigned to the appropriate institute. Applications submitted in response to this announcement will be reviewed and funded on a nationwide basis in competition with all other research grant applications, and in accord with the usual NIH peer review procedures. Applications proposing clinical trials will be evaluated according to criteria developed by NEI (copies available from NEI), and should include a clear statement of the hypothesis to be tested, detailed rationale for the proposed study, an indication of the number of patients needed for statistically valid results, the anticipated recruitment population and location, and an efficient network for sharing resources. A detailed manual of procedures is required for all proposed clinical trials and must be submitted as part of the application.

Applications will be accepted in accordance with the usual NIH receipt dates for new applications.

Applications should be submitted on form PHS 398, which is available in the business or grants and contracts office at most academic and research institutions, or from DRG, NIH. In responding to this program announcement, the phrase "NEI and NCI Ocular Melanoma" should be typed in the space provided on page one of the application.

NEI and NCI encourage potential applicants to communicate with their staffs. Inquiries concerning this announcement should be directed to one of the following:

Bettie J. Graham, PhD., Retinal-Vascular Disorders Program, National Eye Institute, Room 6A52, Bldg 31, Bethesda, Md. 20205, telephone 301-496-5983.

John S. MacDonald, MD, Cancer Therapy Evaluation Program, National Cancer Institute, Rm 4C37, Landow Bldg., Bethesda, Md. 20205, phone 301-496-6138.

Brian Kimes, PhD, Chief, Basic Cancer Biology Section, or Colette Freeman, PhD, National Cancer Institute, 5333 Westbard Ave., Bethesda, Md. 20205, phone 301-496-7028.

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 Contracting Officer or Contract Specialist named, Research Contracts Branch, National Cancer Institute, Blair Building, 8300 Colesville Rd., 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-17375

Title: *Study of the pharmacokinetics of anticancer drugs*
Deadline: *Approximately Jan 20*

The Developmental Therapeutics Program, Div. of Cancer Treatment, is seeking a contractor to collect pharmacokinetic data on new and established antitumor agents in patients undergoing treatment for nonhematologic malignant disease and to analyze these data for individual variability which can be correlated with clinical response or some other pharmacologic parameter.

Specifically, these studies will be primarily concerned with the measurement of drug and/or metabolite levels in the plasma with time (ug/ml x min) after a standard dose (expressed as mg. per meter square of body surface area) and route of administration of the drug. Apparent volume of distribution and plasma protein binding should be determined. Studies may also require measurement of urinary, biliary, and fecal excretion of drug and/or metabolites.

Measurement of other fluids (e.g. cerebrospinal fluid) and tissues may be necessary. A minimum of 25 patients per drug per 6 months must be available to ensure adequate statistical documentation of individual variability in pharmacokinetic behavior. It is expected that two drugs will be evaluated annually and these are to be selected by the project officer in consultation with other investigators of DCT and the principal investigator.

Information on the analytical methodology for the measurement of the drug and/or metabolites in body fluids and tissues will generally be provided by NCI. Circumstances may arise which require modification, use of other analytical procedures, or development of new analytical procedures. One award will be made for a three-year period.

Contracting Officer: Clyde Williams
Cancer Treatment
301-427-8737

RFP NCI-CM-17485

Title: *Synthesis of radiosensitizing agents*
Deadline: *Approximately Jan 20*

The Drug and Synthesis & Chemistry Branch of the Developmental Therapeutics Program (DTP), Div. of Cancer Treatment, is seeking the services of an organization with demonstrated expertise involving the synthesis of radiosensitizers and their preliminary biological evaluation. The objective is to continue to support the design, synthesis, evaluation and development of novel radiosensitizers, a new area of opportunity that has been identified by DCT.

Radiosensitizers are chemical that will selectively radiosensitize hypoxic tumor cells in combination with radiotherapy. The ideal substance would be expected (a) to mimic completely at nontoxic levels the radiosensitizing effect of molecular oxygen; (b) to diffuse rapidly into the hypoxic regions of tumors after administration, and (c) to be nontoxic to normal tissues.

Since nitroimidazoles as a chemical have have been well studied, only limited, well supported work in this area is envisioned. The synthesis of novel compounds that might act as radiation modifiers through mechanisms different from the electron affinic hypoxic cell radiation sensitizers will also be undertaken.

Understanding and awareness of the opportunities and problems of radiosensitizer drug development are necessary. The research team must have the capability to synthesize and evaluate the radiobiological response of radiosensitizers, and to correlate radiobiological response with physical-chemical parameters. The principal investigator must have a PhD in the field of organic chemistry or a PhD in the field of radiation chemistry and the team leader(s) assigned to the in vitro and in vivo tasks must be a DVM with experience in radiation biology or a PhD in the field of radiobiology.

Laboratories should have modern equipment and facilities for the synthesis, analysis, and radiobiological evaluation of compounds and appropriate library facilities must be within the organization or readily available. An adequate radiation source, animal quarters, and cell biology facilities must be located at the same site. The following minimum requirements are:

1. Physical-chemical analytical equipment—UV, IR, NMR, HPLC and polaragraphic or pulse radiolysis equipment to measure electron affinities.
2. Radiation (Co^{60}, Cs^{137} or orthovoltage x-ray) facilities for use with mice and cell cultures.
3. Facilities and equipment to maintain a conventional rodent colony (primarily mice) which will hold a minimum of 3,000 mice a year for periods of one to six months.

A three year period of performance is projected with the following level of effort for each year of six staff years.

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