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Ambitious Radiation Oncology Research Plan Calls For "Concentrated Efforts" In Emerging Areas

"Radiation Oncology--Research Directions 1987," latest in the series of research plans prepared by the radiation oncology community, was presented to the Board of Scientific

(Continued to page 2)

In Brief

Yates To Leave NCI For Roswell Park; Isselbacher Heads MGH Center; Pinsky Moves Up At BRMP

JEROME YATES will leave NCI Oct. 1 to become associate director for clinical affairs at Roswell Park Memorial Institute. Yates has been associate director for centers and community oncology in the Div. of Cancer Prevention & Control for the past five years. He played a key role in development of the Community Clinical Oncology Program and became a champion of cancer centers. At Roswell Park, Yates will head up all clinical activities, including the hospital, and will also oversee cancer control activities . . . . **KURT ISSELBACHER**, chief of the gastrointestinal unit at Massachusetts General Hospital for 30 years and professor of medicine at Harvard, has been appointed director of the MGH Cancer Center. The center, already the largest in New England, has been expanded with new laboratory facilities on the site of the old Charlestown Naval Shipyard. Isselbacher, a member of the National Academy of Sciences, pioneered research of tumor cell nutrient uptake. . . . **LARRY RAY**, who has been administrative officer of NCI's Div. of Extramural Activities, is the new AO of the Div. of Cancer Treatment. He replaces Don Christoferson, now deputy NCI associate director for administrative management. **Dorothy Tisevich**, who has been acting AO of DCT since Christoferson's promotion, has returned to her job as deputy AO. . . . **CARL PINSKY** is now chief medical officer for extramural research in DCT's Biological Response Modifiers Program. He has been replaced as chief of the BRMP Resources Branch by **Stephen Creekmore**. . . . **NCI'S FIRST** Year 2000 Awards were presented to **Benno Schmidt** and **Paul Rogers** for their roles in enactment of the National Cancer Act of 1971. Schmidt chaired the National Panel of Consultants whose recommendations led to enactment of the law and later as chairman of the President's Cancer Panel during its first eight years. Rogers was chairman of the House Health Subcommittee in 1971, and he crafted the compromise bill which became the National Cancer Act.

DCT Board Hears Report On New Plan For Radiation Research, OKs Concepts

(Continued from page 1)
Counselors of NCI's Div. of Cancer Treatment last week. The 19 chapter, two and a half inch thick document covers every aspect of radiation oncology, from basic physics to quality of life.

After hearing discussions of the research plan from the four members of the Steering Committee which headed up its development, the Board approved the concept of two new research programs which were among the plan's recommendations, along with recompetition of an important contract. The concepts set aside a total of $1.4 million a year.

Compilation of the research plan was sponsored by the American College of Radiology, the Inter-Society Council for Radiation Oncology and NCI. Luther Brady chaired the Steering Committee, which included Eric Hall, Alfred Smith and Glenn Sheline. James Cox and Gerald Hanks were ex officio members. John Antoine, director of DCT's Radiation Research Program, and Francis Mahoney of his staff served as NCI liaison representatives.

Brief excerpts from the summary reports on each chapter follow:

Basic and Clinical Radiation Physics--"The six (sub)chapters which are included in this section represent emerging areas of research, but that is not to say that they are entirely new or that considerable work has not already been done. We believe that the time is ripe for concentrated effort in these areas because recent technological advances provide the possibility that these research areas can now be successfully addressed and that some clinical benefit will result from these efforts."

The subchapters are "Dynamic Conformational Radiation Therapy" (a generalization of radiation therapy to a system in which the maximum number of constraints have been reported--the gantry, collimator opening, dose, dose rate and treatment couch are allowed to change under computer control and monitoring during a treament session); "Image Analysis and Processing in Radiation Therapy Planning," involving developing new imaging technologies such as CT, PET and SPECT in treatment planning; "Physics and Engineering of Hyperthermia," with improvements needed in external heating and temperature control, studies of ferromagnetic seed implants, custom tailoring of heat distribution; "Physics of Radioimmunotherapy," to exploit the promise of highly localized radiation therapy; "Physics of Radiation Therapy Under Non-Electronic Equilibrium Conditions," overcoming the problem of adequate dosimetry to heterogeneic areas; and "Tissue Response Modeling," development of the capability of predicting clinical radiation responses of tumors and normal tissues for a population of patients or an individual patient.

The Link Between Physics and Biology--This concentrates on biophysical models which make explicit use of the detailed physical description of the radiation field.

Basic Radiobiology--Includes some research objectives that are essentially pragmatic in nature, intended to support and improve the current practice of radiotherapy, but the central thrust is understanding the mechanisms involved in the biological effects of radiation at the cellular and molecular levels.

Tumor Biology--Organized into seven sections which reflect a progression from the cellular level to tumor and host physiologic levels.

Chemical Modification of Radiation and Chemotherapy--Development of chemical modifiers of radiation damage, such as hypoxic cell sensitizers, shoulder reducing drugs, agents to improve tumor oxygenation, or proliferation dependent radiosensitizers.

Predictive Assays of Tumor Radiocurability--Includes radiosensitivity assays using primary cultures of human tumor cells, the micronucllleus assay, assessment of tumor vasculature and blood flow, measurement of tumor metabolic parameters.

Dose Fractionation and Volume Effects in Normal Tissues and Tumors--Repair of cellular injury, repopulation, redistrubution within the division cycle of cells surviving previous doses, reoxygenation of tumor cells, with emphasis on repair of injury and repopulation.

Combined Modality Therapy Using Cytotoxic Agents and Radiation Therapy--"Much controversy still exists and much carefully controlled work needs to be done. . . Laboratory work is required to improve understanding of tumor and normal tissue radio and chemobiology and interaction of these modalities at the molecular, cellular and tissue levels."

Radiation Therapy and Surgery--First priority should be comparing combined treatment with single treament modalities for

colonic and gastric tumors and nonoat cell carcinoma of the lung.

Monoclonal Antibodies for Use in Radiotherapy and Diagnosis--Problems have emerged with stability of the radiolabel, low tumor uptake, high blood pool and nontarget tissue background, and nonspecific localization.

Brachytherapy--Studies are needed in the radiobiology, physics and dosimetry of brachytherapy. NCI should sponsor a national registry of brachytherapy procedures performed, isotopes used and outcome. Work is needed on instrumentation, reduction of radiation exposures, and brachytherapy use in breast, prostate, cervix and brain cancer.

Biological and Clinical Aspects of Hyperthermia--Priority areas include elucidation of basic HT effects on membrane components, intracellular ion distributions and ion functions, protein phosphorylation, polyamines, cytoskeleton components, protein synthesis and heat shock response.

Particle Radiation Therapy Research Plan--Fast neutron clinical trials vs. photons for prostate cancer stages C and D; sarcomas of the bone, cartilage and soft tissue; inoperable squamous carcinoma of the head and neck; inoperable or recurrent carcinoma of the rectum; squamous carcinoma of the uterine cervix stages 3 and 4A; and inoperable small cell carcinoma of the lung. Expanded studies of low and high LET heavy charged particle therapy are needed.

Oncologic Imaging: State of the Art and Research Priorities--List priorities by body site for MR and CT, including design and testing of techniques to investigate dynamics of tumor perfusion, spectroscopy, better contrast discimination, use with monoclonal antibodies.

Applications of Data Bases and AI/Expert Systems in Radiation Therapy--Lists seven special areas worthy of targeted research.

Design and Analysis of Clinical Trials--Expoiting advances in telecommunications and computing, development of "stopping rules" when appropriate; development of statistical models.

Quality Control and Assurance--Periodic consensus panels are needed to determine best current management for major diseases treated primarily with radiation therapy, in addition to the multidisciplinary consensus panels.

Quality of Life Assessment in Cancer Patients--The need for comprehensive, systematically collected, longitudinal data concerning function is of the higheswt priority.

All three of the concepts approved by the Board fit into the plan's priorities. They include an RFA for grants on research in contrast agents for MRI, a new contract for radiotherapy planning and recompetition of a contract for hyperthermia quality control. The concept proposals follow:

Investigation of tissue composition and function by MRI imaging employing paramagnetic contrast agent formulations and superparamagnetic agents with tissue specific and/or pharmacokinetic properties. Three grants, to be funded for three years at an estimated first year total cost of $400,000. The concept statement:

The number of clinical MRI systems in U.S. medical sites will increase to 500 instruments by 1987 and an estimated 2000 devices by 1990. Technical advances have provided these instruments with sufficient spatial and temporal resolution to study dynamic processes such as tissue perfusion and many other tissue functions.

MR contrast agents, which produce contrast in the MR image by altering the T1 and/or T2 relaxation times of biomaterial to which they are joined, provide molecular probes appropriate to adopt the well known tracer methodologies of nuclear medicine to important clinical problems, since as with the nuclides, very small doses of paramagnetics or superparamagnetics are used.

A variety of paramagnetic contrast formulations have been developed (gadolinium DTPA, gadolinium DOTA, manganese chelate), with useful tissue specific or pharmacokinetic properties. Studies directed toward investigation of tissue composition and function, and localization and/or quantitative measurement of pathological processes are intended by this initiative. For example, gadolinium DTPA is specific for determining kidney function (GFR) and can identify brain lesions when the blood/brain barrier is disrupted. Manganese chelate identifies hepatocytes and performs as a hepatobiliary excretion agent.

The new class of superparamagnetics (ferromagnetic compounds) selectively decrease tissue T2 relaxation time. Being more potent in this latter characteristic than the paramagnetics, they present the enhanced potential of making monoclonal antibodies usable in MR imaging. The ferromagnetic particles are readily phagocytosed by the reticulo-endothelial cells of bone marrow, liver and spleen, thereby providing contrast agents for these organs. These compounds may also elucidate the nature of endogenous materials with apparently similar characteristics seen in normal and pathological tissues with MRI--e.g., distinguishing the iron of hemosiderin of an old bloodclot from normal iron deposition in the brain stem. Quantitative measurement of compounds is determined by a graded intensity scale.

John Antoine, director of the Radiation Research Program, said that not much is going on in developing new contrast agents for oncologic imaging. Francis Ruzicka of RRP added that industry is spending most of its effort on equipment development, not contrasts. "It was initially thought that MRI would produce contrasts in the tissue itself, but it is apparent now that contrast agents are even more important in MRI."

DCT Director Bruce Chabner said that staff had requested $800,000 for first year funding of five to six grants, but the NCI Executive Committee trimmed that to $400,000 for three grants.

Radiotherapy treatment planning tools. Four to five

contract awards for five years at an estimated annual cost of $700,000 a year.

Radiotherapy is one of the most computer intensive disciplines of medical care, primarily because of the anatomical information that is required to define the tumor and treatment volume and to characterize the extent of radiation dose to the tumor and the normal tissues at risk. Computerized tomography scans now play an essential role in the radiotherapy treatment planning process. It is anticipated that the additional information available from magnetic resonance images and diagnostic tools such as PET and SPECT will be adapted to radiotherapy diagnosis and planning. Computerization of CT scans and their use in a new class of computer programs carrying out three dimensional treatment planning have pointed out the need for new tools in the processing and manipulation of the large volumes of data needed for the radiotherapy treatment planning process.

This project calls for the development of computer assisted decision support systems or expert systems that have the following capabilities: (1) To rapidly extract anatomical features from multiple images needed for the definition of the treatment plan, such as the treatment volume (from tumor contours) and critical organs, e.g., spinal cord, kidney, stomach, liver; (2) to assist the physician in the definition and delineation of tumor from normal tissues, using metabolic information available from PET, SPECT, or ultrasound; (3) to assist in the definition and contouring of tumor volumes; (4) to provide three dimensional images in rapid, interactive fashion that yield displays to assist in the optimization of treatment plans; (5) to rapidly and interactively display anatomical information with the treatment plan and radiation dose distribution superimposed; (6) to provide tools that assist the physician in selecting the best treatment plan; and (7) to provide the capability for comparison of images of treatment ports with simulation images as part of the treatment position verification process during treatment delivery. These systems will be designed with a user interface that is acceptable and useful to physicians with respect to fast response and ease of use. Their primary function is to provide tools that support the physician's decision making process. The capability of explaining their reasoning will be essential to physician acceptance.

"It has always bothered me," Antoine said, "that radiotherapy is given in 3D but treatment planning is in 2D." In response to Board member Emil Frei's question on whether industry might support this effort, Antoine said that again, industry is more interested in hardware development. "If this is not done with research funds, I doubt if it will be done. There is no commercial spinoff."

Chabner observed that "the people who make diagnostic machines are not interested in treatment, and those who make treatment equipment are not interested in diagnosis. This falls between the cracks."

"Neither one has been a league leader in supporting research," Board member Robert Goodman added.

Frei asked whether the amount recommended was a realistic figure to support four to five awards. "I thought it would be on the low side," Antoine said. The Board approved the concept without recommending it be increased, however.

Hyperthermia quality assurance program. Recompetition of a contract presently held by Allegheny-Singer Research Corp. A five year contract, estimated annual cost, $300,000.

Hyperthermia is under active evaluation as an effective adjunct to radiation therapy and chemotherapy for the treatment of cancer. The increased interest in this therapeutic modality has caused a proliferation in the number of medical facilities acquiring hyperthermia systems. Continued expansion of the use of this treatment modality is expected, especially since the Health Care Financing Administration and third party payers in several states have approved reimbursement for hyperthermia treatments. Many of the facilities utilizing hyperthermia equipment are doing so without quality control since they are not staffed with individuals trained to recognize the problems. To assure that therapeutic hyperthermia treatments are of the highest quality, an assurance program of national scope is required. This program would ensure uniformly high quality physics and engineering applications at the clinical facilities utilizing hyperthermia, which are actively participating in clinical research protocols approved and supported by NCI. Only with good quality control will the uniformity of data from clinical trials be truly valid and comparable between institutions and/or studies.

The current contractor has developed realistic guidelines for the various types of applicators, thermometry, and ancillary equipment used in hyperthermia. They have tested these guidelines in the various institutions that were site visited. As a result of these site visits, many deficiencies were noted and sources of error were defined. Recommendations were made for identifying sources of error in instrumentation, and suggestions were offered for minimizing these problems. Operator and patient safety were also considered. The contract has developed an excellent working relationship with both the equipment manufacturers and the users. The contractor has served as a resource both by documenting progress in the field and by rapidly disseminating information to the users. The contractor has established an excellent rapport with the appropriate subcommittees of the various scientific societies which have interest in the field of hyperthermia and is jointly trying to set stringent yet achievable standards for the application of this emerging treatment modality. This contractor has identified problems in (1) the accuracy of thermometry (temperature discrepancies ranged from -4.58 to +3.12 degrees C); (2) power reliability (power measured on the instrument panel differed from that at the applicator by a large factor, power indicated/power measured ranged from 0.75 to 1.45); (3) instrumentation uniformity (individual heating devices of the same model from the same manufacturer demonstrated differences in performance characteristics when operated in an identical manner); and (4) EM leakage (leakage for low frequency/high power regional heating devices exceeded the ANSI recommended safe level at every facility site visited at some locations potentially occupied by an operator).

Future plans are to continue providing quality assurance to those institutions conducting clinical trials with NCI support. The importance of external, independent quality assurance as is provided by the Radiological Physics Center has been well recognized in radiation therapy trials. The quality assurance contractor provides a similar service for hyperthermia trials. Since hyperthermia is an emerging modality without the type of standardization achieved in radiation therapy, the importance of quality assurance in hyperthermia trials is much greater than in radiation therapy trials. In addition, the contractor will be required to provide continuing education conferences and meetings. Basically, the contractor will continue as a resource for both the medical community utilizing hyperthermia and the equipment manufacturers.

Board members Karen Fu and Goodman, both radiation oncologists, strongly supported the concept. "The entire radiation therapy community thinks something good will come out of hyperthermia," Goodman said.

Hammer Blasts GAO Survival Report As "Gobbylegook," Praises IL-2 Trials

Armand Hammer, chairman of the President's Cancer Panel, called the General Accounting Office's report on cancer survival "a prime example of bureaucratic gobblygook" in his report to the National Cancer Advisory Board last month.

Hammer did not attend the NCAB meeting, since he was in the Soviet Union at that time; his statement was read by Panel member William Longmire.

"Personally, I happen to believe that the GAO report is simply too pessimistic," Hammer's statement said. "It does not take into account much of the progress that has been made in the past few years, and I believe that certain developments, most especially the exciting work done with biological response modifiers, have justified claims that we are gaining to a significant extent on the enemy that is cancer.

"In fact, you may recall, the GAO report states: 'With regard to the question whether progress has been made against cancer, the GAO concludes that the answer is yes, but the amount of progress is as much a function of the particular definition of the term progress being used, as it is a reflection of what has actually occurred in the field.'

"Such a statement is, in my opinion, a prime example of bureaucratic gobblygook. I know how I define progress, and in my definition, NCI has achieved it to a significant and certainly beneficial extent for many thousands of cancer victims.

"Perhaps the most unfortunate aspect of this matter is its effect on the general public, who are unlikely to read the entire report and attempt to sort out its various inconsistencies. If they read a newspaper account which says in its first paragraph 'Gains in treating cancer over the last three decades have been small according to a detailed analysis completed by a congressional investigative agency,' they are likely to become frightened, discouraged and, especially, confused. And headlines can be even more disturbing. It is true that a careful reading of the various articles does present the rebuttal by NCI and others, but by this time a good deal of the damage in the public's mind has occurred.

"There is little doubt that statistics can be open to many different interpretations, and very often are, but I feel the interpretations made by the GAO investigators in this case were unfair and misleading. I hope somehow we can get this message across to the public and to the Congress as well."

Hammer added that the NCAB's regional public meetings could help in that regard. The first such meeting will be held in Los Angeles in September. Board member Helene Brown is in charge of that meeting.

On another controversy, Hammer said he was "gratified by reports in the 'New England Journal of Medicine' of April 9 by Dr. Rosenberg and his colleagues [of NCI] and Dr. William West and his colleagues from the Biological Therapy Institute reaffirming positive results received with treatment of advanced cancer patients using interleukin-2 with and without lymphokine activated killer cells.

"I was further impressed by the editorial in the same issue written by Dr. John Durant, [president] of Fox Chase Cancer Center regarding these reports. Dr. Durant wrote that he felt the results of Dr. Rosenberg, Dr. West and their colleagues justify rational and vigorous pursuit, and this is just what is taking place.

"I believe Dr. [Vincent] DeVita and NCI have taken a very important step in requesting the Food & Drug Administration to place IL-2/LAK into a modified Group C category and make it available to 38 comprehensive and clinical cancer centers. I have looked over NCI's proposal and am satisfied it is very carefully crafted and designed to maintain stringent controls and appropriate data reporting. I am sure we are all pleased that FDA has approved the NCI request.

"It is encouraging to know that many additional patients with advanced malignant melanoma and kidney cancer will have the opportunity to receive the IL-2/LAK therapy. It is certainly not a panacea, but it does offer some hope to those for whom an effective treatment simply has not been available up to this time. And as the number of patients participating in these trials increase, we will . . . make it as effective in treating these cancers as humanly possible.

"I hope we will be able to move quickly with the cancer centers to enroll qualified patients, for we need to develop this treatment so that one day it, like chemotherapy, surgery and radiation, will be standard treatment and available to all cancer patients who need it. That, indeed, will be progress."

Abbott Offers New Publication, Annual Award In Diagnostics, Tumor Markers

Abbott Laboratories has announced two new educational programs for physicians in cancer diagnostics.

"Recent developments in tumor marker technology and other advances in cancer research are the primary subjects of the educational program, which is directed mainly at practicing oncologists," Abbott said in a statement released during the annual meeting of the American Society of Clinical Oncology.

A new quarterly publication, "Therapeutic Crossroads in Cancer Management," is the cornerstone of the program, Abbott said. It will be supplemented by videotapes, slide/tape modules and other educational materials.

The publication will concentrate, through actual case studies, on a different disease site and the tumor marker or set of markers significant in detection of disease in that area. Practicing oncologists are invited to submit case studies on their uses of tumor markers. They will be paid $500 for each case study chosen for publication.

Abbott also will award a young investigator fellowship of $25,000 each year to the "noted oncologist or pathologist with the most interesting and useful research to cite in the application of tumor marker technology."

Oncologists interested in receiving "Therapeutics Crossroads" may write to Cancer Business Unit, Dept. 94K, Abbott Laboratories, Abbott Park, IL 60064.

RFAs Available

RFA 87-AI-21

Title: National cooperative vaccine development groups for AIDS
Letter of intent receipt date: July 15
Application receipt date: Sept. 15

The National Institute of Allergy & Infectious Diseases announces the availability of an RFA for the funding of national cooperative vaccine development groups for AIDS (NCVDG). The RFA invites applications aimed at the development of effective vaccines for the prevention of AIDS. Scientific approaches to the development of effective AIDS vaccines appropriate to the RFA may range from research on whole virus vaccines, through the production of preparations with recombinant DNA techniques and synthetic approaches, to the use of viral vectors to deliver antigenic materials. Applications directed towards vaccine development for AIDS associated opportunistic infections are not invited. Otherwise, scientific approaches to the development of effective vaccines appropriate to the RFA are broad and limited only by the creativity and ability of the applying group to exploit leads from basic studies in virology, molecular biology and immunology.

Each NCVDG will be assembled by the principal investigator to form a multidisciplinary consortium representing the various skills needed to successfully design and evaluate vaccine entities and strategies for the prevention of AIDS. Inasmuch as it is unlikely that all of the outstanding talents required to exploit fundamental leads from various scientific disciplines will be found in a single institution, each group is envisioned as being multi-institutional as well. Thus each NCVDG will be assembled by the PI and may consist of a number of laboratory projects representing the scientific disciplines required to attain the group's goal and objectives. The various laboratory projects, including that of the PI, may be mobilized from academic or research institutions and industry. It is expected that the rationale for design of potential vaccines, the synthesis or production of specific candidates, and the models for evaluation will originate within the group and be based on leads from their own and others' fundamental research.

Awards will be made as cooperative agreements, to the application institution on behalf of the group as a whole and not to individual laboratory projects within the group. The applicant institution will provide a central operations office for the group.

Complete copies of the RFA and additional information are available from Dr. John Nutter, Chief, Prevention Branch, AIDS Program, NIAID, Westwood Bldg Rm 3A-07, Bethesda, MD 20892, phone 301/496-8200.

RFA 87-TW-01

Title: Special international postdoctoral research program in AIDS
Application receipt date: Sept. 15

The Fogarty International Center of NIH invites applications from U.S. institutions with interest in developing multidisciplinary postdoctoral fellowship programs in AIDS research for U.S. and foreign scientists. Funds will be awarded to encourage basic and clinical research in all biomedical and behavioral disciplines related to AIDS. Applications received in response to this request will be reviewed and considered for funding in a single competition.

The epidemiologic patterns and modes of transmission for the AIDS virus have been shown to vary between men and women and among countries. International cooperation is important in understanding and preventing AIDS. It is in this context that the Fogarty International Center is initiating a special international postdoctoral research program in AIDS.

Objectives of the program are to support collaborative research between U.S. and foreign scientists who wish to enhance their knowledge and skills in the epidemiology, diagnosis, prevention and treatment of AIDS; and to stimulate scientists from nations affected by AIDS to cooperate and share research knowledge in combatting this global problem.

It is expected that the program director will be a recognized scientist in AIDS research, interested in both the basic and clinical aspects of the syndrome, and able to attract as preceptors basic and clinical scientists in his or her institution who are experts in other biomedical and behavioral disciplines related to AIDS.

Under this award the program director will make fellowship appointments to U.S. and foreign scientists varying from three to 24 months. Scientists who are appointed must have an earned doctoral degree (MD, PhD, DVM, DDS) or the equivalent in a health science field, be actively engaged in AIDS research, not be employed by a for profit institution, and if foreign, must have a permanent position in his/her home institution. Postdoctoral scientists at all career

levels are eligible for appointment. It is expected that appointments will cover the full range of scientific disciplines related to AIDS research.

U.S. scientists from the grantee institution will be limited to collaborative study in foreign institutions only. The U.S. appointees must have a letter of invitation from the foreign hosts accepting the fellows and committing the resources of the foreign institutions to the research effort. Foreign scientists will be required to conduct their research at the awardee institution only; each appointee will be assigned to a preceptor from among the participating faculty. Sixty months of appointments will be permitted each budget year.

For further information and copies of the RFA contact Bettie Graham, PhD, Chief, International Research & Awards Branch, Bldg 38A Rm 613, Fogarty International Center, NIH, Bethesda, MD 20892, phone 301/496-6688.

RFA 87-HL-19-B

Title: Inactivation of human immunodeficiency virus and other transfusion transmitted viruses in blood and blood components

Application receipt date: Nov. 16

The Blood Resources Branch of the Div. of Blood Diseases & Resources, National Heart, Lung & Blood Institute, announces the availability of an RFA on the above subject. The program will encourage basic and applied research on the development and evaluation of procedures to remove or destroy the infectivity of HIV and/or other transfusion transmitted viruses in blood and blood components while maintaining the therapeutic effectiveness of these preparations. The emergence of the AIDS epidemic has underscored the serious and urgent need to develop effective means of rendering blood and blood components safe for transfusion. Procedures that are developed should be simple, inexpensive and capable of being used in blood banks and blood centers.

Copies of the RFA may be obtained from Luiz Barbosa, DVM, Blood Resources Branch, DBDR, NHLBI, Federal Bldg Rm 504, NIH, Bethesda, MD 20892, phone 301/496-1537.

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, the Blair building room number shown, National Cancer Institute, NIH, Bethesda MD 20892. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring MD, but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-87226-53

Title: Literature surveillance for natural products with potential anti-AIDS activity

Deadline: Approximately Aug. 7

NCI is seeking a contractor with the capability to conduct a surveillance of published literature in the natural products area to search for new and novel compounds that may be active against AIDS or have biological activities related to antiviral or immunological properties. This will require surveillance for new natural products reported in pertinent current journals, abstracting services and data bases in areas related to the natural product. The surveillance is expected to cover published key journals in natural products, AIDS, virology and immunology and in other fields which may have bearing on activities against AIDS; a comprehensive search of abstracts and data bases as they are published; and a review of the original articles of the references selected from the above.

The contractor shall also perform retrospective taxonomic searches for families and which are sources of active leads. The retrospective searches will be performed on an as needed basis, dependent upon the number of actives found from these searches.

This contract will not involve simple retrieval of articles published, but a selective retrieval, requiring the principal investigator to recognize natural products compounds that could be of biological interest to NCI. It is therefore preferred that the PI possess a PhD in organic, medicinal or natural products chemistry, or a closely related discipline and must have a strong background and recent experience with natural products structures and chemical searches, as well as background and experience with evaluation and interpretation of biological data, preferably in the AIDS area.

The PI should have in depth knowledge of the natural products area and ready familiarity with organic and medicinal chemistry for the selection of articles and chemical structures of probable interest to NCI. Other staff members should possess a bachelor's degree in either chemistry or library science or equivalent experience. The offeror must demonstrate awareness of the type and comprehensiveness of the searches and literature data to be submitted.

The ability to obtain data in a timely fashion is essential as is the knowledge of the appropriateness of journals to be searched. The offeror must have available adequate facilities and equipment. Also, the offeror must possess appropriate organizational qualifications in the field of literature surveillance.

It is anticipated that a single five year incrementally funded contract will be awarded on or about April 1, 1988.

Contracting Officer: Eileen Webster
RCB Blair Bldg Rm 216
301/427-8737

RFP NCI-CM-87225-53

Title: Large scale preparation of anti-AIDS drugs for phase 2 and 3 clinical trials

Deadline: Approximately Aug. 7

NCI is seeking a contractor with the capability to provide and operate a materials preparation laboratory for the development of existing or new processes, procedures and techniques for the preparation of compounds; and for the synthesis of varying amounts of materials, not readily available from other sources in the quantity and/or quality needed.

The offeror will be expected to provide an operating large scale facility with at least one small (20-100 gallons) and at least one and preferably two large (200 gallons or larger) glass lined reactors and the necessary supporting equipment and facilities. In addition, the offeror will be expected to provide a specialized facility for handling hazardous (e.g., explosive or very toxic) reagents and intermediates such as diazomethane, ethyleneamine, hydrogen, sodium azide, etc. Quantities of drugs requested will usually range from 50 grams to multikilograms. Process development for scale up and access to pilot plant equipment is essential.

Specific assignment of the materials for preparation will be made by NCI, and may include synthesis of all types of chemicals and drugs. Quality specifications will be determined by NCI. All materials must be evaluated by the synthesis laboratory for identity and purity before being submitted to NCI.

The principal investigator should be trained in

organic or medicinal chemistry, preferably at the PhD level, or equivalent in experience, and have extensive experience in chemical synthesis and synthetic process development.

It is anticipated that a single incrementally funded contract will be awarded for a three year period on or about April 1, 1988.

Contracting Officer: Eileen Webster
RCB Blair Bldg Rm 216
301-427-8737

RFP NCI-CM-87229-22

Title: Chemical synthesis of anti-AIDS compounds
Deadline: Approximately Aug. 7

The Drug Synthesis & Chemistry Branch (DS&CB) of NCI's Developmental Therapeutics Program, Div. of Cancer Treatment, is seeking contractors to provide the synthesis of a variety of organic/inorganic compounds. The primary focus will be on the resynthesis of compounds that have been identified by DTP as meriting investigations. The compounds scheduled for preparation are unobtainable from the original sources and are needed for biological evaluations. It is anticipated that the compounds will be synthesized in quantities of 0.1 to 5 grams using the original synthetic methods. Occasionally, some method development will be required.

The types of compounds to be prepared will include nitrogen, oxygen, and sulfur heterocycles, nucleosides, peptides, coordination complexes, antisense nucleic acids, etc. All synthesized compounds shall be characterized as to identity and purity.

Each contractor should have available a fully operational facility including all necessary equipment and instrumentation for all aspects of the contract.

Note: Two related RFPs are available; the one following is a 100 percent set aside for small business. Offerors who qualify as a small business are encouraged to submit proposals under both RFPs; however, not more than one award under both RFPs will be made to any single organization.

Contracting Officer: Elizabeth Moore
RCB Blair Bldg Rm 216
301/427-8737

RFP NCI-CM-87231-22

Title: Chemical synthesis of anti-AIDS compounds by small business.
Deadline: Approximately Aug. 7

This RFP is identical to the one above except that it is reserved for organizations which qualify as small business. The standard for small business in this case is 500 employees or less.

Contracting Officer: Elizabeth Moore
RCB Blair Bldg Rm 216
301/427-8737

RFP NCI-CM-87227-22

Title: Preparation of radiolabeled anti-AIDS compounds
Deadline: Approximately Aug. 7

NCI is seeking organizations having capabilities, resources and facilities for the preparation, storage and distribution of radiolabeled materials. The objective of this project is obtaining radiolabeled compounds of high purity via synthesis, fermentation, etc., in 1 to 50 millicuries quantities. The major emphasis will be on the preparation of the desired labeled compounds via synthetic procedures and will involve a wide variety of compounds, such as nucleosides, heterocyclic compounds, alkaloids, peptides, anionic dyes, purines, pyrimidines, etc. Compounds required may include one or more of the following radioactive elements: carbon, tritium, deuterium, sulfur, phosphorous, iodine, nitrogen, etc.

Materials will be stored and shipped by the contractor. The contractor must provide suitable storage for approximately 50 radiolabeled compounds. A broad Nuclear Regulatory Commission or equivalent license is required. Methods will be available for "cold runs" in many but not all instances. All materials must be completely characterized and assayed as to identity, purity and radiopurity.

A well instrumented analysis laboratory including a HPLC dedicated to radiosynthesis work and adequate library facilities should be available. It is anticipated that an incrementally funded contract will be awarded for a period of three years beginning on or about May 1, 1988.

The principal investigator should be trained in organic, medicinal, or radiochemistry, preferably at the PhD level from an accredited school, and should have recent experience in radiochemical synthesis. In lieu of the PhD, equivalent experience may be acceptable.

Contracting Officer: Elizabeth Moore
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RFP NCI-CM-87228-22

Title: Analysis of chemicals and pharmaceutical formulations for anti-AIDS agents
Deadline: Approximately Aug. 7

NCI is seeking organizations with the capability to evaluate bulk pharmaceutical substances and formulated drug products for identity, purity and drug content. Reports of the analytical testing on bulk drugs and dosage forms will be used as a basis for assessing the suitability of bulk drugs or finished dosage forms for use in screening, pharmacology studies, toxicological studies, formulation studies, or for clinical trials. These data will also be supplied to the Food & Drug Administration as part of the NCI investigational new drug (IND) filings for new anti-AIDS agents.

Historical summaries of the data will be used in preparing specifications for the various bulk pharmaceutical substances. These specifications will be used in procurement actions, as well as for the routine quality control of these materials.

In addition, solubility data will be developed, and selected assay methods will be adapted for the quantitation of drug in plasma. These data will be provided to other contract projects to facilitate formulation development, and to aid in the analytical aspects of pharmacology and toxicological testing.

The principal investigator should be trained in chemistry (analytical, pharmaceutical, organic, etc.), preferably at the PhD level from an accredited school, and should have recent experience in the analysis and evaluation of bulk pharmaceutical substances and clinical dosage forms. In lieu of the PhD, equivalent experience may be acceptable.

It is anticipated that an incrementally funded contract will be awarded for a period of five years beginning on or about May 1, 1988. Analyses of approximately 30 lots of bulk pharmaceutical substances and 15 lots of formulated drug products are anticipated per year.

Contract Specialist: Elizabeth Moore
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