THE CANCER LETTER

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NATCHER SUBCOMMITTEE OBJECTS TO BUDGET REDUCTIONS, SQUEEZES FROM DEVITA DETAILS ON PROGRAMS BEING CUT

NCI Director Vincent DeVita as usual had to tiptoe through a minefield laid by members of the House Health Appropriations Subcommittee who were challenging President Reagan's cuts in the 1986 fiscal year budget for the National Cancer Program. A misstep could blow DeVita all the way to the ranks of the unemployed for committing the unforgivable (in D.C.) sin of budget busting. Yet he had

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In Brief

FROZEN PANELS AVAILABLE TO EVALUATE DIAGNOSTIC ASSAYS; PANEL TO MEET AT JOHNS HOPKINS APRIL 22

FROZEN CODED panels of pretreatment sera from patients with various neoplasms, benign disease and healthy controls are available from NCI's Div. of Cancer Biology & Diagnosis for use in evaluating serum assays with potential value in diagnosis of cancer. Promising results may form the basis for subsequent grant applications, DCBD said. Preliminary data documenting useful tests must be submitted and should include a brief description of the assay; results in patients with cancer, nonmalignant disease and healthy controls; reprints of published work, if available. Requests for coded serum panels should be sent to Diagnosis Serum Panels, Project Officer NCI Serum Bank, Diagnosis Branch, Westwood Bldg Rm 10A10, Bethesda, Md. 20205. . . . **PRESIDENT'S CANCER** Panel's next meeting will be April 22 at Johns Hopkins Oncology Center, Hurd Hall, 9 a.m. . . . . **DAN MALDONADO**, who has been staff director and legislative director for Congressman Edward Roybal (D.-Calif.), has joined the firm of Grupenhoff & Endicott, Washington representatives for various medical, academic and voluntary health organizations. A 10 year member of Roybal's staff, Maldonado's responsibilities included work with the Appropriations Committee, where Roybal was a member of the Labor-HHS Appropriations Subcommittee. . . . **STANLEY PARRY** has resigned as deputy director and chief operating officer of the Northern California Cancer Program. He had been with NCCP since 1978 as administrator and associate director of cancer control. . . . **ONCOLOGY NURSING** Society lectures at the 10th annual congress in Houston: Judith Spross, oncology nurse specialist at the NIH Clinical Center, will present the first ONS/Schering Clinical Lecture on "Pain and Suffering: Clinical Lessons from Life, Literature and Legend;" Mary Vachon, research scientist with the Clarke Institute of Psychiatry at the Univ. of Toronto, will deliver the Mara Mogensen Flaherty Memorial Lecture. Carolyne Davis, administrator of the Health Care Finance Administration, will make the keynote address, discussing health care economic issues and the implications for oncology nurses.

EARLY, HOYER LEAD CHARGE AGAINST ADMINISTRATION NCI BUDGET CUTS

(Continued from page 1)

to defend a budget which he knew was grossly inadequate and short sighted, was $300 million less than requested in the bypass budget and even was $265 million less than approved by the Dept. of Health & Human Services.

During the first hour of Monday's hearing before Congressman William Natcher's Labor-HHS Appropriations Subcommittee, DeVita managed to parry or duck the barbed questions and comments critical of the budget. But eventually, Massachusetts Democrat Joseph Early, Maryland Democrat Steny Hoyer, Massachusetts Republican Silvio Conte, the top ranking minority member of the subcommittee, and Illinois Republican George O'Brien pried loose the admissions they were after:

*Hoyer: "In light of the budget request. . . Would it be fair to characterize that as a retreat in the fight against cancer?" When DeVita tried to avoid a direct answer, Hoyer insisted, "I'm asking you as a doctor, as a professional, as someone the American people entrusted with a very important job. We've given you the tools in the past. Is it fair to characterize (the budget cuts) as a retreat? As a professional, can you say you can do everything that should be done through savings in the budget?"

"That's difficult to answer," DeVita said. "We all get our change to argue for our budgets within the Department and the system. I would say that it would be a retreat if the Cancer Program ceased to exist, or if we couldn't fund the highest priority research. Neither of those is true, so it isn't a retreat."

That's how a federal agency head has to answer once the President's budget has been made public. Congressmen are under no such constraints.

*Hoyer referred to the action by the Office of Management & Budget requiring NIH to fund some 1985 grants for three years with 1985 money, thus slashing the total of new and competing grants NIH can fund this year from 6,500 to 5,000. That cuts 240 grants from the total NCI expected to fund this year. Maintaining that level in FY 1986 would take $111 million from NCI's budget, Hoyer pointed out. "Would it be fair if we added $111 million?" Hoyer asked. DeVita managed not to answer the question.

However, when Hoyer asked, "What will we not be able to buy at $1.126 billion (the President's request) that you recommended buying at $1.381 billion?" (the amount approved by HHS), DeVita responded, "We won't be paying 240 grantees that we might have paid."

"Only that?" Hoyer asked.

"That's a lot," DeVita said. "That's 240 laboratories and one center."

Hoyer would not let it go at that. "You are making priority decisions. I'm trying to get what was cut out before the budget got to this committee. There is still another $100 million out there."

DeVita could sidestep the issue no longer. "We originally had increases for cancer control, about $25 million, and a total of $25 million for construction. We had an increase of $15 million on contracts in the epidemiology program, diet and nutrition studies and drug development. We also had an increase of $15 million for the clinical cooperative groups."

Early was even more aggressive in challenging the budget. "In your professional judgment, in light of all the promising things you have in the works, can we afford to do less next year than we are now?"

"No, but that depends on what you say is less," DeVita answered. "I'm no different than any other agency head. I would like to have more." He mentioned NCI's projection at the start of interferon clinical trials that the material would cost $40 million. The cost dropped dramatically when recombinant interferon because available, and NCI spent only $4 million to purchase it.

"That's because you did the research," Early said. He mentioned DeVita's previous comment, that he had had a chance "to make your case for the budget. Did you have a chance to appeal OMB's figure?"

When DeVita tried to hedge, Early demanded, "Yes or no?" DeVita had to admit that he had not been allowed to appeal.

"That is the first time ever," Early said. "You never had a chance to appeal the revised 1985 budget or the 1986 OMB budget." DeVita admitted that that was the case.

*O'Brien brought up the controversial and (to NCI) touchy issue of the expert consultants. The National Cancer Act gave NCI the authority to hire up to 50 experts for as much as two years without going through the normal federal personnel routine. They did not count against NCI's personnel ceiling. Later, the number was increased to 150, but two years ago, OMB ordered the number to be held to 130 and decreed they would count against the total NCI ceiling. DeVita explained that, at O'Brien's insistance.

O'Brien also brought up the shortage of staff, including nurses, at the NIH Clinical Center, and that some wards are not filled. He asked that the cost of providing enough nurses to fully staff all the wards be provided for the hearing record.

*Conte referred to the Year 2000 goals of reducing cancer mortality by 50 per cent, which received the briefest of mention in DeVita's formal

statement. "Are the resources in the budget request sufficient in your opinion to meet that goal?" Conte asked.

"I think they are," DeVita said. "We can cover the high priority programs." That is a statement no one believes, least of all DeVita.

Conte asked what the impact will be on cutting 240 grants from NCI's total this year.

"It never has been possible to fund all approved grants at NIH," DeVita said. "We have always had to leave good research unfunded."

Conte referred to the letter by the Div. of Cancer Treatment Board of Scientific Counselors to the Administration objecting to the cuts and contending they will cripple the research effort. "Are you aware of that letter?" he asked.

DeVita said he was and explained that the four NCI Boards of Scientific Counselors are made up of "outside scientists who frequently express their opinions on things we do. Sometimes they are favorable, sometimes not." The opinions they are expressing on the budget "are understandable," DeVita said, "but the President has an overview of the federal budget the Boards don't have."

Conte mentioned remarks by Armand Hammer, chairman of the President's Cancer Panel, also objecting to the cuts.

Early referred to the statements by the DCT Board and Hammer and asked, "You weren't suggesting their making comments was not the right thing to do?" DeVita said it was their privilege to express their opinions on the budget, but he again defended the Administration in its effort to reduce the federal deficit.

Early exploded. To have any substantial impact on the budget, "we'll have to cut entitlements, and star wars, which has twice your entire budget. You're trying to rationalize. What about the cut in the centers budget. Was that wise?"

"Yes, in the contest of the entire federal budget," DeVita answered.

"What about in the context of the Cancer Program?" Early demanded. "You're rejecting 75 per cent of good, approved science. I know you're coming in here to carry OMB's water." He asked if centers were being funded at recommended levels.

"No, they (center core grants) are negotiated downward," DeVita said.

"Are centers not playing a major role in all the achievements made in cancer research?" Early asked. DeVita responded that they are.

Early noted that HHS Secretary Margaret Heckler, when pressed on the issue of multiple year funding of 1985 grants, agreed that those awards would not be made until July 1. That delays implementation of the OMB directive, and gives opponents in Congress and elsewhere the opportunity to exert pressures, take legal or legislative actions, or attempt to persuade the President to overrule OMB. DeVita said NCI "will abide by the Secretary's comment."

Natcher opened the hearing by noting that "we appropriated $1.196 billion for the 1985 fiscal year. That's a large amount, but it's for the National Cancer Institute and that is good." He queried DeVita on whether physicians are learning quickly enough about new treatment and technology, and on the Year 2000 goal. Finally he asked, "Do you get discouraged as far as research is concerned?"

"No," DeVita answered. The great progress being made is encouraging, he insisted. "We've never seen anything like it. We thought at first the Year 2000 goal was ambitious, but we felt we needed to have our feet held to the fire. But now I think that the goal is conservative."

Natcher noted that since the National Cancer Act of 1971, NCI had received more than $9 billion. "Are the results to date commensurate with the magnitude of this investment?"

"I believe so," DeVita said.te with the magnitude

DCE BOARD APPROVES CONCEPT OF NEW COLLABORATIVE CHEMOPREVENTION GROUPS

The Board of Scientific Counselors of NCI's Div. of Cancer Etiology has given concept approval to four new programs with estimated annual budget totals of $4.5 million, including a proposal to establish three to six National Collaborative Chemoprevention Projects. Two of the programs, including the chemoprevention groups, would be supported through cooperative agreements, the other two through grants.

The two grant supported programs are for basic studies on the development and assessment of retroviral vaccines, with $1.25 million a year to be set aside to support six to eight grants; and studies on feline leukemia virus, with $750,000 a year estimated to support four to five grants.

The other cooperative agreement program will be to support development, validation and application of biochemical markers of human exposure for use in epidemiologic studies. An estimated $1 million a year will be set aside to support up to six awards. Half of the money will come from the NCI-National Institute of Occupational Safety & Health fund, contributed by NCI. The other $500,000 a year, for the first time, will be contributed by the Environmental Protection Agency.

The Board also approved the concept of recompeting DCE's contracts for biomedical computing services, at an annual estimated cost of $1.6 million a year.

The concept proposals written by staff and Board discussion follow:

National Collaborative Chemoprevention Projects. Estimated first year funding, $1.5 million, three to six awards, five years.

Chemoprevention has become an important part of NCI stategic plans. DCE currently supports 58 research grants in this area totaling $6.4 million in FY 1985. RFAs issued in 1981 and 1983 by the Chemical & Physical Carcinogenesis Branch resulted in a total of 39 awards of which 36 are active at this time. The first RFA, issued in 1981, on mechanisms of biological and chemical prevention of carcinogenesis, resulted in 28 grants with a maximum award period of three years. The last of these grants will expire in FY 1985 and to date only three have successfully competed for renewal in the general grant pool. The second RFA, issued in 1983 on new natural and synthetic inhibitors of carcinogenesis resulted in 11 grants which are scheduled to expire in FY 1987. Forty one applications have been received in response to a third RFA on innovative approaches to development of cancer chemopreventive agents which had a receipt date of Dec. 14, 1984. The $1 million set aside for this RFA should be sufficient to fund six to eight meritorious applications in FY 1985. It is estimated that approximately 40-45 grants will be supported in the chemoprevention area by early 1986 based on projected expiration dates of all current grants.

Experience suggests that effective exploitation of new knowledge applicable to cancer prevention, particularly the understanding of basic mechanisms of anticarcinogenesis, often requires diverse laboratory research expertise and material resources beyond the scope of most individual grants and contracts. There are at present a significant number of groups of compounds that have shown some promise as chemopreventive agents. The effective and expeditious development of chemopreventive compounds requires a range of studies beyond the breadth of most conventional investigator initiated research grants and in most cases beyond the capacity of single organizations. For instance, dose response studies, determination of effectiveness in various species, toxicity studies, structure activity determinations and pharmacokinetics are all needed in most cases. For these reasons, National Collaborative Chemoprevention Projects (NCCPs) are proposed for funding with the cooperative agreement mechanism. Each NCCP grant would consist of a number of laboratory research programs representing diverse scientific disciplines and expertise. In this initiative, investigators from scientific disciplines such as experimental carcinogenesis, pharmacology, toxicology, medicinal and organic chemistry, molecular and cellular biology, biochemistry, immunology, and pathology will work together, regardless of organizational affiliation, to generate new approaches and strategies in biological and chemical prevention of carcinogenesis. Thus, scientists in a given NCCP could derive from any combination of the academic, nonprofit and for profit communities, bringing with them to the cooperative ventures the strengths of their organizations' resources and perspectives, as well as their individual scientific backgrounds, expertise and experiences. Components of an NCCP could also be drawn from a single organization possessing necessary diversity and in depth expertise to accomplish project objectives. The selection of institutes and investigators to be included in an NCCP will be completely up to the mutual agreement of the applicant organization(s) and will not be directed by NCI.

It is anticipated that the scope of an individual NCCP will include: (1) in vivo efficacy determinations in significant biological models employed in carcinogenesis studies; (2) demonstration of feasibility of any in vitro bioassays employed, as related to in vivo carcinogenesis/anticarcinogenesis; (3a) pharmacologic investigations of absorption, distribution, metabolism, and excretion with attention to dose/response relationships; (3b) investigations on the range of agent activity relative to organ sites at which chemoprevention is demonstrable and carcinogens/promoters against which activity exists; (3c) investigations characterizing the toxicologic properties of the agent; (4) biochemical investigations on mechanisms of action; and (5) investigations on structure activity relationships elucidating chemical/structural features for agent efficacy, toxicity and pharmacologic properties.

The purpose of the proposed RFA is to support coordinated, basic work in the development of chemopreventive agents in which it is clear that through synergistic interaction of the collaborating components, the whole is greater that the sum of its parts. Discovery in the sense of simply adding to the list of known, potential agents is not a part of this RFA. Neither full scale screening programs nor preclinical/clinical investigations in cancer prevention will be supported by these projects. Those efforts are supported by the Div. of Cancer Prevention & Control.

Several groups of chemopreventive agents appear promising for substantial developmental efforts. These groups include, among others, protease inhibitors, antioxidants, dithiolthiones, dehydroepiandrosterone and related analogs, cyanates and isothiocyanates, inhibitors of arachidonic acid metabolism, and nucleophiles, as well as natural products such as green and yellow vegetables. Since

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CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY: RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

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there is already extensive activity in retinoids research and development, applications in this area will be considered nonresponsive.

The composition of an NCCP is envisioned to consist of a project director, program leaders in several broad scientific disciplines and an NCI coordinator. The project director, in addition to providing scientific and administrative leadership, is expected to contribute to a laboratory program. Program leaders within a project can be derived from one or several institutions, but there must be a high degree of interaction among them. The proposed project must define its own objectives for novel and exploitable approaches to cancer prevention and must develop its own experimental designs and methodologies. An NCI coordinator will be assigned to each NCCP at the time of award and will be expected to provide assistance, advice, and guidance particularly with respect to reducing duplication of efforts conducted in other extramural projects, and through providing resources and information which may not otherwise be available to the group.

David Longfellow, chief of the Chemical & Physical Carcinogenesis Branch, said the program would be patterned after the Div. of Cancer Treatment's National Drug Discovery Groups. It will not be limited to combinations of organizations but could be a single institution with the necessary expertise.

Board member Allan Conney agreed that "there is a need for more in depth studies for some classes. This mechanism can facilitate that."

Board member Renato Dulbecco was skeptical. "There are two classes of substances for which you can anticipate activity. One we know from human epidemiology studies, the rest from animal studies. But we don't have any idea of their role in human cancer. It may be that the majority will not have anything to do with human cancer. I'm not convinced."

Board member Lee Wattenberg said, "There is a category of chemopreventive agents which work on a straightforward chemical basis, independent of species. . . The reality is that carcinogens in animals many times are also carcinogens in humans."

DCE Director Richard Adamson mentioned vitamin C as a possible anticarcinogen, preventing the formation of nitrosamines in the stomach. "That may be the reason stomach cancer is disappearing." He credited that discovery to studies at Eppley Institute by former Eppley Director Philippe Shubik and Sidney Mirvish.

The vote to approve the concept was unanimous. Longfellow and Carl Smith are program directors.

Basic studies on the development and assessment of retroviral vaccines. Estimated first year funding, $1.25 million, six to eight grants, five years.

The principle of prevention of virus induced disease by prophylactic immunization against the virus has been successfully used to conquer such diseases as smallpox, yellow fever and poliomyelitis. However, the knowledge and use of similar approaches for the prevention of retrovirus induced cancers and immunosuppressive diseases of man and animals are in a rudimentary stage. Recent advances in vaccine technology, such as the packaging of genes coding for immunogenic protective proteins into appropriate expression vectors (such as vaccinia virus) and other recombinant DNA methods, are currently being exploited to produce safe and effective vaccine preparations for diseases caused by viruses such as hepatitis B virus, herpes simplex viruses, and foot and mouth disease virus. Similar, modern approaches need to be explored for the prevention of equally important and devastating diseases caused by retroviruses.

While NCI is considering approaches for the development of a vaccine for the AIDS retrovirus, HTLV 3, there are at present no RO1 grants or contracts funded by NCI dealing generally with the development of vaccines for retroviruses. As a first step towards the consideration of an RFA to stimulate extramural studies of prevention of retrovirus infections through vaccination, the RNA Virus Studies 1 component of the Biological Carcinogenesis Branch conducted a workshop entitled "Vaccination Approaches for Retrovirus Infections" last December to determine the state of the art in the field of vaccine technology and to assess those aspects of pertinent research that may be important from the standpoint of future vaccine development. The meeting was chaired by Hilary Koprowski, a member of the DCE Board. A total of 108 participated including many world leaders in viral vaccine technology. The workshop recommendations were for:

1. Development of naturally occurring retrovirus animal models to systematically evaluate strategies for immunogen preparation, vaccination schedules, use of suitable adjuvants, determination of host target cells, induction of a protective immune response, and development of an appropriate measure for in vivo protection against challenge.

2. Basic studies to determine how retroviruses interact with and/or escape from the host immune surveillance system, such as by genetic recombination/antigenic shifts/drifts involving env gene alternations.

3. Characterization of retroviral components presumed to be immunosuppressive.

4. Identification and characterization of antigenic determinants of retroviruses that are most associated with their presentation and immunogenicity.

5. Utilization of newer methodologies to produce and evaluate retroviral vaccines such as recombinant/subunit vaccines prepared in yeast, bacteria, and/or mammalian cells; DNA sequence derived synthetic peptides; modified live recombinant DNA retroviral vaccines; retroviral gene segment expression vectors such as vaccinia and adenovirus; and antiidiotype antibodies against retroviral components employed as immunizing antigens.

6. Investigations to develop quantitative serological procedures to assess the in vivo immune status against retrovirus infections.

"We're asking basic questions," Adamson said. "We will not get into commercial development."

The concept was approved without objection. Padman Sarma is the program director.

Studies on feline leukemia virus. Estimated cost, $750,000 a year, three years, four to five grants.

Among the retroviruses, the leukemia inducing viruses of the cat (feline leukemia viruses, FeLV), are unique in many respects, First, they are responsible not only for malignant diseases, such as leukemia, lymphosarcoma, and other neoplastic conditions, but they also cause other serious diseases such as anemia, immunosuppression, and reproductive failure. More cats die of complications arising from immunosuppression caused by FeLV than through tumor induction. In this respect, a parallel exists between FeLV and the recently discovered human retrovirus, human T cell leukemia/lymphoma virus (HTLV), especially HTLV-3. The fact that FeLV has the potential to induce diverse disorders in the cat poses the question of whether differences in the induced diseases are a result of differences in the nature of the virus isolates.

Differences between viral strains responsible for differences in the induced diseases in cats have not been elucidated and research remains to be done in this area. Second, an examination of oncogene sequences in feline sarcoma viruses has revealed an abundance and diversity of the oncogenes which they acquire through recombination from the cat genome, suggesting that the cat is a reservoir of many different cellular oncogenes. Since ongogenes of different species appear to be similar and to be well conserved, the cat cellular oncogenes may have important implications for cancer in other species, including man.

A third feature of the eline retroviruses, just beginning to be recognized, is the unexpected finding that certain leukemia inducing FeLV strains acquire, retain, and transduce the oncogene myc in a manner reminiscent of the avian myelocytomatosis virus, MC-29. This finding, previously unknown for a mammalian retrovirus, remains to be fully studied for its relevance in the etiology of cancer and other diverse disorders attributed to FeLV.

There are at present only six active RO1 grants in the program dealing with FeLV. Only three of these grants are addresssing the important questions at issue, especially those concerning the role of FeLV in causing immunosuppressive disorders in the cat. As a first step towards stimulating additional extramural studies through grants, the RNA Virus Studies 1 component of the Biological Carcinogenesis Branch sponsored a workshop on FeLV last November. Myron Essex, a member of the DCE board, was chairman. Workshop participants agreed that studies should be encouraged on the biology, immunology, and molecular biology of feline leukemia virus. Examples of important areas of research emphasis (which are not all encompassing) are (1) elucidate the mechanisms of feline retroviral pathogenesis/cell transformation/oncogenesis, with attention to the newer knowledge of oncogene chromosomal translocations and other interactions; (2) explore the origin and significance of virus subgroups in feline leukemia virus induced disease and immunity; (3) to understand the immune effector mechanisms in feline leukemia, identify and define feline hemopoietic and lymphoid cell populations, and identify the target cells in immunosuppressive disorders. Additional studies that might be addressed are (1) define the significance of subgroup C FeLV envelope component and its apparently protective antibodies against feline leukemia; (2) characterize myc-containing feline leukemia viruses and determine their role in feline leukemia; and (3) determine the etiology of virus negative cat tumors which generally appear under natural conditions in cats raised in FeLV infected environment.

Because of limited funds currently available for FY 1986, program staff will first issue this research initiative as a program announcement (soliciting RO1 grant applications but without any commitment of funds set aside for the program). Should additional funds become available for FY 1986 or 1987 and responses to the program announcement be insufficient to appropriately strengthen this area of research, this initiative will be reissued as an RFA (with commitment of the $750,000 per year).

Board member Charlotte Friend commented, "Padman Sarma (the NCI program director for this effort) is a pioneer in this field."

"This is not a new area," Adamson said. "There are scientists out there working in this area. I think that with the program announcement, we may get enough grants."

Essex suggested that NCI may have to develop a colony of cats for the research. "They are expensive." Although Adamson said that availability of cats has not been a problem, Sarma said, "It would be better if we had a source."

The concept was approved unanimously.

Development, validation and application of biochemical markers of human exposure for use in epidemiologic studies. Estimated first year funding, $1 million, four years, maximum of six cooperative agreement awards.

Establishment of association between exposure of interest and the subsequent development of disease is particularly difficult in chronic disease epidemiology where a long latent period may separate exposure and clinical onset. The difficulty extends over a broad range of exposure types. For the purpose of this initiative we are primarily, though not exclusively, interested in exposures to toxic chemicals occurring in the occupational setting where heavy and prolonged exposures are likely to occur. Many approaches to classifying past exposure have been utilized in existing epidemiologic studies with varying degrees of success. Such approaches include, for example, the assignment of individuals to exposed and unexposed categories on the basis of past employment in a particular industry, a record of job types held in the past, or use of ambient air monitoring data, soil or water quality measurements. The extent to which these surrogate measures of exposure reflect reality is always questionable, particularly when exposure is to complex mistures or

agents. The classification errors which may result have serious effects on study outcome. The inability of these methods to assess delivered dose to target tissues is a serious limitation.

It would be advantageous to have available biochemical measures (preferably minimally invasive) which would provide unambiguous markers of past exposure and perhaps permit a quantitative assessment of the extent of exposure. Certain substances are either passively accumulated or activcely incorporated into body tissues. Others may react chemically with target molecules in the body or evoke immunologic or enzymatic responses which could persist for extended periods. Such tests would also allow one to study how humans with shared exposure vary in biological response. This would be of great value in defining groups at varying risks, an essential prerequisite for preventive intervention.

The activities to be supported under this initiative will be investigator initiated. Although program staff has identified an area of research activity in need of stimulation, the specific scientific approaches and methodologies best suited to accomplish the objective will be proposed by the extramural scientific community and evaluated for their scientific merit through the usual peer review process. The initiative will support basic research studies having as their principal objective the generation of information which is critically important to the extramural research community for the conduct of future epidemiologic efforts. The organizations supporting the initiative feel that achieving the stated objectives could be significantly facilitated by substantial programmatic involvement on the part of staff members. It is anticipated that persons responding to the RFA will be primarily basic scientists with extensive experience in the development and use of biologic markers in research settings, but with limited experience in the application of such methodology in epidemiologic settings. A small group of NCI, NIOSH and EPA staff members will be established to work with the award recipients. They will assist them by consulting on proposed methodologies to maximize their epidemiologic utility; providing a resource of information on the extent and distribution of exposures; and providing information on cohorts or exposed individuals which could provide material for methods development and validation.

Necessary preliminary investigations in animal systems may be proposed under this announcement. Because the methods to be developed will ultimately be utilized in epidemiologic studies, it is important that consideration be given at the outset to feasibility in this context. Such factors as ease of conduct and expense as well as collection, storage and transport problems should be considered along with the accuracy and validity of the method. For markers demonstrated to have utility, assessment of the extent of intra and interindividual variability is important.

The range of materials for which exposure markers are of interest is extremely diverse. Included would be markers of exposure to any substance which has been proposed to alter the risk of malignancy or other significant disease and is so distributed that significant human exposure is likely to have occurred.

"Are you concerned about novel methods, or just blood samples?" Conney asked. "I would like to see methodology on more of a frontier basis."

"These will be reviewed as research grants," answered John Cooper, who with Aaron Blair and Thomas Cameron are NCI program directors for this RFA. "It is unlikely that any application so pedestrian as to use blood samples would get a fundable score."

"This could be viewed as supplementing our effort to develop biochemical markers," Board member Gilbert Omenn said. "Going from reviewing employment records to measuring anything in the marker is a big step, and badly needed. It is appropriate to the participating agencies' missions."

The concept was approved without dissent.

Biomedical computing for the Epidemiology & Biostatistics Program. Estimated annual cost, $1.6 million, four years. Multiple contracts may be awarded. Present contractors are Capital Systems Group and Information Management Services.

The Epidemiology & Biostatistics Program is attempting to consolidate its request for concept approval of contracting activities for computer support. Four years of level funding (with an appropriate inflation factor) are requested for the Environmental Epidemiology Branch whose contract with Capital Systems Group will terminate March, 1986. Three years of level funding (with an appropriate inflation factor) are requested for the Biostatistics Branch whose contract with Information Management Services terminates in August, 1987. Currently, these contracts also provide support for the Radiation Epidemiology Branch and are planned to support the Clinical Epidemiology Branchy. The first year of the contract will be at a level of $1 million a year, with annual funding of $1.6 million during the second year.

Contractors will provide services in data base development and management, systems analysis, systems design and implementation, computer programming, technical documentation and data technician support related to computer applications. These services will be applied to data already collected as well as to data in the process of being obtained from ongoing and planned intramural research projects for which computer support is not provided by other means.

Project officers are Michael Stump, Thomas Mason, John Boice and John Mulvihill.

The concept was approved without dissent.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions.

Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda, MD. 20205. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring, Md., but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

NCI-CM-57707-16
Title: Large scale isolation of antitumor agents from natural sources--master agreement
Deadline: Approximately June 1

The Developmental Therapeutics Program of the Div. of Cancer Treatment is interested in receiving contract proposals from, and establishing master agreement order contracts with, offerors with the capability to extract, isolate, and purify antitumor agents from plant and animal materials on a pilot plant scale.

The successful offerors must provide a pilot plant facility capable of storing and processing up to 5,000 kg of bulk crude material and must have experience in development of natural products isolations. The government will supply the plant and animal materials to be processed. The successful offerors will supply all equipment, solvents, reagents and other materials needed for the project.

The antitumor agents isolated must be of high purity suitable for subsequent manufacture of clinical dosage forms, and all work must be carried out under current good manufacturing practice standards. A minimum mandatory requirement is that the contractor be registered as a manufacturer of bulk drugs with the Food & Drug Administration at the time of award.

Master agreements are competitively negotiated and awarded to more than one contractor. It is planned that such agreements will be awarded on or about March 1, 1986, for a three year period of performance, but will not be funded per se. After award, groups of qualified master agreement holders will be invited to bid competitively on appropriate master agreement orders as they are issued. Each master agreement order will be designed to accomplish a specific task as promptly as possible and will be awarded on a completion or level of effort basis, as determined by the contracting officer.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and reported in The Cancer Letter Oct. 26, page 3.

Contract Specialist: Elizabeth Moore
RCB Blair Bldg Rm 228
301-427-8737

SOURCES SOUGHT

Title: Literature surveillance of natural products
Deadline: Approximately March 25 for statement of qualifications

The Div. of Cancer Treatment is seeking small business firms (no more than 500 employees) with the capability to conduct a surveillance of currently published literature in the natural products area. The objective is to obtain the names and structures of new and novel compounds, especially those exhibiting biological activities, i.e. antitumor activity, cytotoxicity, antiviral activity, etc., for the purpose of acquisition of compounds of potential antitumor activity.

Surveillance is to cover at least 150 journals in the natural products and related fields. The findings are to be reported every two months.

Interested sources must demonstrate the following:

1. A proposed team with the following qualifications and experience--the principal investigator should have a degree at the PhD level in organic, medicinal or natural products chemistry or a closely related discipline and must be familiar with natural products structures and chemical searches,s as well as having background and experience with biological activity, preferably in the cancer area. The PI should also have at least two years experience in working with literature surveillance; staff members on trhe project should have a degree at the bachelors level in either chemistry or library.

2. 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 knowledge of the appropriateness of journals to be searched, proposed research methods, and the format of the output.

3. Availability of adequate facilities and equipment:

A. Library--ready access to a large library with extensive holdings in the areas of biology, chemistry, microbiology, pharmacology, biochemistry and medicine is required for the project.

B. Other--adequate space for offices, filing, record keeping, etc., should be available.

4. Appropriateness of organizational qualifications in the field of literature surveillance and availability of in house consultation and support to this project.

Sources who believe that they have the capability necessary to undertake this project should submit complete documentation, including their total number of employees, which demonstrates their ability. Each of the above requirements should be addressed specifically. Ten copies of this documention should be addressed to the contract specialist.

Contract Specialist: Patricia Shifflett
RCB Blair Bldg Rm 228
301-427-8737

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