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## ADMINISTRATION SEEKS AUTHORIZATION BILL REPEALING NATIONAL CANCER ACT, OTHER NIH SPECIAL AUTHORITIES

Just when the biomedical research community had concluded that the Reagan Administration had pulled off one of the all time dirty tricks with its order to fund some grants in 1986 and 1987 with 1985 money,
(Continued to page 2)

*In Brief*

### HCFA OFFERS GRANTS FOR RESEARCH ON IMPACT OF DRGs; ACCC LEADERS DISPUTE HCFA CHIEF

**HEALTH CARE** Finance Administration is supporting research on the impact of prospective payment (diagnosis reimbursement groups) including effects of DRGs on cancer clinical research. Grants and cooperative agreement awards are available. Contact Frances Larivieri, HCFA, Office of Research & Demonstrations, Office of Operations Support, Area 2-B-12, Oak Meadows Bldg, 6325 Security Blvd., Baltimore, Md. 21207, phone 301-594-7476. Meanwhile, the Eastern Cooperative Oncology Group released results of a small study it conducted on determining the proportion of patients on ECOG protocols that would have been affected by DRGs in 1983. The answer: three per cent. However, the DRG system had not been fully implemented in 1983, which may have affected the numbers. Also, patients in the four waivered states were excluded, although reimbursement is also limited in those states despite their exemption from the DRG system. Finally, a recent article in "JAMA" (Feb. 1) by John Yarbro, president of the Assn. of Community Cancer Centers, and ACCC Executive Director Lee Mortenson supported the case for "DRG 471," ACCC's answer to the problem. DRG 471 would be a category for all patients in NIH approved clinical trials, for which reimbursement would be on a cost basis. Yarbro and Mortenson contend that while HCFA has not in the past paid for the research costs of data collection and analysis, experimental drugs, etc., it has reimbursed for patient care costs, including extra costs required for protocol patients, such as more intensive care. That point was disputed in an accompanying editorial by Carolyne Davis, HCFA administrator, who said HVFA never has and is forbidden by law from reimbursing those costs. . . . **WILLIAM BLOT,** who has been chief of the Analytical Studies Section in NCI's Environmental Epidemiology Branch, has been appointed chief of the Biostatistics Branch by Div. of Cancer Etiology Director Richard Adamson. . . . **HENRY PITOT,** director of the McArdle Laboratory for Cancer Research and former chairman of the National Cancer Advisory Board, is the new chairman of the selection committee for the annual Bristol-Myers Award for Distinguished Achievement in Cancer Research. He succeeds Albert Owens, director of the Johns Hopkins Oncology Center.

## WHITE HOUSE SEEKS NATIONAL CANCER ACT REPEAL; CONGRESS WON'T GO ALONG

(Continued from page 1)
thus slashing 1,500 grants from the number NIH can fund this year, another bomb was dropped on them this week: the Administration intends to seek only biomedical research authorization that relies on the broad language of Section 301 of the Public Health Services Act and which strips NCI and the National Heart, Lung & Blood Institute of their special authorities. Specifically excluded would be renewal of the National Cancer Act. The Administration's decision was announced at a retreat of NIH institute directors.

That would mean, in effect, the end of the National Cancer Program. The President's Cancer Panel would be abolished. The National Cancer Advisory Board would revert to the status of an NIH advisory council, with reduced responsibilities and appointment by the HHS secretary rather than the President. The NCI and National Heart, Lung & Blood Institute directors would be secretarial rather than presidential appointments. The NCI bypass budget would no longer exist. The special authorities in the National Cancer Act for cancer centers, public education, cancer control, and nutrition research would end. NCI's authority to review its own grants and contracts (except RO1s) would end.

Cancer research would be squeezed back under the thumb of NIH which, with the pressures exerted by other constituencies would inevitably deemphasize cancer.

It was an arrogant, mindless decision which ignores history and the vast progress in biomedical research that is a direct result of the National Cancer Act of 1971.

NCI Director Vincent DeVita has for several months been telling anyone within hearing that the most important business facing the cancer research community this year was renewal of the National Cancer Act. Last week, he told the Div. of Cancer Etiology Board of Scientific Counselors that HHS had decided to oppose all NIH reauthorization. Afterward, he declined further comment. The announcement at the director's retreat confirms that the intent to return to pre-1971 authorization is now an official White House policy.

The policy will not go unchallenged.

"The American Cancer Society strongly supported the National Cancer Act of 1971 and worked hard for its passage by Congress and signature into law by the President," ACS President Robert McKenna said. "The Society repeatedly worked to secure its renewal each time it has come up since that time. This unique legislation has brought more benefits to the people of this nation than any other health research legislation in our history. Progress against cancer continues to accelerate rapidly because of the National Cancer Act. A great many Americans are alive and well today as productive members of society who, without the benefits of the National Cancer Act, would not be with us.

"To summarily repeal this law as part of action to eliminate NIH authorizations," McKenna continued, would abruptly and severely retard progress against cancer and would work against the interests of the cancer patient. The American Cancer Society strongly opposes repeal of the National Cancer Act and will work vigorously to secure renewal of the current law, or passage of legislation which will assure continuation of the same level of independence and the same special authorities for the National Cancer Institute contained in the current law."

The National Cancer Program was created by Congress and has been nurtured and defended by Congress against attacks by every Administration since 1971. It has been a bipartisan effort, and spokesmen for the key health legislators in both houses indicated they would pay little attention to HHS or White House opinions on this issue.

"We will introduce legislation similar to that which was vetoed last year," a spokesman for Sen. Orrin Hatch (R.-Utah), chairman of the Labor & Human Resources Committee, said. President Reagan pocket vetoed the reauthorization bill last year after Congress had adjourned, precluding any opportunity to override. There may be a few minor technical amendments, possibly including those sought by NCI which would maintain its authority to review its own grants, left out of last year's bill. "There is no interest on Sen. Hatch's part in turning back the clock to 1971. We're not interested in repealing the National Cancer Act. We will produce a bill which is quite favorable to the cancer research community."

In the House, a spokesman for Congressman Henry Waxman (D.-Calif.), chairman of the Health Subcommittee of the Committee on Energy & Commerce, said the vetoed bill would be reintroduced intact, again possibly with minor technical amendments. "It unanimously passed both houses," he pointed out, a suggestion that if the President vetoes it again, it be overridden.

Reagan vetoed the bill, he said, because it established two new institutes at NIH, one for arthritis and another for nursing research, and because it added unnecessarily to codification of certain authorities.

NCI executives were not totally dismayed by the veto because the bill did not include the provisions of the National Cancer Act which authorized NCI to review its own program project, cancer center, cancer control, construction and training grant applications.

## 5,000 GRANTS A FLOOR, NOT CEILING, OMENN SAYS; 76 ON FIRST "HONOR ROLL"

The Office of Management & Budget has attempted to justify its action in limiting NIH to 5,000 new and competing renewal grants this year by contending that it was only living up to the policy of several years standing that grants would be stablized at 5,000 a year. The 5,000 figure, OMB claims, is supposed to be a ceiling as well as a floor.

Not so, says one of the former Administration officials who participated in establishing the policy.

Gilbert Omenn, dean of the School of Public Health & Community Medicine at the Univ. of Washington, was one of President Carter's science advisors when the 5,000 grants policy was established. "There should be no doubt in anyone's mind, that 5,000 grants is a floor, not a ceiling," Omenn said last week at the meeting of the Div. of Cancer Etiology Board of Scientific Counselors, of which he is a member. "I was involved in that decision." It was made, he said, after NIH funded only 3,800 new and competing grants in 1977. "We agreed that 5,000 should be the minimum, to be funded if necessary through economies in other areas at NIH. There is no question, 5,000 was a floor."

OMB spokesmen have accused Congress of breaking faith with the Administration by going over the 5,000 number with FY 1985 appropriations, putting enough money in the RO1-PO1 pool to fund 6,500 grants.

NCI Director Vincent DeVita, who was present at the DCE Board meeting when Omenn made those remarks, said the policy "was a mistake. OMB is wrong to establish any figure. First, it did become interpreted as a ceiling, and in any case, 5,000 does not take into account things that might be happening in subsequent years." Last year, DeVita objected to the Administration's abortive attempt to support funding 5,000 grants by gutting the cancer centers program.

"I'm concerned that if we continue to go in this direction, there won't be any biomedical research 10 to 20 years from now," Board member Allan Conney said. "If only one fourth or one third of approved grants are funded, why should a young person go into it?"

**Seventy six investigators, including some of the nation's outstanding cancer scientists, may be asking themselves that question.**

They are grant applicants who, in any other year, would have been funded without question because of the superb priority scores their applications achieved—from 159 to 175. But because of OMB's decision to force NIH to reduce the number of grants to 5,000 by funding some FY 1985 grants for three years with 1985 money, the payline will be 158. That decision did not affect grantees approved for funding in the first cycle of 1985, and those were paid at least through 170, in some cases 175. The second cycle, however, will be hit hard, the third cycle even harder, with NCI slated to take a cut of 240 grants.

The list of 76 martyrs to the Administration's folly might be considered an honor roll of cancer scientists. They are, by state:

Alabama

David Baker, Univ. of Alabama, with a priority score of 159.

Arizona

Robert Roemer, Univ. of Arizona, 162.

California

Edward Profio, Univ. of California (Santa Barbara), 161; Walter Schimmerling, UC (Berkeley), 162; Richard Moran, Los Angeles Childrens Hospital, 162; Nicholas Petrakis, UC (San Francisco), 166; Edward Acton, SRI International, 167; John Whiteley, Scripps Clinic Research Foundation, 167; Debrah Spector, UC (San Diego), 167; Howard Sussman, Stanford, 169; John Elder, Scripps Clinic, 172; Dennis Dean, UC (San Diego), 174; Mary Claire King, UC (Berkeley), 174; Barbara Mills, UCLA, 175.

Colorado

Lewis Schiffer, AMC Cancer Research Center, 161.

Delaware

Daniel Simmons, Univ. of Delaware, 165.

Florida

Kurt Hofer, Florida State Univ., 159; Robert Pauley, Univ. of Miami, 171.

Illinois

Geoffrey Cordell, Univ. of Illinois (Chicago), 163; Dan Vesselinovitch, Univ. of Chicago, 175.

Indiana

Rita Young, Ball State Univ., 166; James Morre, Purdue, 169.

Iowa

Marit Nilsen-Hamilton, Iowa State Univ., 163; Robert Woolson, Univ. of Iowa, 168.

Kentucky

Marion Steiner, Univ. of Kentucky (Lexington), 161; Stephen Zimmer, Univ. of Kentucky (Lexington), 163.

Maryland

Jeffrey Harmon, Uniformed Univ. of Health Sciences, 160; Thomas Kensler, Johns Hopkins Univ., 171.

Massachusetts

John Wagner, Dana-Farber Cancer Center, 169; Barry Snider, Brandeis Univ., 161; Ganesa Ogeeswaran, Boston Univ., 164; Thomas Griffin, Univ. of Massachusetts Medical Center, 165; Mark Greene, New England Medical Center, 165; Richard Gange,

Massachusetts General Hospital, 166; Madhukar Pathak, Harvard, 174; William Haseltine, Dana-Farber, 174; Michael Czech, Univ. of Massachusetts, 161; Emil Frei, Dana-Farber, 171; Steven Burakoff, Dana-Farber, 179.

Michigan

Steven Tanis, Michigan State Univ., 162.

Minnesota

Thomas Hoye, Univ. of Minnesota, 159; James O'Leary, Univ. of Minnesota, 162; Kathryn Held, Mayo Clinic, 163.

Missouri

James Swierkosz, St. Louis Univ., 160.

North Carolina

Randy Jirtkle, Duke Univ., 168.

New Hampshire

Thomas Curphey, Dartmouth, 171.

Oregon

Richard Scanlan, Oregon State Univ., 169.

New Jersey

Alice Liu, Rutgers, 161; Malcolm Steinberg, Princeton, 166.

Ohio

Thomas Pretlow, Case Western, 162.

Pennsylvania

James Pipas, Univ. of Pittsburgh, 160; Renato Iozzo, Univ. of Pennsylvania, 161; Sam Sorof, Institute for Cancer Research, 162; Dennis Leeper, Thomas Jefferson Univ., 162; David Boettiger, Univ. of Pennsylvania, 163; Mary Conner, Univ. of Pittsburgh, 165; Madeline Joullie, Univ. of Pennsylvania, 168; Prasanta Chakraborty, Medical College of Pennsylvania, 169; Frank Waterman, Thomas Jefferson Univ., 173.

Rhode Island

Shih-Hsi Chu, Brown, 164.

South Carolina

Aubrey Thompson, Univ. of South Carolina, 163.

Tennessee

Leas Huang, Univ. of Tennessee (Knoxville), 165; Kenneth Hande, Vanderbilt Univ., 163; Lee Washburn, Oak Ridge Associated Universities, 166.

Texas

Shiang Yang, Texas Tech Univ., 162; Freddy Hendler, Univ. of Texas (Dallas), 162; Michael Brattain, Baylor, 165; Harold Dunsford, Univ. of Texas Health Science Center (Houston), 165; Naguib Samaan, Univ. of Texas System Cancer Center, 169.

Utah

Chris Ireland, Univ. of Utah, 168.

Washington

Christopher Badger, Fred Hutchinson Cancer Center, 166; Paul Neiman, Hutchinson, 168; James Lewis, Hutchinson, 174.

Virginia

Prem Veer Reddy, Univ. of Virginia, 165.

Wisconsin

James Zagzebski, Univ. of Wisconsin (Madison), 166.

Foreign

Umberto Veronesi, UICC, 160.

Steven Burakoff of Dana-Farber was included in the "honor roll" despite a funding score slightly above the previous payline because his grant is considered by NCI to be a very important program project. The possibility still exists that Burakoff's PO1 could be funded as an exception, a prospect that applies to any of those listed.

The statement made last week by Chairman Armand Hammer of the President's Cancer Panel that President Reagan"s science advisor, George Keyworth, had said he would ask the President to consider an FY 1985 supplemental appropriation for NCI was in effect denied this week by Keyworth's office.

Bruce Abell, spokesman for the Office of Science & Technology Policy which Keyworth heads, told **The Cancer Letter** that Keyworth had met with Hammer at the latter's request "to discuss some recent promising clinical results that had been brought to Dr. Hammer's attention (the very early results from the study by NCI's Steven Rosenberg using interleukin-2). Dr. Keyworth promised to look further into the results and said that if it appeared that the particular research was on the verge of a major breakthrough and if substantial additional funding would speed that process, then he would see what could be done to find that support. We are following up on that meeting."

## FACILITIES SURVEY FINDS $25 MILLION A YEAR NEEDED FROM NCI BY YEAR 1990

Preliminary findings of the cancer research facilities survey commissioned by Armand Hammer and the American Cancer Society conclude that NCI support of $25 million a year for the next five years will be required to meet currently identified needs in the year 1990.

The survey, carried out under contract with Hammer and ACS by CDP Associates, found that 6.1 million additional net square feet which would cost an estimated $1.5 billion. That figure is an extrapolation to all 197 institutions eligible for NCI construction support, made from 84 institutions which participated in the survey; the estimate of required NCI support applies only to those institutions which responded to the survey, and it amounts only to NCI's share of an estimated $580 million total the responding institutions have identified for alteration, renovation, completion of shell space and new construction. Needs include basic and clinical research and animal facilities.

## DCT BOARD RECOMMENDS POLICY CHANGE ON HEAVY PARTICLE THERAPY STUDIES

NCI's policy of not supporting new studies in heavy particle radiotherapy until the current neutron therapy effort can be evaluated has been reversed on the advice of the Div. of Cancer Treatment Board of Scientific Counselors. The Board's action opens the door for consideration of a grant application for heavy particle development and studies which DCT Director Bruce Chabner said could cost as much as $100 million.

Coordinated clinical trials of the neutron therapy program are just getting under way and probably will require at least another five years for evaluation.

The Board's unanimous vote to change the policy came after a presentation on the prospects for heavy particle therapy by Edward Alpen, Lawrence Laboratory, and Joseph Castro, Univ. of California. They argued that since the DCT policy limiting new heavy particle studies was established in 1979, sufficient progress has been made in heavy particle research to warrant reconsideration.

The Dept. of Energy pays the operating cost of the Lawrence heavy particle facility and will continue to do so, Alpen said. But, "we know full well we will need a line item in the congressional budget. We are also looking for private support."

"The support should be broader based," Board member Alan Rosenthal commented. "If it is primarily a program of NCI, it is very likely to encroach in ways that will surprise us every year on the rest of the NCI budget."

Castro said that phase 1 and 2 clinical trials have been completed "and we're ready now to begin phase 3 trials." He estimated it would require four to five years to accumulate enough patients for phase 3 studies.

The Board recommended that DCT staff develop guidelines for the grant applications which would limit NCI support before accepting new applications. Chabner agreed, noting that the policy change and any guidelines would have to be submitted to the NCI Executive Committee.

The Board approved concepts for two new contracts in the Radiation Research Program, including converting the headquarters grant for heavy particle radiotherapy clinical trials to a contract, and also approved the concept for a new grant supported initiative in dose fractionation and late effects studies using animal models.

The Board also gave concept approval for grant supported studies of differentiating agents in human malignancies requested by the Cancer Therapy Evaluation Program. The concept proposals as written by DCT staff follow:

**Studies of dose, fractionation, and volume late effects in normal tissues using animal models.** Total estimated first year cost, $1.5 million, six-eight awards, four years. Staff description and rationale:

Research is needed to determine appropriate animal models for a variety of human tissues which are dose limiting for curative radiotherapy; to select endpoints and evaluation criteria and develop statistical considerations for dose, fractionation, and volume effects studies; to determine the dose response relationships for late effects for fractionation schemes relevant to radiotherapy; to determine whole organ and partial volume dose response relationships for late effects for fractionation schemes relevant to radiotherapy; and to identify methods for predicting and/or measuring the onset of regeneration in irradiated normal tissues.

There is an urgent need to develop a rational basis for selecting the optimal radiation fractionation schedule in an individual patient. Studies of dose fractionation and volume effects are important in developing treatment strategies which minimuze radiation injury to normal tissues. Fractionation schedules used either to reduce overall treatment time (accelerated fractionation) or to increase total dose (hyperfractionation) offer a new range of possibilities for improving the results of clinical radiotherapy by readily available low linear energy transfer beams.

**Group headquarters for heavy particle radiotherapy clinical trials.** Estimated annual cost, $585,000, four years.

The headquarters grant, now held by the American College of Radiology in Philadelphia, supports heavy particle clinical trials and is now in its seventh year of funding. The present grant, a program project, will expire in April, 1986. The objective of the heavy particle therapy program is to determine whether heavy particles are superior to the best current treatment methods in the management of locally advanced cancer. Specifically, the program aims to improve local control rates for bulky cancers or, with unchanged control rates, decrease the incidence of late effects. The group is primarily concerned with conducting randomized clinical trials; however, dose searching pilot studies are also being carried out.

The aims of the headquarters group are to provide administrative support for the particle clinical trials to include coordination of protocol development and review of submitted protocols; entry of patients into studies; monitoring of individual study achievements and institutional contributions to the group; provision of data management, statistical design and evaluation for all studies; coordination of group quality control; coordination and management of group meetings; and distribution of reports of meetings and study results.

NCI staff has determined that the PO1 mechanism is no longer appropriate for funding this project and recommends that a contract be used instead. Due to the large funding levels of the heavy particle clinical facilities and the problems experienced in

the past with these clinical trials, the entire heavy particle grant program is currently being converted to the contract mechanism. It is appropriate that the headquarters grant also be funded under the contract mechanism in order to ensure adequate staff direction of the management of the phase 1/2 clinical trials.

The headquarters group will provide the administration, management, quality control, coordination and data management necessary to conduct multi-institutional clinical trials using heavy particles. The recipient shall have the necessary resources and clinical trial experience to carry out this work.

The NCI program staff will be actively involved in the overview of this program and the program official who is the project officer for the neutron therapy clinical trial contracts and program director for the charged particle clinical trial grants will also be the project officer for this contract.

The level of funding requested is at the current funding level for the grant and includes a six per cent annual increase. The funding should begin at the end of the current headquarters group PO1 funding period (5/1/86) and continue six months past the termination date of the neutron therapy contracts which expire in September, 1989.

Chabner told the Board that NCI has not been entirely pleased with the headquarters group but "because it is a grant, we can't do anything about it."

"Can't you tell them that if they don't straighten up their act, they won't have a chance of getting the contract?" Rosenthal asked.

"That's going to be a factor in making the award," Chabner said.

Francis Mahoney, Radiation Research Program staff member, said, "We're not unhappy with everything they've done. The problem is at the treatment end, not with data management."

"Can you assure us that if you go ahead with the contract, the performance will be satisfactory?" Rosenthal asked.

"I can assure you that if it isn't, the contract will be cut," Chabner said.

**Improvement and development of radiopharmaceuticals for employment with single photon emission computed tomography.** Estimated annual cost, $500,000, three years (contract).

Positron emission tomography (PET) has represented a major advance in nuclide imaging since it provides not only anatomical but also functional information. Its applications have been mainly in the areas of brain and heart metabolism. Its cost, however, has been extraordinarily high since its use requires a cyclotron in the immediate vicinity for production of very short positron emitting nuclides and specially trained personnel. The positron course in tissue results in an annihilation of the positron with the generation of two gamma rays which travel in opposite directions at 180 degrees and are detected by specially dedicated cameras which have no other use.

Single photon emission tomography (SPECT) would employ a type of longer lived isotope that would be readily available throughout the country. The need for a cyclotron is eliminated. The gamma camera used to detect the emitted x-rays is readily adaptable for use in making other routine nuclide scans. Hence, such equipment would be available to practically all medical institutions. The problem that exists is that the isotopes that appear to be promising (technetium and iodine) for use with SPECT are not now available in appropriate chemical formulation.

This project which is part of a larger initiative that was proposed one year ago was reviewed and approved in principle by the Board of Scientific Counselors. The larger initiative which originated from a workshop held in 1983 included not only development of the radiopharmaceuticals but also further refinement of the SPECT instrumentation.

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**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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The development of the radiopharmaceuticals is considered to be the most important part of the original initiative. It is reasoned that once the radiopharmaceuticals become available, industry will concentrate on improvement of the SPECT system.

The final decision on the original larger initiative was to use the program announcement mechanism. This has been done. The present proposal for an RFP is intended to provide additional stimulus in this important research area should an insufficient number of proposals be funded as a result of the program anmnouncement.

Objectives of the contract will be:

1. To study the relationships between chemical structure and in vivo transport and metabolic disposition of potential biochemically useful technetium 99m and/or 123 iodine radiotracers as probes of physiologic processes.

2. Development and validation of 99m technetium and/or 123 iodine radiotracers for the study and/or detection of primary cancers, cancer metastasis, and for the study of metabolism of normal and cancer tissue, including monitoring of response to treatment.

3. Development of methods and procedures for evaluating possible toxicity of radiotracers that will allow prompt dissemination of useful tracers into clinical medicine.

Francis Ruzicka, acting director of the Radiation Research Program, said that the RFP will not be issued until staff looks over the grant applications generated by the program announcement.

The staff had recommended that the RFP be listed as a small business set aside because, Chabner said, "we thought it would be very likely to be directed there." Board member David Bragg objected. "There's not enough profit in it," he said. "It would be better for a large company, or more likely, an academic institution." Chabner and the Board agreed to remove the small business designation; however, the Small Business Administration could still determine otherwise.

**Differentiating agents in human malignancies.** Estimated first year total, $750,000, three grants, three years each.

A series of clinical observations has led to the current interest in differentiating agents as potential therapy for human malignancies. Over half a century ago, regression of tumors in patients was described as occurring either spontaneously or following the administration of blood. Some tumors, such as teratocarcinoma and CML, appear to undergo maturation following therapy, but retain the capacity for dedifferentiation at a future date. The recent concept that cancers are composed of cells blocked at an early stage of normal maturation stimulated a search for agents with potential differentiating effects. Such agents are particularly attractive since, in principle, they spare normal tissue and therefore avoid many of the toxicities of chemotherapy or radiation therapy. Retinoids were one of the first class of agents studied and were observed to induce differentiation in a number of in vitro systems. A wide range of compounds have subsequently been discovered, including polar solvents, fatty acids, vitamin D3, and several types of chemotherapy (pyrimidines, purines, anthracyclines) which cause differentiation in vitro at doses below the cytotoxic level. A broad spectrum of cellular alterations have been observed after treatment of established human tumor cell lines with these compounds. In most cases, however, there is no clear cause and effect relationship and the specific sites of growth control at the cellular level remain obscure.

Such in vitro observations have led to empirical clinical trials of several differentiating agents. These trials, however, have not been uniformly successful. For example, with similar schedules of low doses of ara-C, complete response rates in acute leukemia and myelodysplastic syndromes range from 10 per cent to over 50 per cent while the drug has appeared to act as a maturational agent in some series and as a cytotoxic agent in others. There are several possible explanations for these and other discrepancies. First, the tumors which have been most extensively studied include AML, myelodysplastic syndromes, and neuroblastoma, which are relatively uncommon and have been studied sporadically and insufficiently. Second, there is at present no biochemical effect for these agents at the cellular level which has been correlated with clinical efficacy. Indeed, there are limited data as to the clinical relevance of any of the laboratory phenomena described thus far. Finally, there has been considerable difficulty distinguishing between cellular differentiation and cytotoxicity followed by regeneration. Currently, there are limited, spontaneous correlative studies ongoing and many tumor types remain unaddressed.

The concept is to support grants in basic research and concurrent clinical trials involving differentiating agents in human tumors at three institutions. The realization of this goal would require (1) identification of in vitro measures of differentiation/maturation that could have clinical applicability; and (2) establishment of correlations between this clinical utility and other cellular features such as histopathology, immunopathology, cellular phenotyping and cytogenetic analysis. Applications will be sought which propose a series of projects comprising the program described above. It is envisioned that these applications will closely resemble a program project.

"We need to increase coordination between laboratories and clinical centers," Robert Wittes, director of the Cancer Therapy Evaluation Program, said. Responding to Board member John Kersey's query on how many RO1 or PO1 grants were involved in this type of research, Wittes said, "I can't think of a single one. This area is not adequately covered. It's like clinical trials were being conducted on a different planet, as far as laboratory work is concerned."

Board member Dani Bolognesi suggested that the staff's original proposal, for $400,000 a year to support one or two grants, was not enough. "We felt we couldn't afford more," Wittes said.

"Is there any possibility, to enhance the number funded, that this could be a contract, so it doesn't dig into the grants pool?" Board member David Goldman asked. "We have to be as creative as OMB (referring to the Office of Management & Budget's manipulations to reduce the number of NIH grants.

Donald Christoferson, DCT administrative officer, suggested that it possibly could be a cooperative agreement. Chabner said he would explore that possibility, and the Board approved the concept at the increased level of $750,000 a year.

**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-CP-51015-60**
**Title: Master agreement for literature review for carcinogenesis information**
Deadline: May 15

The Div. of Cancer Etiology of NCI conducts studies on the occurrence and significance of environmental carcinogens in various media including air, water, food, drugs, cosmetics and the workplace. Information obtained in these studies is disseminated in special reports to the scientific community.

This RFP is available for a master agreement to review the literature for data relevant to the areas of carcinogenesis and toxicology with respect to the presence of carcinogens in various environmental media. The contractor selected will perform under master agreement order a wide range of simple and complex tasks such as supplying bibliographies covering specific topics of interest, providing critical analyses in defined areas of carcinogenesis and toxicology, preparing special reports with specific formats requested by the project officer, organizing and entering data for computer based files and other activites such as updating, modifying or editing previously prepared reports for DEC.

Reports may contain reviews of large amounts of published data which encompass several scientific disciplines including chemical/physical parameters, in vivo and in vitro carcinogenesis, environmental occurrence and fate, exposure information, pharmacokinetics and epidemiology. Previous reports have included compilations of literature data on the occurrence and biological activity of carcinogens in various environmental media including air, water, drugs, cosmetics, food and the workplace. The subject matter, format and complexity of these reports has varied from summary tables of biological activity to evaluations of the potential carcinogenicity of various chemical agents.

**This RFP was derived from a concept approved by the DCE Board of Scientific Counselors last fall and reported in The Cancer Letter Nov. 16, page 7.**
Contract Specialist: Thomas Porter
RCB Blair Bldg Rm 117
301-427-8888

**RFP NCI-CM-57724-30**
**Title: Evaluation of congeners of new lead compounds**
Deadline: May 16

The Developmental Therapeutics Program of NCI's Div. of Cancer Treatment is seeking an organization having the necessary experience, scientific and technical personnel and facilities to evaluate series of structurally related compounds in experimental tumor models in vivo. Structure activity studies with congeners and prodrugs of newly identified lead compounds (synthetic and natural product) will be conducted under well controlled experimental conditions in order to guide future synthetic efforts and identify the most promising members of a class for further development. Approximately 300-400 compounds will be tested per year. The offeror shall be expected to help design and conduct appropriate preclinical antitumor experiments to answer questions that arise during any stage in the preclinical or clinical development of specific agents.

As compounds of a commercially confidential nature may be evaluated, pharmaceutical and chemical firms will be excluded from the competition. Since some of the test systems will involve human tumor lines growing in athymic mice, the proposed organization will be required to have a barrier facility as a minimum requirement.

It is anticipated that one award will be made for this effort. A multiyear, incrementally funded contract will be awarded for a period of three years. Each increment will be for a 12 month period.

**The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and reported in The Cancer Letter Oct. 26, page 5.**
Contract Specialist: Elsa Carlton
RCB Blair Bldg Rm 228
301-427-8737

**AMENDMENT**

RFP NCI-CP-51020-64, titled "Biological Carcinogenesis Branch repository for storage and distribution of research resources," published in **The Cancer Letter** Feb. 22, has been amended to remove the requirement that it is a 100 per cent small business set aside. The deadline for proposals also has been extended to approximately May 18.

**NCI CONTRACT AWARDS**

TITLE: Systems planning services for NCI
CONTRACTOR: Prospect Associates, $1,388,131.

TITLE: Center for Radiological Physics Program
CONTRACTORs: Univ. of Washington, $635,416; Allegheny-Singer Research Institute, $989,167; American Assn. of Physicists in Medicine, $834,488; West Coast Cancer Foundation, $1,016,374; Univ. of Texas System Cancer Center, $742,303; and Univ. of Wisconsin, $1,073,976.

TITLE: Rodent production centers
CONTRACTORS: Charles River Breeding Laboratories, Wilmington, Mass., $804,991; Southern Animal Farms, Prattsville, Ala., $614,247; Harlan Sprague Dawley, Indianapolis, Ind., $740,980; Simonsen Laboratories, Gilroy, Calif., $951,534; Taconic Farms, Germantown, N.Y., $598,490.

**The Cancer Letter** _Editor Jerry D. Boyd
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