THE CANCER LETTER

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ACCC TO ASK CONGRESS TO EARMARK APPROPRIATIONS FOR CONSTRUCTION OF COMMUNITY CANCER CENTERS

A line item in the fiscal 1976 HEW appropriations bill earmarking funds for construction of community cancer centers is one of the goals that will be sought by the Assn. of Community Cancer Centers. The association has not yet determined how much money it will seek, but one estimate was that it would be in the $5-7 million range.

ACCC leaders are aware of the Administration's opposition to federal funding for new health facilities. The Office of Management & Budget is still refusing to release money appropriated by Congress in the current fiscal year for new construction of cancer centers. That money is not carried as a separate line item in NCI's budget; congressional instruction that the appropriation included funds for new construction was contained in the Senate report on the bill and not in the bill itself. Executive Branch agencies ignore such instructions at their peril, but they do not have the force of law.

"That's why we will ask for a line item in the bill," said James Dono-

(Continued to page 2)

In Brief

EDWARDS TAKES A PARTING SHOT AT CANCER PROGRAM; "FORWARD PLAN" CALLS FOR EMPHASIS ON PREVENTION

HEW'S "FORWARD Plan for Health," Asst. Secretary for Health Charles Edwards' legacy to his as yet unnamed successor, included an implied threat against the cancer program as Edwards and HEW planners continue to mis-state the facts. Increased emphasis on cancer and heart disease "have thrown the research effort out of balance," the Forward Plan says. "As a result of the designation of cancer and more recently heart and lung diseases as high health priorities (with attendant large increases in funds for those programs), important, fundamental, cross-cutting areas of knowledge have not received the support they merit. . . . Progress in many of our national health objectives in disease control and prevention efforts is hampered by gaps in our knowledge of the fundamental normal and pathological process at work. These areas include immunology, cell membrane research and the cellular and molecular basis of growth, aging and disease." The fact is, basic research in cell biology and immunology has been vastly increased since the National Cancer Act was adopted in 1971; NCI probably supports more such projects than all other sources combined. . . . THE PLAN isn't all bad. It calls for major emphasis on prevention, including efforts to reduce cancer by eliminating environmental and occupational hazards. It also asks for more immunization programs, development of health care standards for physicians and hospitals, and an inventory of clinical trials to speed up information flow to practitioners on their results. The Forward Plan assumes that a national health insurance plan will be in operation by 1980.

LINE ITEM IN BILL WOULD PREVENT OMB FROM BLOCKING CONSTRUCTION DOLLARS

(Continued from page 1)

van, ACCC president. "That's the only way we can be sure the money would be released."

Donovan said his group estimated the average cost of building a new community center would be close to $1 million. The federal share would be 50%, although Donovan feels the program should be flexible, permitting the government to pay a greater share in communities with more limited resources.

Some communities will be able to make use of existing facilities and might require as little as $200,000 for upgrading, Donovan said.

ACCC will have the support of at least one other lobbying organization when it goes before the congressional appropriations committees. The Citizens' Committee for the Conquest of Cancer has offered its help. The committee, in a recent report, said it would ask Congress to authorize a "single adequate grant" to ACCC to support its activities. Legislation may not be necessary. NCI's Div. of Cancer Control & Rehabilitation has invited ACCC to submit a sole source proposal for a contract to help carry out the association's program.

The report of the Citizens' Committee included notice that the group would revive the issue of "umbrella grants" for comprehensive cancer centers.

"Originally each comprehensive center was to receive a large yearly grant to enable it to carry out its missions," the report said. "This large grant . . . was supposed to cover many activities. It would reduce the enormous paper work, red tape and waste of time that accompanies sending in a separate grant application for each project. Since the comprehensive centers are centers of excellence, they could be relied upon to function effectively.

"Unfortunately," the report continued, "some officials and advisors in HEW do not want to relinquish any of their authority. Accordingly, they have managed to block all or most of the umbrella grants. The Citizens' Committee views this situation as intolerable. It is a clear violation of the legislative intent of the Cancer Act of 1971. Accordingly, we intend to ask the Congress at the proper time to write into the appropriations bill an absolute requirement that substantial umbrella grants be awarded to the regional cancer centers. This should reduce greatly the red tape and time wastage that is now hindering the progress of the regional centers."

NCI decided not to award umbrella grants after the National Cancer Advisory Board and NCI staff advised against them. "Everyone felt the grants would be so large and so numerous that they could never be adequately reviewed by a single reviewing committee," Director Frank Rauscher said.

NCI does award core grants to the comprehensive centers, covering salaries of key personnel, equipment and other start up costs. The centers also receive funds to finance the start up of new research projects by younger investigators, permitting them to bring their projects along to the point where they can then apply for regular grant support.

Other efforts planned by the Citizens' Committee this year include presentation of its arguments for increased funding for NCI and an attempt to speed up the drug approval process of the Food & Drug Administration.

"After a crude natural product is shown to have definite anticancer effects on mice," the report said, "it still takes seven to 12 years before it is ready for clinical trials on patients with cancer. In part, this delay is due to generally inadequate funding, in part to priorities that were set up in the past that are now being modified, and in part to arbitrary, bureaucratic regulations by FDA which the Citizens' Committee will be working to correct."

The committee believes that adequate funding for the cancer program would be from $1.2 to 1.5 billion a year. The National Cancer Act amendment of 1974 authorizes $896 million for NCI for fiscal 1976. "However, certain elements of the federal bureaucracy will undoubtedly try to reduce the appropriation to a much lower figure," the report said. "For fiscal 1977, Congress authorized $985 million. That is coming close to the amount needed, but it will not be easy to get that sum appropriated."

The report included arguments against OMB's intention to cut the health research budget to fight inflation. "Funds spent to conquer cancer and for other medical research programs do not contribute to inflation, they help fight inflation. Serious illness costs a lot of money. When treatments are found for serious illnesses, they lower the costs to the individual, his family, the community, and the national economy. This is not merely theory. Careful studies show that the government actually makes a profit on its medical research investment. People who are cured or restored to health return to work and pay income and excise taxes. Each year, the income and excise taxes paid by people who were cured or restored to health through medical research paid for by federal funds actually exceeds the amount paid out by the government for medical research in that year. Therefore, medical research helps fight inflation. Cancer now costs the nation over $15 billion per year in medical care costs and loss of wages.

"In comparison with other government expenditures, the amount needed to conquer cancer is quite reasonable. A single Trident submarine costs about $1.5 billion. . . . At its peak, the space program received over $6 billion per year, and it still receives over $3 billion per year. The amount needed per year for an effective conquest of cancer campaign is considerably less than one-half of one percent of the yearly spending of the government."

BEHAVIORAL CONFERENCE TO EXPLORE MANAGEMENT, REHABILITATION PROBLEMS

A behavioral science conference sponsored by NCI's Div. of Cancer Control & Rehabilitation is scheduled Jan. 20-22 in San Antonio, Texas. Speakers will include professionals in the behavioral science field who will discuss problems related to the management and rehabilitation of cancer patients.

Objectives of the conference are to determine the state-of-the-art of behavioral principles as they relate to chronic disease and cancer in particular, and to strengthen interest among behaviorists toward applying their knowledge and skills to cancer patients and the general public at risk to cancer.

Topics will include delay and secondary prevention; problems of high risk populations and high risk non-responders; role of the health care system in affecting the attitudes and behavior of practitioners and patients; negative and positive roles of groups in influencing health behavior; communication; problems of physicians and patients in confronting the diagnosis; adjustments of patients and practitioners to the consequences of cancer; and the terminal patient.

PREVIOUS ARTICLE IN ERROR -- CIDAC RFP AVAILABLE TO ANY ORGANIZATION

The statement appearing in *The Cancer Newsletter* Dec. 20 that bidding on contracts to establish four Cancer Information Dissemination and Analysis Centers (CIDAC) would be limited to cancer research centers was not correct.

The RFP, which will be available in about two weeks, will be offered to any organization that feels it has the capability of performing the work, NCI said. The RFP will spell out the requirements for staff and facilities for the CIDACs, a key element in the International Cancer Research Data Bank program.

Contract Awards

CANCER PATIENT JOB DISCRIMINATION SUBJECT OF $2 MILLION, 3-YEAR STUDY

The growingsuspicion that many of the 300,000 or more cancer patients who are successfully treated every year are encountering employment discrimination because of the disease has impelled NCI to support a $2 million, three-year effort to do something about it.

The Div. of Cancer Control & Rehabilitation has awarded four contracts and is negotiating a fifth aimed at "modification of employers' attitude toward the employment of work-able cancer patients." The four contracts already awarded went to Westinghouse Electric Corp., $354,007; American Institutes of Research, $467,699; Human Resources Research Organization, $495,763; and University Research Corp., $485,680.

Each award will cover three years of work, and with the fifth now in negotiation, the commitment will approximate $2 million. The first-year total will be $800,000.

Phase I of the project includes a survey each contractor will undertake to determine if job discrimination is a problem for cancer patients and if so, the extent to which it exists. If NCI determines that data show the problem is not significant, the project will be terminated at that point. Otherwise, the contractors will proceed to Phase 2, which will be development of methodology to improve employment practices.

Other contract awards:

Title: Continue to provide human hematopoietic tissue culture cell lines and related technical services
Contractor: Associated Biomedic Systems, Inc., $195,453.

Title: Continuation of support of the international classification of tumors
Contractor: National Academy of Sciences, $158,745.

SOLE SOURCE

Proposals are listed here for information purposes only. RFPs are not available.

Title: Murine mammary tumor virus production facility
Contractor: Meloy Laboratories.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology and Diagnosis Divisions are located at: NCI, Landow Bldg. NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NO1 CP-55657-56

Title: *Studies on an in vivo/in vitro system as a potential bioassay for chemical carcinogens*
Deadline: *March 7, 1975*

The primary goal of the Carcinogenesis Program is to prevent cancer in man by identifying carcinogenic compounds and formulations that may affect humans, as well as by identifying the mechanism of action of known carcinogens. Both these approaches require ex-

tensive bioassay and other analytical technologies, as well as a continuing vigorous program for refinement and innovation of the same technologies.

NCI is interested in the development of rapid, sensitive, reproducible, and quantitative methods for detection of potential carcinogenic substances. It has been observed, after administration of diethylnitrosamine (DEN) to guinea pigs and prior to the appearance of liver tumors that there is a selective decrease in the serum concentration of complement component C4. This coupled with the fact that both components C2 and C4 are synthesized by macrophages provided a basis for further studies on a host-mediated in vivo/in vitro system.

In this system, guinea pigs were injected with the chemical, peritoneal exudate (PE) was obtained and the PE cells tested in vitro for synthesis of C2 and C4. It was found that DEN effectively reduced the rate of C4 synthesis while dimethylnitrosamine (DMN) reduced biosynthesis of both C4 and C2. The non-carcinogenic analog diphenylnitrosamine not only failed to inhibit C2 and C4 synthesis but appeared to enhance production of both these complement components by isolated PE cells.

The objective of the project proposed is to investigate and standardize this in vivo/in vitro system using a guinea pig macrophage system and a series of known chemical carcinogens run in parallel with non-carcinogenic analogues. Consideration must be given to factors which could influence the in vivo response. These include route of administration of the compound, dosage, strain, sex and age of the animal at the beginning of the test. The methods for inducing the PE exudates, preparation of reagents and hemolytic titrations are described below.

The proposals written in response to this RFP should consider the following as some of the parameters for study.

1. In the initial phase, groups of Hartley stock and strain 2 guinea pigs will be compared using DMN, diphenylnitrosamine, and the appropriate vehicle controls. The sex and age of the animal, and time response between injection of the chemical and induction of the peritoneal exudate for the in vitro assay must be determined. This will provide the information necessary to start to envolve a standard protocol. The following studies will be done.

a) Dimethylnitrosamine will be given intramuscularly at a dose of 30 mg/kg body weight at 72 and 24 hours before harvesting the PE cells.

b) Diphenylnitrosamine will be given under the same conditions as for DMN at a dose of 30 mg/kg body weight three days before harvesting the PE cells.

2. If a standardized approach can be established with these compounds, the second phase of the study will consist of testing at least 50 known chemical carcinogens and a representative number of non-carcinogenic analogs for their activity in this system. The carcinogens will be suppled by NCI.

3. In vitro assay

a) Biosynthesis of C2 and C4 in PE cells from experimental and control animals placed in culture, will be determined over a 72 and 96 hour period. The method of inducing a peritoneal exudate and preparing the in vitro plates will be as follows: Ten ml of a sterile 3% starch solution will be injected intraperitoneally. Seventy-two hours later, the resulting peritoneal exudate will be harvested by washing the peritoneum with 100 ml of Hank's balanced salt solution containing 10 units of heparin per ml. The cells will be washed three times in Medium 199 (M199) and suspended in M199 supplemented with 10% heat inactivated fetal calf serum.

Total and differential cell counts will be performed and the cells placed in 60 x 15 mm petri dishes ($3x10^6$ cells/plate) and incubated in M199 for 2 hours at 37° C. After this period of incubation, the dishes will be washed four times to remove non-adherent cells and 4.0 ml of M199 plus 10% fetal calf serum will be added to each dish.

b) Hemolytic titrations for C2 and C4 will be performed as described in Opferkuch, W., Rapp, H.J., Colten, H.R., and Borsos, T., *J. Immunol,* 106: 927, 1971, with rat CEDTA (rat serum diluted 1:5 in EDTA buffer, final molarity of EDTA 0101). Preparation of reagents, including sheep erythrocytes (E), rabbit antibody to boiled stromata of E (A), cell intermediates EAC 1 and EAC 1,4, veronal-buffered saline (VBS), Veronal-buffered saline-sucrose (VBS-sucrose, μ=0.065), EDTA buffer 0.01M, pH 7.5 and isolation of partially purified guinea pigs C1 and C2 are given in Rapp, H.J., and Borsos, T., *Molecular Basis of Complement Action,* Appleton-Century-Crafts, New York, 1970.

Contract Specialist: Melvin Hamilton
Cause & Prevention
301-496-6361

RFP NO1-CP-55664-69

Title: *Operation manual for small rodent long term carcinogen bioassay studies*

Deadline: *March 21, 1975*

NCI is interested in establishing a contract for the development of an operation manual for use in long term carcinogen bioassay studies in small rodents. The objective of this project is to develop a manual to provide investigators with guidelines, procedures and background information on each of the elements that need to be considered for a well designed and properly conducted carcinogen bioassay study.

The manual is to include material which will enable the investigator to understand, plan, design, implement, conduct, evaluate, and report the study.

Contracting Officer: D.J. Dougherty
Cause & Prevention
301-496-6361

RFP NO1-CO-55219-04

Title: *Rapid screening and initial processing of biomedical literature*
Deadline: *Probably mid-March*

The Associate Director for Internation Affairs of NCI is requesting proposals for a contract to rapidly screen 1,000 biomedical journals and other documents on a high priority basis, in order to identify all articles related to cancer, and to process them so that they may be used by the International Cancer Research Data Bank (ICRDB) Program for the preparation of abstracts.

The selected contractor will also prepare a tape containing the most current citations of the identified cancer-related documents, and provide it monthly to other ICRDB contractors.

The organization selected must be prepared to provide the above in the shortest possible time using trained personnel experienced in screening cancer literature.

Contracting Officer: Hugh E. Mahanes Jr.
Control & Rehabilitation
301-427-7984

RFP NO1-CO-55220-04

Title: *Preparation of cancer-related abstracts*
Deadline: *Probably late March*

NCI is requesting proposals for a contract to prepare abstracts from cancer-related literature for the International Cancer Research Data Bank (ICRDB) Program. This project involves the preparation of concise, informative abstracts in English, averaging about 300 words and typed using a standard optical character recognition type font. The documents to be abstracted will be provided by the ICRDB Program office. The majority will have been written in English, but some will be in Slavic, Oriental, European, and other languages.

The organization selected must be prepared to provide staff consisting of highly qualified biomedical abstractors with advanced degrees (MS or PhD) in biomedical subject areas who are experienced in preparing abstracts covering all disciplines related to cancer research (molecular biology, biochemistry, immunology, hematology, pharmacology, toxicology, clinical medicine, virology, organic chemistry, cytology, histology). The staff must be skilled in preparing abstracts from documents written in many foreign languages (particularly Eastern European and Asian area languages). The abstracts must be prepared within three weeks after documents to be abstracted are received, and are to be provided with no restriction on their future use by the ICRDB Program.

In addition, the selected organization must be qualified to translate foreign language abstracts into English and to provide index terms when necessary, and to maintain tracking records of all documents received, abstracted, and delivered to the ICRDB Program office.

Contracting Officer: Hugh E. Mahanes Jr.
Control & Rehabilitation
301-427-7984

RFP NO1-CO-55221-04

Title: *Computer support for cancer information dissemination*
Deadline: *Late March, 1975*

The Association Director for International Affairs of NCI is requesting proposals for a computer support contract which will provide services related to cancer information dissemination for the International Cancer Research Data Bank (ICRDB) Program.

The organization selected must demonstrate a high level of competence and extensive experience in the use of magnetic tapes containing bibiographic information (citations and abstracts) to provide selective dissemination of information (SDI) services to groups and individuals. It must be staffed with individuals experienced in interacting with subject specialists who prepare the SDI profiles and must demonstrate experience in methods of collecting user feedback and using it to optimize the SDI service.

The organization selected must also be experienced in the use of bibliographic data from magnetic tapes to prepare camera-ready copy of technical monographs, including the ability to rearrange records in the monograph, add section headings, and automatically prepare KWIC and other types of indexes.

In addition to the prime requirements just listed, the organization must demonstrate capabilities related to the following types of services which will also be required by this contract: converting tapes from other NCI contractors to input format required by the National Library of Medicine, updating and correcting errors on existing tapes, converting abstracts typed with an optical character recognition type font to magnetic tape with the use of an optical character reader, maintaining mailing addresses in a computerized file, keyboarding of abstracts to produce bibliographic records on magnetic tape, and developing new (or modifying existing) computer programs for use in processing and correcting errors on input data tapes before they are added to the existing ICRDB data base.

Contracting Officer: Hugh E. Mahanes Jr.
Control & Rehabilitation
301-427-7984

RFP NCI-CB-53916-31

Title: *Procurement of melanoma cell vaccine and in vitro assays for humoral and cellular cytotoxicit toxicity*
Deadline: *Feb. 7, 1975*

Activities required under this RFP include preparation of a quantity of melanoma cell vaccine for use in

treatment of patients with melanoma and growth of additional tumor cell lines.

The contractor will prepare batches of melanoma cell line RPMI-8072 grown in sterile PPLO-free suspension culture in McCoys 5A medium with human serum modified for suspension culture. Each batch will consist of at least 1×10^{10} cells, grown at maximum density and maximum viability. A batch will be prepared each 4 weeks, for a total of at least 13 batches in each contract year providing a total of at least 1.3×10^{11} cells each year. The project officer will provide the necessary human serum; all other materials and equipment are to be supplied by the contractor.

Once a week, appropriate amounts of frozen vaccine will be thawed, washed, suspended and brought to NIH for administration to patients. The contractor will provide appropriate delivery service.

The contractor will grow and provide small batches of several other melanoma cell lines and other tumor cell lines.

The contractor will be prepared to do all tissue culture such that cells are PPLO free and will also be prepared to do appropriate studies and maneuvers to get rid of PPLO should it develop.

Because of the need to provide freshly thawed, washed and suspended vaccine of high viability, the contractor must be within a 45 minute drive of the NIH Clinical Center.

This project also involves procurement of a service in which the contractor shall carry out in vitro assays for humoral and cell-mediated cytotoxicity.

The contractor will be provided with patient blood samples by the project officer. Each blood sample will be tested for complement-dependent cytotoxic antibody, cell-dependent cytotoxic antibody, and direct cell-mediated cytotoxicity. It is anticipated that there will be at least 1,000 patient blood samples in the course of a year. The contractor will be expected to provide normal blood samples for controls. Tests will be performed as described by the project officer to test reactivity, as well as specificity of reactivity.

The contractor will be provided with 30 solid tumor samples in the course of a year. Cells will be dispersed mechanically and enriched for viable tumor cells on discontinuous BSA density gradients. Viable tumor cells will be used in complement-dependent cytotoxic antibody tests. Each tumor will be tested with 4-5 different antisera to be provided by the project officer.

The contractor will be expected to maintain by in vitro passage 2 human tissue culture lines other than melanoma cells. These cells will grow in Eagles media with 10% fetal calf serum and will be used in tests for cell-dependent cytotoxic antibody. Seventy-five serum samples will be provided by the project officer in the course of a year.

To facilitate exchange of biologic materials between NIH and the contract site, the contractor's laboratory must be within a 45 minute drive of the NIH Clinical Center.

Contract Specialist: Robert S. Townsend
Biology & Diagnosis
301-496-5565

RFP NCI-CB-53912-31

Title: *Preparation of reagent antisera and antigens*
Deadline: *Feb. 15, 1975*

NCI wishes to procure the following services in support of intramural research:

Preparation and supply to the government of reagent antisera and antigens. This task shall consist of:

1. Preparation of antisera to the following immunoglobulins:
   a. All classes of human H chains and L chains.
   b. All classes of murine H chains and L chains.
   c. Fragments of human and mouse immunoglobulins of all classes.
2. Preparation of antiserum to human T cells and B cells.
3. Preparation of F(ab')2 fragments of the IgG antibodies derived from selected antiserum.
4. Conjugation of selected antisera or antigens with fluorescent material at F/P ratios to be specified by project officer.

In order to carry out the work in numbers 1) and 2) above, it will be necessary for the contractor to be able to obtain, isolate, and purify all antigens needed for preparation of antisera. The project officer may provide certain categories of materials that would be difficult to obtain. Absorptions of all antisera will be performed by solid phase immunoabsorption. It is required that the contractor prepare each antiserum in 100cc quantities, at a potency of at least 1 milligram per ml of specific antibody. Species of animals to be immunized will be determined by the project officer. Each reagent prepared and supplied must meet the criteria for specificity established in consultation with the project officer.

Contract Specialist: Robert S. Townsend
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