THE CANCER LETTER

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NCAB Cancer Centers Committee Recommends Ratio Cap To Limit Growth Of Largest Grants

Advisors to NCI's Cancer Centers Program have recommended that if a limitation needs to be placed on the size of cancer center support grants, it should be based on a ratio determined by the amount of peer reviewed research that is conducted at each center. The National Cancer Advisory Board's Committee on Cancer Centers at its recent meeting reviewed 12 different cap models developed by centers program

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In Brief

House Hearing On NCI Budget Is March 16; NIH Reauthorization Sent To Senate Floor

HOUSE LABOR, HHS, Education Appropriations Subcommittee will hear testimony from NCI Director Samuel Broder on NCI's fiscal 1993 budget as recommended by the President, March 16, at 2 p.m., Rayburn House Office Bldg. At the annual hearing, the NCI director must try to defend the President's budget, and this year will be no exception, even though the President has recommended only a $30 million increase for the Institute, for a total of $2.01 billion. NCI's bypass budget for FY93 requested $2.7 billion. . . . **SENATE LABOR** & Human Resources committee last week passed the NIH reauthorization bill introduced by Sen. Edward Kennedy last summer. There were no significant changes; it now goes to the floor of the Senate. . . . **SILICONE BREAST IMPLANTS** will be discussed by FDA's General & Plastic Surgery devices advisory committee at a meeting Feb. 18-20, particularly "information which has come to light since the panel met" last November. New data include "case reports of autoimmune diseases in women with breast impants, information not included in the manufacturers' original submissions to FDA and evidence that some early models may have leaked excessively," according to FDA. . . . **INTERNATIONAL CONFERENCE ON AIDS** is scheduled for July 19-24, in Amsterdam, the Netherlands. Abstract deadline is March 2. For information, contact Harvard AIDS Institute, 617/495-0478. . . . **FORMER SPEAKER** of the House Thomas "Tip" O'Neill and the late Rep. Silvio Conte were selected by the board of the Federation of American Societies for Experimental Biology as recipients of the 1992 FASEB Public Service Award. The were selected for their support of biomedical research funding and legislation throughout their public careers. . . . **BURTON EISENBERG** has been named chairman of Fox Chase Cancer Center's surgical oncology department; he has been acting chairman since 1990.

Cancer Centers Committee Advises Ratio Cap On Center Core Grants

(Continued from page 1)

staff. For the past nine months, the committee and NCI staff have discussed the issue of equitable distribution of funds in the Cancer Center Support Grants ("core" grant) budget. Approximately 15 percent of the core grant budget is awarded to two centers that have been in program the longest--Memorial Sloan-Kettering and Fox Chase.

Though fiscal 1992 has seen about a $15 million increase in the core grant budget, that amount of growth is an anomally. Under the President's FY93 budget released recently, the centers budget would be held level.

As its meeting last month, the centers committee reaffirmed its belief that NCI should consider some type of cap that redistributes the existing budget more equitably to centers that win favorable peer review. By itself, peer review is inadequate to perform redistribution, since budget requests are based on the center's previous year's budget, not a comparison the budgets of all centers, Brian Kimes, director of NCI's Centers, Training & Resources Program, has told the committee in the past (**The Cancer Letter,** May. 17, 1991).

Under cap scenarios Kimes' staff developed, the number of funded cancer centers would drop from the current 57 to less than 40 by the year 2001 if there is no cap and the budget rises at an average of 4 percent per year.

"No model is ideal," said committee chairman John Durant. "We settled on a modified approach." The ratio model allows for differences in core grants based on the size of their research base, rather than a flat dollar cap.

The committee recommended that if a cap is adopted it should be based on the following:

▶A ratio in which the overall size of the core grant is determined by the size of the peer reviewed research based. Thus, cancer centers with larger peer reviewed research bases would be eligible to receive larger core grants.

▶The ratio selected should result in an overall budget need that is coincident or slightly lower than the predicted growth of the Cancer Center Support Grant budget. In the model presented, a ratio of .2 satisfied this condition.

Under a 10 percent ratio cap model, 14 of 21 centers selected as examples would be capped, while others would continue to grow. Under a 20 percent cap model, seven centers would be capped.

▶Any centers over the cap would not have their core grants reduced below the current level but would receive no cost of living increases or be eligible for larger awards until their research bases increased appropriately.

▶The research base of each center applicant should be based on: a) all NCI research support, b) all NIH research support in which NCI received a secondary referral designation, c) all American Cancer Society support, d) all other support submitted to the Cancer Centers Program and found to comply reasonably with the official NCI Grant Referral Guidelines.

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Epstein Criticizes 'Lavishly Funded Cancer Establishment;' NCI Replies

Like a comet that appears once a decade, NCI critic Samuel Epstein flew in to Washington last week to grab media attention with his predictable attack on NCI's cancer prevention programs.

Epstein, professor of environmental medicine at the Univ. of Illinois School of Public Health, held a press conference at the National Press Club to denounce what he calls "the lavishly funded cancer establishment" and to demand that NCI redirect funding for treatment research to research on prevention and environmental risks.

"The cancer establishment is fixated on diagnosis and treatment," and "has trivialized the risk of environmental causes," Epstein said. The news conference was sponsored by Food & Water Inc., a nonprofit organization that has campaigned against irradiated food.

Those are the same charges Epstein leveled in 1987 in a statement titled, "Are we losing the war on cancer," in which he charged that industry, the American Cancer Society and NCI are all on the wrong track (**The Cancer Letter,** Nov. 6, 1987).

Trailing after Epstein were former senator Gaylord Nelson, another sporadic NCI critic, and Eula Bingham, professor at Univ. of Cincinnati Medical Center and former assistant secretary of labor, as representatives of a group of 60 occupational and environmental health academics who share Epstein's views.

Epstein distributed a 17-page press release titled, "We're losing the war on cancer, experts say," containing an amalgam of pseudo-fact, at least one conspiracy theory, and a list of recommendations including overhaul of the National Cancer Act, removing its special authorities such as Presidential appointment of the NCI director.

Hot on the comet's tail were NCI executives and American Cancer Society representatives to set the record straight.

Edward Sondik, deputy director of NCI's Div. of Cancer Prevention & Control countered two statements in Epstein's press release:

►Epstein stated, "A Canadian National Breast Cancer Screening Study (based on 50,000 volunteers from 1980-88) found a 52 percent increase in breast cancer mortality in women aged 40-50 given annual mammograms and physical exams over women who had physical exams only."

Sondik's response: "The Canadian National Breast Cancer Screening Study has not released any mortality data. In fact, the Canadian investigators have not completed their analysis of mortality. The dissemination of the 52 percent figure, without any scientific basis behind it, nor the expressed endorsement of the Canadian investigators, is unethical.

►Epstein asserted that, "Safe alternatives to mammography, such as MRI and transillumination with infrared light scanning, are available. A crash program should be mounted to refine and market them with a goal of phasing out screening mammography."

Sondik's response: "Mammography, coupled with physicial exam, is the most useful tool we have for finding breast cancer early, when the results of treatment are most successful. Five year relative survival figures for breast cancer found in the local, regional, or distant stage are, respectively, 92, 71 and 18 percent.... Studies of mammography show that it has the potential to reduce mortality from breast cancer by at least 30 percent in women over 50. Studies in women aged 40-49 have not been conclusive, and NCI is continuing to study the issues involved. However, some evidence to date has suggested that breast cancer screening can be a useful regimen for women of this age group. NCI has recommended screening every one to two years for women aged 40-49 and annual screening for women over 50....

"NCI does not view mammography as the ultimate technology for detecting breast cancer at an early stage. Research is underway on many new technologies including MRI, infrared light scanning, optical imaging, as well as digital mammography. Considerable research is also underway on biomarkers."

Richard Adamson, director of NCI's Div. of Cancer Etiology, noted that NCI spends a third of its budget on cancer causation and prevention related research, including the study of environmental agents in the workplace that may contribute to cancer risk.

"NCI's efforts in researching cancer biology, cancer causation, cancer treatment and cancer prevention and control are well balanced and peer reviewed," Adamson said.

The Insitute also supports numerous studies of the total environment contributing to cancer causation, including viruses, chemicals, diet and nutrition, UV radiation, and others.

However, he noted the "single most identifiable cause of cancer--and other diseases--in the U.S. is tobacco smoking."

NCAB Oks LANs To Link NCI Staff With Each Other And The World

The National Cancer Advisory Board has given concept approval to a new contract for installation, management, and maintenance of local area computer networks for NCI programs that lack this capability, expected to cost $2.8 million over the next five years.

The Board, which provides concepts review of projects within the NCI director's office, also gave concept approval to continuation of support for the activities of the U.S. National Committee of the International Union Against Cancer (UICC).

Most of the annual expediture of $30,000 to the U.S. committee covers travel and per diem of the participants to the committee's annual meeting and partial support for a National Academy of Sciences staff member. The Board committed $160,000 to the contract for five years.

Following is the concept statement for the computerized local area network (LAN), presented by Aaron Greenberg of NCI's Management Information Systems Branch:

NCI Intramural LANs. New RFP concept, total $2.860 million, five years.

A large part of the NCI staff (primarily in administrative and

extramural organizations) has been given access to local area networks which allows them to share information among themselves; with other components of their divisions, with other NCI and NIH organizations on the NIH campus and at the Frederick Cancer Research & Development Center; and with their contractors, grantees, and other researchers throughout the world. Moreover, connection to LANs will give these individuals access to computing facilities located at DCRT and Frederick as well as to the myriad research facilities connected to the worldwide Internet.

NCI now proposes to provide a similar capability to the rest of the NCI staff, primarily in the intramural program. The planned capability will not only provide those features currently available at NCI but will also provide those the infrastructure to take advantage of the benefits of the High-Performance Computing Act of 1991 which promises multi-gigabit per second data highways for research and education by 1996. Known as the National Research and Education Network, it willlink research and educational institutions, government, and industry in every state.

NCI proposes a centralized strategy to the design, implementation, maintenance, and management of these new LANs. This approach will povide economies of scale for program, administrative, and contract staff in all areas from procurement of hardware and technical support through management of contract resources, planning, and network support. This centralized strategy will insure more efficient communication throughout NCI as well as superior LAN management and user support than would be accomplished with individually procured LANs.

The project includes cabling those NCI locations which have not been cabled, pruchase and installation of network servers and network interface cards, purchase and loading of appropriate network software, and continuing administration and management of the LANs. It is anticipated that cabling will be contracted through existing NIH telecommunications contracts while purchase and installation of servers and interface cards, loading of software, and the continuing administration, management, and maintenance of equipment will be done through the proposed contract.

News Roundup

'We'd Ban Cigarettes' If Nicotine Were Defined A Drug, Kessler Says

President's Cancer Panel Chairman Harold Freeman queried FDA Commissioner David Kessler at his recent appearance before the National Cancer Advisory Board about the agency's view of tobacco, a substance that kills 400,000 Americans per year, but which is not regulated by FDA.

"FDA so far has had no relationship with tobacco; could this change in the future?" Freeman asked, following the commissioner's prepared remarks (**The Cancer Letter,** Jan. 31).

Kessler said it has to do with FDA's jurisdiction as set by Congress.

"The definition of a drug is anything used in a cure, medication, prevention, or treatment of disease," Kessler said. A 1977 case, Action on Smoking and Health v. Califano, raised that issue, and legislative history of the Food & Drug Act did not support that view, he said.

"Congress never intended cigarettes to be a part of the jurisdiction of the agency. Our jurisdiction is vast; it's a trillion dollars worth of products, it's 25 cents on every consumer dollar. There are a few things, some medical devices, cosmetics, and cigarettes, that fall between the cracks," Kessler said. "I share your concern."

"It's a paradox that FDA does not look at nicotine. Why did this happen? Was it political? Was it economic?" Freeman asked.

"Let me walk through your scenario," Kessler said. "If it were a drug, there's no way that we can assure the safety of cigarettes--it's an oxymoron. So, once you classify cigarettes as a drug, or nicotine as a drug, we would ban all cigarettes. There is no other alternative."

"I'm not opposed to that," Freeman said, to supportive laughter around the conference room.

"I understand. But a lot of people don't understand that once it is classified as a drug, effectively, approval would have to be denied," Kessler said.

"That's the idea," one Board member said.

Freeman continued: "I think we're playing a little trick with ourselves as a country, by denying that this thing does exist, and that it is the number one cause of death in America."

"There's really no question," Kessler replied. "This HHS Secretary, Louis Sullivan, feels very strongly, he agrees with you."

"But what can be done, what can we do?" Freeman asked.

Kessler said a petition has been filed with FDA arguing that cigarettes labeled "low tar" or "low nicotene" are making a health claim, and since no cigarette can be shown to be healthy, manufacturers should not be allowed to make those health claims.

"Would it be in the public health benefit to remove these products from the market?" Kessler asked. "I think that is an open question."

"What is the patholigical lesion that does not allow us to act intelligently on this issue, considering that it is a drug that kills people?" Freeman asked.

"It's what we have as jurisdiction," Kessler replied. "Congress sets the mandate for the agency. Unless we have jurisdiction over it, we cannot act."

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The breast cancer committee being formed by the President's Cancer Panel is expected to be announced this week (past **The Cancer Letter's** presstime), following final clearance by HHS and the office of the Vice President. The committee will be made up of 16 members, chosen from 165 nominations, representing a "broad spectrum of expertise" on breast cancer,

according to Panel Chairman Harold Freeman. Vice President Dan Quayle asked Freeman to form a committee to investigate progress and opportunities for research in breast cancer.

The Cancer Panel's next meeting is scheduled for Feb. 21 in San Francisco on "Cancer Research and Technology Transfer for the 1990s."

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Short list of approved oncologic drugs for which certain unapproved uses ("off-label") are reasonable clinical practice, based on data, according to staff in NCI's Div. of Cancer Treatment:

--Carboplatin for non small cell lung carcinoma.

--Cisplatin for NSCLC and small cell lung carcinoma, sarcomas, and head and neck cancer.

--Etoposide for NSCLC, Hodgkin's disease, non-Hodgkin's lymphoma, and acute leukemias.

--5-FU for ovary, head and neck, and superficial bladder cancer.

FDA has said it plans to streamline the process for approval of secondary indications for already approved cancer drugs. NCI staff say these are the ones to start with.

These are a few of the most important, but there are other examples, including several drugs that have activity in Ewings cancer, for which no drug is approved.

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NCI awarded $1.27 million to a research consortium to study production of taxol in plant cell cultures in an attempt to develop alternative means of taxol production. The consortium members are Cornell Univ., Colorado Univ., Phyton Catalytic Inc., Hauser Chemical Research and the U.S. Dept. of Agriculture Research Service.

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NCAB member Irene Pollin continues to lead the NCI/National Basketball Assn. Mammography Initiative, which consists of the wives of NBA players who are collaborating with cancer centers in their local areas to promote community outreach and early detection of breast cancer in minority and underserved populations.

Last month, representatives from 27 NBA teams met at NCI for an orientation. NCI Director Samuel Broder symbolically "deputized" them to return to their communities and "spread the word" about mammography. Future plans by the NBA initiative are to create public service announcements with with players and their mothers to be aired around Mother's Day, which is during the NBA playoff season.

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NIH strategic plan will be discussed at four regional meetings: Feb. 12 in Los Angeles, jointly hosted by Drew Univ. and Occidental College; Feb. 25 at Univ. of Connecticut, Farmington, CT; March 3 at Emory Univ., Atlanta, GA; and March 5, Washington Univ., St. Louis, MO.

Due to "overwhelming" interest in the strategic plan, NIH has changed the format of the regional meetings. Oral public testimony will be deferred in favor of panel discussions; five panels will meet concurrently at each session, and the meeting will end with a plenary session.

NCI Director Samuel Broder is scheduled to chair the Critical Technologies panel at the Feb. 25 meeting in Farmington.

NIH formally unveiled the "Framework for Discussion of Strategies for the NIH" this week at a symposium in San Antonio, TX.

Copies of the "Framework" and information about the regional meetings are available from the office of NIH Associate Director for Science Policy & Legislation Jay Moskowitz, phone 301/496-3152.

NIAID Advisors Ok Two New RFAs, Recompetition of Pediatric ACTGs

Advisors to the National Institute of Allergy & Infectious Diseases have given concept approval to a new grant program to encourage research on model systems and assays for evaluation of mucosal immunity to HIV and SIV.

The four year program would cost $7.2 million over four years and would begin in fiscal 1993. It was approved last month by NIAID's Combined Division Advisory Committee.

The committee also gave concept approval to:

--Recompetition of cooperative agreements for 15 institutions involved in the Pediatric AIDS Clinical Trials Cooperative Group, and committed $100 million over four years to the program.

--Recompetition of the National Cooperative Drug Discovery Groups for HIV and opportunistic infections through 1997. New RFAS for these programs will be issued early next year. The institute has set aside first year costs of $3 million for the NCDDG-HIV program and $3.5 million for the NCDDG-OI program.

The advisors deferred two concepts for screening services and production suport to NCDDG scientists working on opportunistic infection therapies. The committee nominated some of its members to work with NIAID Div. of AIDS staff to rewrite the concepts, and suggested that supplemental funding was needed for NCDDG-OI researchers. The rewritten concepts may be availabe in several months.

Following are the concept statements:

Pediatric AIDS Clinical Trials Cooperative Group. RFA recompetition, first year cost $25 million, four years; total $100 million.

This initiative will support pediatric clinical trial units which conduct research to evaluate potential therapies for HIV disease and its associated opportunistic infections, malignancies, and other complications. The pediatric clinical trial units will link with obstetrical and perinatal facilities and social services for mothers and children infected with HIV.

The AIDS Clinical Trials Group (ACTG) was formed in December 1987. Today, the ACTG consists of three components: 15 pediatric AIDS Clinical Trials Units (ACTUs) and 32 adult ACTUs; the Div. of AIDS Clinical Research Program (CRP) and Treatment Operation Research Program (TROP); and, the Statistical and Data Analysis Center (SDAC). In addition, contractors for site monitoring and operations support the functioning of the ACTG.

The ACTG performs a wide range of scientific planning and coordinating functions related to the conduct of adult and pediatric clinical trials. The group assesses treatment research needs, establishes scientific priorities, develops new research protocols, conducts and reports the results of clinical studies, and establishes quality control programs to ensure the accuracy of data. In addition, CRP and TROP facilitate the functioning of the ACTUs and the application of clinical trials results to the practice of medicine.

The pediatrict effort consists of 15 institutions which conduct clinical trials in pediatric ACTUs and 12 institutions which conduct pediatric trials as a part of a larger research effort in adult ACTUs. Collectively, these pediatric ACTUs and pediatric components in adult ACTUs comprise the pediatric AIDS clinical trials program. The cooperative agreements supporting the current 15 pediatric ACTUs will be recompeted in fiscal 1993 (the adult ACTUs are now being recompeted and will be awarded in March and April of 1992). Applications from existing pediatric ACTUs and from new pediatric sites wishing to join the ACTG will be reviewed during this recompetition.

Even though the pediatric and adult ACTUs are being recompeted separately, the concepts upon which both RFAs are based are identical. Essential features of the pediatric recompetition plan include the following:

The RFA for pediatric ACTUs will describe required and optional components. All applications must contain a clinical trials component. An optional component for laboratory sciences may be included. Each component will be budgeted separately. Phase I, I/II, and III trials to evaluate potential therapies will be supported under this cooperative agreement.

1.) Under the clinical trials component, funds will be provided to pediatric ACTUs on the basis of research activities and provision of crucial ancillary services and outreach required to recruit and maintain an agreed upon minimum number of patients into an array of protocols each year of grant support. The cost of new protocols will be estimated in advance so that institutional budgets reflect the number of new pediatric patients, the number of patients continuing on study, and the cost of the individual pediatric protocols in which the ACTU is participating. This funding is designated as core clinical base funding. In each budget period, a portion of the total ACTG pediatric budget may be set aside and designated as incentive funding. These monies will provide supplemental funding for additional patient accrual above the minimum number and for certain high priority studies. Core clinical base funding will support patient recruitment, personnel costs for clinicians, pharmacists, study coordinators, nurses, patient care costs, protocol mandated flow cytometric immunophenotyping, processing of clinical specimens, and data management.

The clinical trials component will emphasize enrollment of study participants from populations currently underrepresented in ACTG clinical trials relative to the national demographics of the HIV epidemic. Applicants will be encouraged to participate in clinical trials involving therapies for antiretroviral agents, opportunistic infections, perinatal transmission and active and passive immunotherapies. These areas will be emphasized as areas of high priority. Since neurologic and cognitive development are significantly influenced by HIV infection and because of their importance as end points, all units will be required to demonstrate capabilities to conduct routine neurologic testing as part of clinical trials. Research on ways to use neurologic and cognitive measures as end points will be supported through several possible mechanisms which may include the incentive funding pool.

2.) Core laboratory funding in virology, pharmacology and special immunology will support professional and technical laboratory personnel and laboratory costs associated with performing protocol mandated tests. Core virology laboratories will have minimum capabilities to conduct HIV cultures, p24 antigen determinations and implement new assays as diagnostic technology evolves. Core pharmacology laboratories will have capabilities to conduct therapeutic drug level assays for agents utilized in the treatment of HIV disease and develop new assays for therapeutic drug monitoring as needed. Core special immunology laboratories will have the capabilities to conduct tests which may be required for intensive study of active and passive immune-base therapies. The number of core laboratories awarded for virology, pharmacology and special immunology will be determined by the needs of the ACTG and available funds. Core laboratory funding to support protocol mandated tests and assays in pharmacology, virology and special virology will be an optional component of the RFA. Applicants not applying for these options or not awarded funds for these components will be required to establish agreements with a funded ACTG core laboratory to obtain protocol mandated testing. (In contrast, protocol mandated flow cytometric immunophenotyping is required at all clinical trials sites, and therefore is included in the clinical base funding).

3.) Applications for the developmental (applied) research component will be optional and contingent upon receiving core laboratory funding in virology, pharmacology or special immunology. The scope of this component will be dependent upon available resources. Applicants will be encouraged to form collaborative arrangements with any appropriate research laboratory regardless of its location. Developmental research funds will provide support for specific projects that will assist in the development and assessment of appropriate therapies for HIV disease. Applications for developmental research will be accepted in virology, pharmacology and/or special immunology. Research is encouraged, but not limited to, the following areas: a.) the effect of therapies on the progression of infection and organ system pathology, b.) development of surrogate markers to evaluate therapeutic responses, and c.) drug resistance. Clinical trials to evaluate the safety and/or efficacy of therapies or studies of the basic pathogenesis of HIV disease will not be funded under this component.

The new cooperative agreements awarded to support the pediatric ACTUs will be administered under the following conditions which are consistent with grants management policy and cooperative agreement policy:

--The ACTG investigators and DAIDS staff will continue to develop and establish research goals and priorities.

--The cost of conducting each study will be determined prior to protocol implementation. ACTUs will be funded on a reimbursement basis for participation in specific protocals

according to patient accrual. Funding will include adjustments for the variation in the costs of conducting protocols among institutions.

--The TROP will conduct reviews of each ACTU twice a year, and allocate fiscal resources based on analysis of ACTU accrual, timely submission of accurate data, observance of protocol requirements, authorship, scientific contributions and leadership, complexity of protocols, and accrual of special populations, according to the reimbursement formula previously negotiated.

National Cooperative Drug Discovery Groups for the Treatment of HIV Infection. Reissuance of RFA, first year cost $3 million, four years, two to three awards.

This program, launched in 1987, has been successful in providing a framework for academia, industry and government to cooperate in the design and development of novel anti-HIV modalities. NCDDG supported research on viral and cellular factors involved in HIV replication has expanded the knowledge base on how HIV replication may be halted. The discovery and/or development of several HIV inhibitors targeted to different stages in the replication cycle have been greatly facilitated by the NCDDGs (D4T, AZdU, sCD4, protease and tat inhibitors, ribozymes). Reissuance of the RFA will allow new applicants to compete with eight of the currently funded groups for 1993 funds. Two to three awards are expected.

This project will continue to support innovative basic research for the identification of innovative therapeutic modalities in areas including: i. interference with viral targets critical to the HIV life cycle; ii. exploiting cellular factors that enhance or repress viral functions, such as NFkB, tat and Rev binding factors; iii. identifying neurological receptros and/or factors involved in neurological consequences of HIV infection; iv. designing immune based therapies such as immune reconstitution with multipotent cells or cells engineered to confer protection against HIV infection; and other novel, high risk approaches. Strategies currently under intense investigation in the private or public sectors will be excluded from this competition.

National Cooperative Drug Discovery Groups for the Treatment of Opportunistic Infections Associated with AIDS. Reissuance of RFA, first year cost $3.5 million, four years, five to seven awards.

To stimulate the search for improved anti-OI drugs, the NCDDG-OI program was launched in FY 1990 with the funding of seven applications. Two of four new awards were made in FY91, and two to four are anticipated in FY92, bringing the total to 13015 groups. In FY 1993, five of the original seven awards will terminate. Funding five to seven groups in FY93 will continue the infusion of new ideas and state of the art technologies.

This program of investigator initiated research consists of diverse and independent approaches to discover new potential therapies to treat the opportunistic infections associated with AIDS. Research considered responsive to this RFA may include but is not necessarily restricted to the following:

1. Studies to identify and characterize molecular targets in opportunistic pathogens that may be exploited in discovering selective therapeutic agents, 2. studies leading to greater understanding of the biochemical differences between the selected pathogen and mammalian cells, 3. establishment and utilization of assay systems for selected molecular targets to identify active compounds and biologicals, including natural products, and 4. development of novel and innovative animal models to determine the therapeutic efficacy of compounds and to facilitate comparisons of normal and immunocompromised animal models for evaluating potential therapies.

Development of model systems and assays to evaluate mucosal immunity to lentiviruses. New RFA, first year cost $1.8 million, four years; cooperative agreements.

Objective of this project is to develop animal models, methodology, and assay reagents to study mucosal immunity to HIV (and SIV) in primates and humans. a) To identify serological and cellular immune responses that might be effective in preventing HIV transmission; b) To develop and test various vectors designed to induce a mucosal immune response to HIV (and SIV) antigens that could protect against infection; c) To identify and characterize specific T-cell responses that might be a front-line defense in gut-associated immunity against HIV; d) To develop methods and to evaluate mucosal immunity in humans and primates.

A primary route of infection of HIV is through the mucosal surfaces. Induction of virus-specific mucosal immunity capable of preventing or minimizing the earliest infectious events may provide the greatest opportunity to avert HIV disease in an individual.

It is necessary to evaluate mucosal immunity in humans and higher primates. To develop a vaccine that induces protective immunity at mucosal surfaces, basic information about transmission of HIV and SIV across these surfaces is needed. Currently the availability of tools to examine mucosal immunity in humans and animals lags far behind the ability to study serological immunity Panels of IgA monoclonal antibodies (Ab) do not exist, even to neutralizing or Ab-dependent, cellular cytotoxicity epitopes of HIV or SIV. Reagents for mucosal immunity studies in monkeys are lacking, or limited to a few polyclonal reagents. A small number of studies have documented the presence of Ab to HIV at mucosal surfaces or in milk from infected persons. However, these studies have not evaluated either Ab specificity or effectiveness in blocking transmission. Support for research on mucosal immunity and transmission is both timely and essential for effective vaccine development.

Vectors have been developed that have been shown to induce mucosal immunity these include bacterial (Salmonella) and viral (adenovirus) vectors which are delivered orally. Through this initiative, SIV and HIV genes will be cloned into these or additional vectors that will be assayed for their ability to induce mucosal immunity. The ability of mucosal immunity to prevent infection can be assayed in the monkey model system. This initiative will stress both the development of new vectors capable of inducing a mucosal immune response, and systematic assay and comparison of vectors currently available.

This initiative would also focus investigative efforts on specific T-cell responsiveness in the gut which gives us another approach to examine the potential responses of gut immunity to HIV. Investigators are encouraged to use the macaque model for studies of rectal/vaginal mucosal immunity if possible, and to attempt to identify the specificity and MHC restriction of such populations.

This initiative would expand existing support contracts performing and developing novel serological and cellular assays of immune responses to AIDS viruses. These studies would include women-infant transmission studies, men's AIDS cohort studies, heterosexual AIDS transmission studies, and interaction with anticipated studies in the AIDS Vaccine Evaluation Group on vaccines to mucosal surfaces.

These studies would have broad ranging impact on other vaccines to sexually transmitted diseases. It would also support the development and application of mucosal immunity assays to vaccinated primates and human volunteers at AIDS Vaccine Evaluation Units, particularly where live vectors or mucosal delivery systems are being studied.

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 Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CB-21026-32

Title: Master agreement for cancer vaccine development

Deadline: Approximately March 20

NCI is seeking experienced firms to provide needed support services in the emergent cancer vaccine field. The required support will be defined by master agreement orders issued during the period of performance. The MAOs will be awarded based upon competition between members of the master agreement pool.

MA holders selected for award shall provide one or more of the following: clinical grade recombinant vaccinia virus CEA constructs, other recombinant tumor associated antigen vector constructs, monoclonal antibodies and peptides for use in clinical protocols to elicit specific active immunotherapy responses in colorectal carcinoma, mammary carcinoma, and lung carcinoma patients.

Specific tasks may include one or more of the following: production of clinical grade recombinant CEA and other tumor associated antigen constructs, including pox virus vectors, baculovirus vectors, purified peptides, monoclonal antibodies, and testing of constructs in rodent and nonhuman primates for immunogenicity and safety.

Agreements will be awarded to all firms whose technical proposal is considered acceptable. Multiple MAOs may be issued in each year.

An MA holder is free to respond to any particular RFP without having any affect on its MA.

Contract Specialist: Richard Hartmann
RCB Executive Plaza South Rm 620
301/496-8611

RFP NIH-ES-92-17

Title: Evaluation of toxic and carcinogenic potential of isoprene, indium phosphide and gallium arsenide when inhaled in Fischer 344/N rats and B6C3F1 mice

Deadline: Approximately March 12

The purpose of this contract is to evaluate the toxic and carcinogenic potential of isoprene, gallium arsenide, and indium phosphide when inhased in Fischer 344/N rats and B6C3F1 mice. The base contract award will include work activities associated with bulk chemistry, generation and monitoring developmental work, and health and safety concerns. The government may, pending the availability of funds, exercise options for: an inhalation study of glutaraldehyde, a 104 week chronic study of glutaraldehyde, a 104 week chronic study of isoprene; a 104 week chronic study of gallium arsenide, a 13 week study of indium phosphide and a 104 week chronic study of indium phosphide. These studies shall be conducted in accordance with the FDA Good Laboratory Practice Regulations.

Award of one cost reimbursement completion type contract with an estimated period of performance for the base contract of approximately one year on an open competition basis is contemplated as a result of this solicitation. Exercise of all options under this solicitation may result in a multi year cost reimbursement type contract with a total term of four years nine months that would be incrementally funded.

Copy of the RFP is available from Marilyn Whaley, Contract Specialist, National Institute of Environmental Health Sciences, 79 TW Alexander Dr. 4401 Bldg., PO Box 12874, Research Triangle Park, NC 27709, phone 919/541-5770.

RFP NIH-ES-92-18

Title: Evaluation of the toxic and carcinogenic potential of sodium fluoride and methyleugenol administered orally in laboratory animals.

Deadline: Approximately March 12

The purpose of this contract is to evaluate the toxic and carcinogenic potential of sodium fluoride and methyleugenol administered orally in laboratory animals. The base contract award will include work activities associated with bulk chemistry, dose formulation and dose analusis developmental work, and health and safety concerns. The government may, pending the availability of funds, exercise options for: a study of anthraquinone, a 13 week study of anthraquinone, a 104 week chronic study of anthraquinone, a 104 week chronic study of sodium fluoride, and a 104 week chronic study of thethyleugenol. Laboratory animals that will be used in these studies are Fischer 344/N rats and B6CF1 mice. These studies shall be conducted in accordance with FDA Good Laboratory Practice Regulations.

Award of one cost reimbursement complete type contract with an estimated period of performance for the base contract of approximately 10 months on an open competition basis is contemplated as a result of this solicitation. Exercise of all options under this solicitation may result in a multi year cost reimbursement type contract with a total term five years 10 months that would be incrementally funded.

Copy of the RFP is available from Marilyn Whaley, Contract Specialist, National Institute of Environmental Health Sciences, 79 TW Alexander Dr. 4401 Bldg., PO Box 12874, Research Triangle Park, NC 27709, phone 919/541-5770.

RFP NIH-ES-92-19

Title: Evaluation of the toxic and carcinogenic potential of sodium nitrite and o-nitrotoluene administered orally in laboratory animals

Deadline: Approximately March 12

The purpose of this contract is to evalaute the toxic and carcinogenic potential of sodium nitrite and o-nitrotoluene administered orally in laboratory animals. The base contract award will include work activities associated with bulk chemistry, dose formulation and dose analysis developmental work, and health and safety concerns. The government may, pending the availability of funds, exercise options for: a study of cinnamaldehyde, a 13 week study of cinnemaldehyde, a 104 week chronic study of cinnemaldehyde, a 104 week chronic study of sodium nitrite, and a 104 week chronic study of o-nitrotoluene. Laboratory animals to be used are Fischer 344/N rats and B6C3F1 mice. These studies shall be conducted in accordance with FDA Good Laboratory Practice Regulations.

Award of one cost reimbursement completion type contract with an estimated period of performance for the base contract of approximately 10 months on an open competition basis is contemplated as a result of this solicitation. Exercise of all options under this solicitation may result in a multi year, cost reimbursement type contract with a total term of five years six months that would be incrementally funded.

Copy of the RFP is available from Marilyn Whaley, Contract Specialist, National Institute of Environmental Health Sciences, 79 TW Alexander Dr. 4401 Bldg., PO Box 12874, Research Triangle Park, NC 27709, phone 919/541-5770.