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Congress Renews National Cancer Act, Including Most Key Amendments Sought By NCI And Allies

Biomedical research reauthorization, including renewal of the National Cancer Act, finally made it through a bleary eyed Congress in the last hours before adjournment last week. The bill which will go to the White House preserves the Cancer

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In Brief

Wyngaarden Delays Gene Transfer Study, Seeks All Information; Rosenberg Wins Griffuel Prize

NIH DIRECTOR James Wyngaarden has delayed approval of the gene transfer protocol developed by Steven Rosenberg and Michael Blaese of NCI and French Anderson of the National Heart, Lung & Blood Institute (**The Cancer Letter**, Oct. 7). When the protocol was submitted to the NIH Recombinant DNA Committee at a public meeting, some information had been withheld because the investigators felt that disclosure might jeopardize publication in a scientific journal. Committee members objected but voted 16-5 for approval anyway. "That is not acceptable to me," Wyngaarden said later. "The RAC will not be held hostage to the "New England Journal of Medicine." The RAC subcommittee which had reviewed the protocol and had asked for the additional information will meet Dec. 9; the investigators will have the oppportunity to present the data then. . . . **STEVEN ROSENBERG** will receive the 1988 Griffuel Prize Nov. 14 in Paris for his work in development of immunotherapy of cancer. Rosenberg is the third NCI scientist to win the prize, worth this year about $50,000; Vincent DeVita won it in 1980 and Robert Gallo in 1983. . . . **KENNETH OLSON**, clinical oncologist who has edited the Florida Society of Clinical Oncology newsletter since 1981, will turn over at least part of that job to an associate editor familiar with the economics of oncology, at his suggestion. Olson's newsy publication has included this statement on the back page: "Flasco's newsletter is published a few times a year at the caprice of the editor. Any errors are produced by others and the editor is irresponsible. Brief contributions. . . [including] gripes are welcomed and will be published subject to the libel laws of the state of Florida". . . **M.D. ANDERSON** Associates (all current and former professional staff and trainees) are invited to the annual business meeting and reception Nov. 3, 5:30-7:30 p.m., in the Clark Clinic Building, in conjunction with the 32nd annual clinical conference Nov. 2-5.

Biomedical Reauthorization, Including National Cancer Act, OKd By Congress

(Continued from page 1)
Act pretty much intact, and includes most of the amendments sought by NCI, its advisors and cancer program advocates.

The reauthorization is only for two years, however, which means that the process will have to be undertaken all over again in the next Congress. The original National Cancer Act of 1971 and its subsequent renewals have always been for three years. The National Cancer Advisory Board had asked for five years this time.

The new legislation in the 1990 fiscal year will not establish a maximum appropriation for NCI, for the first time since 1971. The bill authorizes $1.5 billion plus $100 million for cancer control in FY 1989, but for the next year, the bill calls for "such sums as may be necessary."

In the first years after 1971, the authorized figures in the National Cancer Act were seen as optimal amounts and as levers to encourage higher actual appropriations. More recently, the authorizations have been ceilings, against which the appropriations frequently bumped.

Cancer program advocates feel that "such sums as may be necessary" now is a preferable approach, offering more flexibility in development of the bypass budget and in justifyhing budget requests to Congress.

The bypass budget, incidentally, is one of NCI's special authorities which remain in the new legislation, along with Presidential appointment of the NCI director and the National Cancer Advisory Board, the President's Cancer Panel, cancer centers, cancer control, public and professional education, and the right to establish its own review committees.

One amendment avidly sought by NCI involved only one word, changing from "may" to "shall" in the directive on distribution of appropriations by the White House Office of Management & Budget. "Shall" was in the original National Cancer Act. When "may" crept in a few years ago, OMB took advantage of it and caused no end of consternation at NCI by micromanaging how funds could be spent. That limited flexibility and reprogramming of funds, leading NCI to plead to Congress, the NCAB and anyone else who would listen for some relief.

OMB backed away in the face of congressional pressure, but NCI and its allies sought the change anyway. It was in the bill passed by the Senate, but did not make it through in the compromise. Some members of the conference committee expressed reluctance to make the change without better understanding its implications.

That may not be a negative factor, as long as the appropriations committees continue to include language in their bills ordering OMB to distribute NCI's money directly, without the noxious apportionment directives.

The NCI director's authority to appoint members of NCI review committees and advisory groups, without approval of the NIH director, had been left out in a previous renewal of the National Cancer Act. Restoration of that authority was in the Senate bill, but was not included in the compromise. That was never a major problem, but NCI liked the old way better and campaigned for it in the new bill.

NCI's legislative office, lobbyists and others were pouring over the bill as it came out in the "Congressional Record" in attempts to nail down its contents. That is not easy, since amendments to existing law frequently are hard to decipher, referring to sections and numbers rather than specific language. Some key issues remain unclear:

* Construction. Did Sen. Edward Kennedy's provision for a new NIH wide construction grant authority, which included retention of NCI's separate authority, survive?

* Did Kennedy's effort to retain NIH scientists through establishment of a new Senior Biomedical Research Service with higher salaries make it through?

Tune in next week.

Three senators influential in health issues bowed out with adjournment. Not running for reelection are Sen. John Stennis (D-MS), chairman of the Appropriations Committee; Sen. Lawton Chiles (D-FL), chairman, and William Proxmire (D-WI), of the Labor-HHS Appropriations Subcommittee. If Democrats retain control of the Senate, Ernest Hollings of North Carolina is the likely new chairman of that subcommittee. Robert Byrd, who is stepping down as majority leader, probably will succeed Stennis as chairman of the full committee. Republicans Mark Hatfield of Oregon and Lowell Weicker of Connecticut will head the full committee and subcommittee, respectively, if the GOP wins control.

No leadership changes are expected in the authorizing committees of either house nor in the House appropriations committees.

Fischinger Named VP For Research At MUSC; To Develop Cancer Center

Peter Fischinger, who has been AIDS coordinator for the Dept. of Health & Human Services for the past year, will leave Jan. 1 to become vice president for research at the Medical Univ. of South Carolina in Charleston.

Fischinger, who is still officially the NCI deputy director, will have among his responsibilities the task of developing a new cancer center in Charleston. He will head research activities at the university, with emphasis on immunology and molecular biology, and will oversee development of new centers for molecular biology and for immune deficiency.

When Fischinger was detailed to the office of the assistant secretary for health last year to coordinate the department's AIDS activities, he said then that he did not expect to be in that job for more than a year. Maryann Roper was named acting deputy director at NCI and continues in that position.

Fischinger was appointed by then NCI Director Vincent DeVita as scientific director for the Frederick Cancer Research Facility in 1981. He played a major role in implementing the present contractual arrangement at FCRF, when it was split from one into five separate contracts, and he oversaw recompetition of those contracts last year. He continued as FCRF scientific director after DeVita made him his deputy in 1985.

Much of NCI's AIDS research activities are located at FCRF, including the vaccination program. Fischinger also coordinated other NCI AIDS activities.

The Medical Univ. of South Carolina has made a major commitment to build a strong biomedical research program. The state has allocated $12 million for development of the cancer center.

Fischinger, who has been in the government 22 years, 20 of it with the Public Health Service, will take his federal retirement when he leaves.

In another major cancer center development, Frank Meyskens, director of cancer control and prevention at the Arizona Cancer Center in Tucson, has been named director of the new cancer center at the Univ. of California (Irvine), effective in February.

Meyskens is credited with building one of the best cancer control programs by a cancer center in the country, an innovative effort which involves local organizations and carries out detection and prevention programs throughout Arizona. Meyskens also has been principal investigator for a number of chemoprevention studies.

The UC-Irvine School of Medicine has been developing its research capabilities, including plans for a cancer center.

Robert Young, who had only six months in his job as director of NCI's Cancer Centers & Community Oncology Program, before learning he had been elected the new president of Fox Chase Cancer Center, experienced both exhiliaration and frustration in the job he will leave in December.

Exhiliaration over how successful those programs have been--centers, the Community Clinical Oncology Program, the cancer research facilities program. "These were all good ideas when they were created, they fullfilled the criteria set forth for them, and they are now very important to the National Cancer Program," Young told **The Cancer Letter.**

"A Tragedy"

Frustration, over level budgets and budget cutbacks, a total wipeout in the case of facilities. "People in the centers and CCOPs have made those programs work. They now require additional support to reach anything close to their potential. They're not getting it, and that is a tragedy. The same is true for facilities."

Young called Fox Chase "one of the truly great comprehensive cancer centers, remarkably balanced in all areas, basic and clinical research and cancer control." He sees as one of his most crucial tasks "the long term challenge of recruiting and replacing the outstanding senior scientists at Fox Chase as they retire."

Noting that Fox Chase has always been known for its outstanding basic research developed under the stewardship of founding President Timothy Talbot, Young said the cancer control program under Paul Englstrom "is one of the best anywhere. Under John Durant and Bob Comis, clinical research has improved enormously, hiring people like Bob Ozols (recently recruited from NCI to head medical oncology), with outstanding people in surgical oncology and radiotherapy, and strengthening the ties with ECOG."

Durant left last April after five years as Fox Chase president to become vice president

for health affairs at the Univ. of Alabama in Birmingham.

Young said he intended to continue Durant's efforts to develop ties with community hospitals in the region, especially encouraging them to participate in Fox Chase protocols while retaining their patients.

DCT Board OKs Clinical Trials, DTP, BRMP Recompetitions, BNCT Grants

The Div. of Cancer Treatment Board of Scientific Counselors has approved recompetition of the Cancer Therapy Evaluation Program's contracts for phase 1, 2 and 3 clinical studies at an estimated $4.25 million a year. The new awards will be for five and a half years for phase 1 studies and seven years, including followup, for phase 2 and 3 studies.

The Board also gave concept approval at its meeting earlier this month for an additional $3.5 million worth of contract recompetitions and modifications, and for two new grants for development of boron neutron capture therapy compounds.

The phase 1, 2 and 3 studies are currently being performed, at a total level of a little more than $4 million a year, by Memorial Hospital, Mayo Clinic, Univ. of Maryland (Baltimore), Univ. of Wisconsin (phase 1 only), Ohio State Univ. (phase 1), Univ. of Texas Health Science Center (San Antonio, phase 1), Johns Hopkins Univ. (phase 1) and Univ. of Texas M.D. Anderson Cancer Center.

Board member Emil Frei expressed concerns about the fact that CTEP "has two mechanisms for phase 2 and 3 studies. I'm not sure you need both." Frei is chairman of Cancer & Leukemia Group B.

"These do not overlap with the cooperative groups," CTEP Director Michael Friedman said. "They are complementary. We use them when we need to move faster, which you can do with a single institution. I think the groups are becoming more sophisticated and will do the more complicated and toxic studies. We use [the contract mechanism] for the very creative, very toxic, very difficult studies. There is no danger this mechanism will preclude groups from doing very interesting and very creative studies."

The recompetition concept was approved without opposition, although Board members Charles Balch and James Cox, M.D. Anderson, and John Mendelsohn, Memorial, abstained because of their institutions' participation in the program. John Niederhuber, of Hopkins, did not vote because as chairman he was not required to.

The Board without dissent approved recompetiton of the Developmental Therapy Evaluation Program's contract with Southern Research Institute for detailed drug evaluation and development of treatment strategies for chemotherapeutic agents; and DTP's contract with ORI Inc. for computer task orders. The computer contract "is the only way we can compensate for lack of staff," DTP Director Michael Boyd said.

John Antoine, director of DCT's Radiation Research Program, asked the Board for concept approval of two contracts to support development of boron neutron capture therapy, following the Board's recommendation to proceed with the plan to use the Dept. of Energy's neutron facility in Idaho (**The Cancer Letter**, July 1).

One of the contracts would have been for synthesis of compounds for BNCT, the other for biological screening of boron compounds. The sythesis contract was estimated to cost $475,000 a year for five years; the screening contract, $250,000 a year, also for five years.

Board members felt, however, that there is not yet enough knowledge about BNCT to proceed with those efforts as straight procurements. They decided instead to approve the concepts as grant supported research, at the same levels of support. RFAs, rather than RFPs, will be issued to solicit research applications from investigators.

Growing opportunities in development of monoclonal antibodies in cancer treatment resulted in a request to the Board from the Biological Response Modifiers Program to double the amount allocated for phase 1 clinical contracts for MABs, from $2 million a year to $4 million.

Contracts had been awarded to six institutions for the phase 1 studies, with each doing two clinical trials a year. The additional money will support more imaging and therapy related dosimetry studies, for development of an increasing number of new murine and murine-human chimeric monoclonal antibodies.

"Since the original BSC approval of the budget ceiling, a larger number of antibodies and immunoconjugates are becoming available, the concept statement said. The increased ceiling wills allow their development.

Concept statements for the recompetitions and new grants follow:

Phase 1 and clinical pharmacokinetic studies of anticancer drugs (Task A); phase 2/3 clinical studies of anticancer drugs (Task B).

Objectives of the phase 1 clinical trials contracts are to characterize drug toxicity, the maximum tolerated dose and pharmaco-kinetics of drugs entering clinical trials. The agents studied primarily have been obtained from the NCI drug development program, although some compounds were made available to NCI from the pharmaceutical industry for collaborative development.

The phase 2/3 clinical trials contracts have primarily been used as a resource for the phase 2 evaluation of the antitumor activity of new agents that have completed phase 1 trials. These contractors have also conducted other phase 2 studies which were of a high priority to NCI, such as the initial pilot studies of combination regimens and studies which were technically difficult to perform.

Although the focus of the phase 1 contracts has been the evaluation of new agents arising from the DTP screeing program, the contracts are also being used for phase 1 evaluation of biochemical modulatory combinations, differentiating agents, radiosensitizers, and phase 1A trials of biological response modifiers. The eight phase 1 contractors have demonstrated that the toxicity of new agents can be assessed qualitatively and quantitatively across several institutions, with the determination of appropriate and reliable pharmacokinetics.. Since 1985, 30 investigational cytotoxics, one radiosensitizer, and five biological agents have been studied. In addition to this, the differentiating agent HMBA has also been evaluated on these contracts, and six commerically available cytotoxics have been reevaluated in combination with biochemical modulating agents in an attempt to significantly enhance their therapeutic index. A median number of 44 trials were accomplished per year (ranged 35 to 50).

Pharmacokinetic evaluations have been completed for virtually all of the agents studied under these contracts. Analytical methodology for these assays are now established during preclinical testing so that pharmacokinetics can be determined in animals prior to the phase 1 evaluation of the agent in man. Improved pharmacokinetic evaluations have permitted the following:

A. Establishment of the relationship between pharmacokinetic measurements in animals and man, which has permitted more rapid dose escalation schema in phase 1 trials, thereby reducing the number of patients treated at subtherapeutic doses.

B. Determination of dose dependent elimination of anticancer drugs, providing safer drug administration for those agents showing saturability of elimination with increasing doses.

C. Determination of active and inactive metabolites, yielding better understanding of the parent compound and, at times, the identification of active new substances for therapeutic evaluation.

D. The evaluation of pharmacokinetic elimination of these agents in patients with abnormal organ function, establishing safe, predictable dosing regimens in patients with abnormal renal or liver function.

Although the phase 2/3 contracts were written to permit the conduct of phase 3 studies, the primary emphasis has been phase 2. Since June 1, 1985, 1,763 patients have been accrued to 104 trials involving the evaluation of 30 different investigational agents. In addition, tumor and normal tissue specimens from 332 patients have been supplied for basic science studies on antineoplastic drug resistance with clinical correlations.

Of 101 trials performed under the contract to date, 70 were standard single agent phase 2 trials, three were phase 3 and the remainder were combination and combined modality studies. While phase 3 studies were uncommon, the pivotal study of carboplatin plus etoposide vs. cisplatin plus etoposide in good risk germ cell tumors and a randomized study of continuous infusion cisplatin plus 5-FU vs. 5-FU alone were conducted under these contracts and will answer important scientific questions. Of 39 high priority clinical trials identified by CTEP in the past six-eight months, 16, or 41 percent, of them are now in development on the contract.

The project plan will be divided into two parts as follows:

1. Phase 1 trials and pharmacokinetics of new anticancer agents.

Program staff anticipates the award of six to eight contracts for these efforts at a total estimated cost of $3.1 million. The specific goals of this project will be to define the acute toxicities of new anticancer agents in patients with advanced cancer; to redefine the acute toxicities and pharmacokinetics of existing anticancer agents administered in combination with colony stimulating factors; to provide information on the pharmacologic characteristics (absorption, distribution, metabolism, and elimination) of selected antitumor agents; and to determine a treatment regimen for evaluation of antitumor activity in phase 2 trials.

The agents to be studied will include the following:

a. New cytotoxic chemotherapeutic agents identified by NCI's drug screening program.

b. Existing chemotherapeutic agents which, when administered with colony stimulating factors, can be given in doses substantially higher than those previously tested.

c. Agents developed by the pharmaceutical industry and provided to NCI for collaborative development.

Each contractor will be expected to perform at least three phase 1 trials per year with an average of 25 to 30 patients per trial. Each contractor will perform at least two pharmacokinetic studies per year on the compounds evaluated in the phase 1 trials.

2. Phase 2/3 clinical trials.

While the workscope for these contracts will include the conduct of phase 3 trials, most of the effort will be devotged to the conduct of phase 2 trials. Program staff anticipates the award of three to five contracts for these efforts at a total estimated cost of $1.15 million for the first year. The purpose of this project is to provide a resource for the conduct of early and high priority phase 2 trials. The objectives of this project (1) when testing new agents which have just completed phase 1 trials, to confirm that the dose and schedule chosen can be safely given in subsequent phase 2 studies; (2) to determine the spectrum of antitumor activity for new agents across a variety of human cancers; (3) to determine the antitumor activity of existing antitumor agents which can be administered in significantly higher doses when used with colony stimulating factors; and (4) to determine the antitumor activity of combinations of antitumor agents. While the contract will continue to permit occasional phase 3 trials, major emphasis will be on early phase 2 studies, pilot protocols that explore promising combination therapies and high priority studies that are pivotal for drug development and require rapid initiation, completion and data reporting.

Agents to be studied in this project will include:

a. New cytotoxic chemotherapeutic agents that were identified by NCI's drug screening program and have completed phase 1 testing.

b. Existing chemotherapeutic agents for which significant dose escalation was possible when used in combination with colony stimulating factors.

3. Agents developed by the pharmaceutical industry and provided to NCI for collaborative development.

Combinations of agents for which the individual toxicities are known.

Each institution will be expected to accrue at least 200 patients per year and complete on average for the

length of the contract at least seven phase 2 trials a year. In all categories of disease, patients to be selected for trial will be those with excellent performance status and the minimum amount of prior treatment that is consistent with ethical medical practice. For any proposed trial, the offerors will be required to document their ability to accrue the required number of patients within a reasonable time period. For rare tumors intercontract studies will be encouraged.

Detailed drug evaluation and development of treatment strategies for chemotherapeutic agents. Recompetition of a contract held by Southern Research Institute. Estimated annual amount, $750,000, five years.

This contract provides the drug development program of DTP with a resource for detailed in vivo antitumor evaluations of agents selected for development to clinical trial or undergoing initial clinical trials. The principal objective of the contract is to optimize the antitumor activity of agents identified by the primary screen. To achieve this objective studies using a variety of in vivo experimental tumor models are conducted in which drug concentration and exposure time of the tumor cells and host to the drug are varied. Results are interrelated with pharmacokinetic, toxicologic biochemical and immunologic information to devise and recommend treatment strategies for clinical trial, and are included in the investigational new drug applications filed with FDA. Other tasks involve comparing the activity of parenteral formulations with the original bulk material; evaluating the influence of route of administration on activity; cross resistance profiles; collaboration with outside investigators to explore new chemotherapeutic strategies (e.g. the antiangiogenesis approach of Dr. J. Folkman); and evaluating the modulating effects of agents on the efficacy of standard clinical agents (e.g. Dr. R. Warrington's histidinol findings). To accommodate changes in DTP's drug discovery projects, emphasis during the course of the contract has shifted to the use of human tumor xenograft models in athymic mice.

During the past year and a half, a variety of detailed antitumor evaluations using both mouse tumors and human tumor xenografts were conducted on approximately 28 potential antitumor agents and classes of antitumor agent. Most compounds had been identified as agents of interest from previous in vivo screens, but a few were from the human tumor colony forming assay (HTCFA) and the human tumor cell line project. Illustrative examples of the type of studies conducted include (1) penclomedine, one of a few compounds demonstrating good activity against the two breast tumors in the 1976-82 NCI tumor panel, produced 100% complete responders in mice bearing advanced stage human breast tumors following oral administration. The compound also was effective orally against two additional breast tumors. Activity did not appear to be highly schedule dependent and was retained after i.v. administration of a recently developed parenteral formulation; (2) an apparent antitumor effect against a human lung tumor xenofraft was observed with chloroquinoxaline sulfonamide (CQS), a compound selected for development based on its activity in the HTCFA using primary human tumors. In order to demonstrate the in vivo activity of CQS, unusual drug schedules were employed involving bolus doses to saturate protein binding sites and concomitant infusions to maintain free plasma levels of the compound; (3) the effort devoted to new chemotherapeutic strategies included studies to evaluate the biochemical modulating effects of histidinol and buthionine sulfoximine (BSO) on the antitumor activity of alkylating agents, the ability of calcium antagonists and membrane interactive agents to circumvent resistance to adriamycin, and the ability of antitumor agents to affect established metastases. Two results from these studies showed that pyrazine diazohydroxide (PZDH) reduced the metastatic burden of the lungs of mice inoculated with the human LOX melanoma, and BSO enhanced the activity of melphalan against the LOX melanoma using schedules designed to optimize the effects of glutathione depletion and possible diurnal variation.

Major emphasis will be placed in the new contract on evaluating compounds identified by the human tumor cell line screen. With these agents it will be important to ascertain whether a compound exerts selective antitumor toxicity in a tumor bearing host. Human tumor xenograft models, developed by other contract resources using tumor cell lines from the in vitro screen, will be employed. Some capacity in this recompeted contract will be maintained to explore exciting new chemotherapeutic approaches requring in vivo evaluation and to provide a resource for specialized in vivo expertise for the National Cooperative Drug Discovery Groups.

Computer support task orders. Recompetition of the contract held by ORI Inc. Estimated annual amount, $330,000, five years.

Objective of this contract is to provide quick response to data processing needs which may arise in the performance of the various computer support commitments of the Information Techynology Branch and to provide support for ongoing operations which evolve over time. The task order managed contract has been chosen for this, as it provides the necessary contractual flexibility for assigning diverse jobs as well as for monitoring their progress.

A great variety of tasks has been performed under this contract in the past. These have included the conversion of computer programs from one format to another, the transfer of programs from one machine to another, the development of specifications for new machine design for hosting the DTP Drug Information System, the development of robotics software support, and development of graphics programs for improving the quality of printed chemical structures. Under this contract a relational database design is currently being developed to handle in vitro drug screening data. A major ongoing task of this contract is the operation of DTP's high speed laster printer. This device is used for printing large volumes of graphic reports, which are sent to suppliers of materials sent to DTP for screening.

As the volume of data generated by the in vitro drug screening program grows, the need for computer support of this type will also grow. In the past year these needs proved urgent enough to require an accelerated rate of spending under this contract. For this reason, recompetition must be performed early. The level of effort anticipated for the new procurement corresponds to the level currently used.

Synthesis of compounds for boron neutron capture therapy. New five year grants, with a total of $475,000 for first year awards.

Boron neutron capture therapy represents a promising modality for selective irradiation of tumor tissue. The localization of ^{10}boron in tumors and the subsequent irradiation of the tumor with low energy (epithermal) neutrons results in the production of heavy charged particles (alpha particle and positively charged lithium ion) which have the range of approximately 10 microns in tissue. Although there has been clinical activity utilizing this modality, the currently used boron compounds do not achieve sufficient tumor tissue levels to be therapeutically effective, although some of these compounds are tumor selective. The further development of new boron compounds with greater tumor selectivity is needed if this promising treatment modality is to be properly evaluated.

It is anticipated that three to five grants will be awarded to synthesize a variety of chemical classes of

boron containing compounds in sufficient quantities for in vitro and in vivo preclinical biological testing. Those chemical classes that show acceptable biological activity will be further explored by synthesizing various analogues of that class.

Biological screening of boron compounds for BCNT. New five year grant, with an estimated first year award of $250,000.

The major problem area that needs to be resolved before boron neutron capture therapy can be properly evaluated as treatment modality for cancer is the lack of a boron compound with high tumor selectivity, i.e., a high tumor tissue to blood ratio. The proposed increased activity in the synthesis of new classes of boron compounds will require the capability for testing these compounds for biological activity.

It is anticipated that one grant will be awarded to screen the compounds submitted by the synthesis contractors for biological activity. This testing will include biodistribution and pharmacokinetic studies once the compound has been shown to have acceptable biological activity.

RFAs Available

RFA 89-CA-04
Title: Radiolabeled immunoconjugate dosimetry
Application receipt date: Jan. 6, 1989

The Radiation Research Program of NCI's Div. of Cancer Treatment announces the availability of an RFA for the above program. The main objective is to develop and validate techniques to estimate radiation dose to neoplastic and normal cells and tissues from the in vivo administration of antibodies and antibody fragments labeled with radioactive nuclides. Alpha, beta and photon emitters have been proposed as potential labels and, therefore, proposals are invited that develop dosimetry for any or all of the proposed radionuclides.

Radiolabeled immunoconjugates directed against tumor cell surface antigens have shown promise as both diagnostic and therapeutic agents in vitro and in human tumor implants in animals. The prospect of an agent directed specifically against neoplastic cells has led to clinical trials in humans. While calculating the dose delivered by the low activity used in diagnosis is desirable, it is mandatory in therapy when a large activity of radiolabeled immunoconjugate must be delivered to the neoplastic tissue in order to achieve the desired improvement in patient survival. Being able to calculate dose requires that one can determine the distribution within the body, for both normal and neoplastic tissue, through measurement or through the extrapolation of experimental or theoretical data.

Recent measurement by microdosimeters and observations from autoradiography have shown the distribution in tumors to be much more inhomogeneous than could be appreciated by available nuclear medicine imaging, including SPECT. Dosimetry, to date, has not accounted well for this aspect or for irregularly shaped tumors. The use of an extended MIRD type calcuation has been proposed, but MIRD's major assumption is homogeneous distribution of radionuclide. Present methods provide an estimate of dose, but clearly some modification of "normal' methods or new development must be made. The dosimetry may even have to be modified for each antibody, radionuclide (alpha, beta or gamma emitter) and/or target. Thorough evaluation of cancer therapy using radiolabeled immunoconjugates requires the best calculation of dose that can be performed.

It is anticipated that approximately three or four scientifically meritorious applications can be funded.

Requests for copies of the complete RFA and further information are available from Robert Morton, M.S., Program Director, Radiotherapy Development Branch, RRP, DCT, NCI, NIH, EPN Rm 800, Bethesda, MD 20892, phone 301/496-9360.

RFPs Available

Requests for proposals 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, Executive Plaza South, room number shown, National Cancer Institute, NIH, Bethesda, MD 20892. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CP-95614-56
Title: Radiation dosimetry for epidemiologic studies
Deadline: Approximately Dec. 1

The Radiation Epidemiology Branch of the Epidemiology & Biostatistics Program of NCI's Div. of Cancer Treatment is seeking a contractor who will support dosimetry for epidemiologic studies of populations exposed to ionizing radiation, conducted by the REB. This support is essential to REB's ability to quantify radiation risks and provide information on dose response relationships.

The contractor shall evaluate the radiotherapy records collected by the REB and determine whether the data are adequate to calculate organ doses, and provide organ doses for individual study subjects to the REB for analysis.

The contractor shall provide the support necessary to make measurements on patients, anthropomorphic phantoms, or water phantoms in order to reconstruct radiation doses to specific organs following medical exposures. The contractor shall:

1. Determine the manner in which physical dosimetry can be best applied to the epidemiologic studies of interest.
2. Coordinate dosimetry data collected or prepared by other medical physicists who are participating in the studies.
3. Compare measured doses with calculated organ doses to validate consistency and accuracy of simulation models measurements to allow a separation of organ doses into the contribution from (a) head leakage and collimator scatter, and (b) scatter within the patient from the useful beam.
4. Continue dosimetry of neutron distributions from betatrons and other high energy linear accelerators as well as from primary neutron sources.

Contract Specialist: Donna Winters
RCB Executive Plaza South
301/496-8611

NCI CONTRACT AWARDS

Title: Tracing through credit bureau to determine the vital status and current address of persons treated for retinoblastoma in childhood
Contractor: Johns Holding Co., $1,152

Title: Facility for housing and preparing virus infected mice, genetically manipulated mice, and chimeric mice
Contractor: Bioqual Inc., $2,295,282

Title: Preclinical pharmacology of anti-AIDS agents
Contractors: Arthur D. Little, $794,614; Southern Research Institute, $954,916; Vermont Regional Cancer Center, $702,721

Title: Primary extraction of the barkwood of taxus brevifolia
Contractor: Hauser Chemical Research, $50,322

NCI Advisory Group, Other Cancer Meetings For Nov., Dec., Future

Critical Perspectives in Hematology & Oncology--Nov. 1, Chicago. Clinical Trials Program, 1988 fall meeting. Contact American Hospital Assn., 840 N. Lake Shore Dr., Chicago, IL 60611.

Bladder Cancer Symposium--Nov. 2-4, Cairo. Contact Symposium Secretariat, Dr. Nazli Gad El Mawla, National Cancer Institute, Cairo, Egypt.

Optimizing Management of Primary Bone Tumors--Nov. 2-5, Houston. 32nd annual clinical conference, an international symposium emphasizing the multidisciplinary approach. Contact Office of Conference Services, M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, phone 713/792-2222.

Progress in Regional Cancer Therapy--Nov. 3-5, Vienna. Contact Brigitte Schick, 1 Chir. Univ.-Klinik, Alser-Str. 4, 1090 Vienna, Austria.

Cancer Research Manpower Review Committee--Nov. 3-4, Guest Quarters Hotel, Bethesda, MD, open Nov. 3 7-7:30 p.m.

DNA Probes in the Practice of Medicine--Nov. 3-4, San Diego. Contact Bill Silberg, 312/645-4417.

12th Annual Cancer Symposium and 8th Annual Cancer Symposium for Nurses--Nov. 7-9, Sheraton Harbor Island Hotel East, San Diego. Sponsored by Scripps Memorial Hospital Cancer Center. Contact Nomi Feldman, Conference Coordinator, 3770 Tansy St., San Diego, CA 92121, phone 619/453-6222.

Update on Cancer of the Head and Neck--Nov. 11-12, Cleveland. Contact Barbara Guy, Assistant to the Director, Ireland Cancer Center, Lowman Bldg-211, University Hospitals of Cleveland, 2074 Abington Rd., Cleveland, OH 44106, phone 216/844-7856.

Institutional Review Boards and Clinical Trials: Protection and Progress in Biomedical Research--Nov. 11, New York Univ. Medical Center. NIH and FDA regional conference on the protection of human subjects. Phone 212/340-6697.

Nausea and Vomiting: A Multidisciplinary Perspective --Nov. 12-13, Ottawa. Contact Dr. R.K. Harding, Physiology Dept., Univ. of Ottawa, 451 Smyth Rd., Ottawa, Ontario, K1H8M5, Canada.

Inter-American Society for Chemotherapy--Nov. 13-16, Buenos Aires. Fifth meeting. Contact Dr. R.W. Sidwell, IASC, Utah State Univ., Logan, UT 84322.

Death of a Parent: Impact on School Age Children--Nov. 15, Calvary Hospital, Bronx, NY. Contact Sr. Patricia Sheridan, phone 212/518-2259.

Franco-Egyptian Cancer Conference--Nov. 15, Cairo. Reports on breast cancer, pediatric lymphoma, virology, and cytokinetic studies. Contact Dean's Office, National Cancer Institute, Kasr El-Aini Str., Fom-El-Khalig, Cairo, Egypt.

Innovative Cancer Chemotherapy for Tomorrow--Nov. 16-18, Sheraton Centre Hotel, New York. Chemotherapy Foundation Symposium V111. Will include discussion on use of tamoxifen in prevention of breast cancer. Contact Jaclyn Silverman, Div. of Medical Oncology, Box 1178, Mount Sinai School of Medicine, One Gustave L. Levy Pl., New York 10029, phone 212/241-6772.

Monoclonal Antibodies and Breast Cancer--Nov. 17-18, San Francisco Hilton & Tower. Third international workshop. Contact Kelly Travers, John Muir Cancer & Aging Research Institute, 2055 N. Broadway, Walnut Creek, CA 94596, phone 415/943-6314.

Directions in Pediatric Hematology/Oncology Care--Nov. 17-19, Harbour Island Hotel, Tampa. 12th annual seminar sponsored by the Florida Assn. of Pediatric Tumor Programs. Contact Cindi Butson, Seminar Coordinator, FAPTP, PO Box 13372, University Station, Gainsville, FL 32604, phone 904/375-6848.

Developmental Therapeutics Contract Review Committee--Nov. 17-18, Bethesda Holiday Inn, open Nov. 17 8-8:30 a.m.

Early Detection of Cancer: Potential for Increased Survival and Cures--Nov. 18-19, Western William Penn Hotel, Pittsburgh. Third annual Mary A. Davis Memorial Symposium. Contact 412/624-1023.

Div. of Cancer Biology & Diagnosis Board of Scientific Counselors--Nov. 21, NIH Bldg 31 Rm 9, 9 a.m.

Frederick Cancer Research Facility Advisory Committee--Nov. 21-22, FCRF, open Nov. 21 8:30-11 a.m.

Cooperative Group Chairmen--Nov. 22, NIH Bldg 31 Rm 6, 9 a.m., open.

11th Annual San Antonio Breast Cancer Symposium--Nov. 29-30, San Antonio. Contact Terri Coltman, RN, 4450 Medical Dr., San Antonio, TX 78229.

Facing the Challenge: Meeting the Spiritual Needs of Persons with Cancer--Dec. 1, Calvary Hospital, Bronx, NY. Contact Sr. Patricia Sheridan, phone 212/518-2259.

American Society of Hematology--Dec. 3-6, San Antonio. Phone 609/848-1000.

Mechanisms of Antimutagenesis and Anticarcinogenesis--Dec. 4-9, Ohito, Japan. Second international conference. Contact D.M. Shankel, Cochair, Organizing Committee, Dept. of Microbiology, Univ. of Kansas, Lawrence, KS 66045.

National Cancer Advisory Board--Dec. 5-6, NIH Bldg 31 Rm 6, 8:30 a.m., all open. Annual program review.

Advances in Cancer Treatment--Dec. 7-9, Hyatt Regency Hotel, Los Angeles. American Cancer Society national conference. Contact ACS, 3340 Peachtree Rd NE, Atlanta, GA 30026.

FDA Oncologic Drugs Advisory Committee--Dec. 19-20, Parklawn Bldg Rms D and E, 5600 Fishers Lne, Rockville, MD. 9 a.m. both days, all open.

FUTURE MEETINGS

St. Jude 23rd Annual Clinical Symposium--Feb. 24, 1989, St. Jude Children's Research Hospital, Memphis. Open to all physicians. Contact Director, St. Jude Children's Research Hospital, Box 318, Memphis, TN 38101.

Chemotherapy of Infectious Diseases and Malignancies--March 5-8, 1989, Montreux, Switzerland. Second biennial conference. Contact Biennial Conference, PO Box 70 0640, D-8000 Munich 70, FRG.

Nice Symposia--April 9-11, 1989, Immunology and Biologic Control of Cancer; April 12, Cancer in Patients with AIDS; April 13-15, Perspectives and Trends in Cancer Prevention and Detection. Beach Regency Hotel, Nice, France. Contact H.E. Nieburgs MD, ISPO, 217 E. 8th St., Suite 303, New York 10028, phone 212/534-4991.

Oncology Nursing Society--May 17-20, 1989, San Francisco. 14th annual Congress. Contact ONS, 1016 Greentree Rd., Pittsburgh, PA 15220, Attn: Nancy Berkowitz.

Centennial of Johns Hopkins Medicine--June 7-11, 1989, Baltimore Convention Center and the Johns Hopkins Medical Institutions.

16th International Congress of Chemotherapy--June 11-16, 1989, Jerusalem. Contact Scientific Secretariat, 16th Congress of Chemotherapy, PO Box 983, Jerusalem 91009, Israel.

The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams

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