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NCI To Fund Two Construction Grants With $2 Million From Special NIH Fund

NIH has allocated $2 million of a special $15 million pool of construction funds to NCI to be awarded to cancer center construction projects that have been reviewed and approved, but have been languishing for lack of construction funding in the NCI budget.

NCI Director Samuel Broder told **The Cancer Letter** that the $2 million will fund "approximately two construction projects with very good priority scores, projects that were in the system and recommended for

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In Brief

Lasker Foundation Will Not Make 1990 Awards; Michigan Cancer Elects Fischer Vice Chairman

ALBERT AND Mary Lasker Foundation has decided not to make its medical and scientific awards this year in order to review its future commitments. The foundation, begun in 1942, has assets of about $2.4 million, down from $4.5 million in 1980. The awards of $15,000 each are among the most prestigious American prizes in science and medicine. . . . **PHILIP FISCHER** was elected vice chairman of the Board of Trustees of the Michigan Cancer Foundation. **Paul Nine** was named secretary. The foundation gave Distinguished Service Awards to **Marie Swanson,** formerly vice president of epidemiology, for her pioneering work in the study of the occupational epidemiology of cancer; and **Sam Brooks,** director of the foundation's breast cancer programs, for his contributions to the development of new malignant and nonmalignant cell lines. . . . **TAYLOR WHARTON** has been appointed to the Charles Barker Chair in Surgery at Univ. of Texas M.D. Anderson Cancer Center. Wharton, an expert on gynecological cancers, is chairman of the gynecology department at M.D. Anderson and medical director of the center's cancer prevention and detection programs. . . . **NIH WORKSHOP** on "Promotion of Integrity and Responsible Practice in Biomedical Research," will be held April 20-21 at the Holiday Inn Crowne Plaza in Arlington, VA. It is the first of four regional workshops following up on the proposed conflict of interest guidelines withdrawn by NIH in December. The remaining workshops will be held in Boston, St. Louis and San Diego. Contact Leah Valadez, George Washington Univ. Medical Center, 202/994-2801. . . . **DEADLINE FOR** mail registration for Methods Workshops to be held in conjunction with the American Assoc. for Cancer Research annual meeting May 23-26 in Washington is March 30. For information and forms contact AACR, Public Ledger Bldg., Suite 816, 6th & Chestnut Sts., Philadelphia, PA 19106, phone 215/440-9313.

NCI Receives $2 Million From NIH; Will Fund Two Construction Grants

(Continued from page 1)

approval by the NCAB." He declined to name the two projects until the grantees had been notified this week.

Congress mandated the creation of the $15 million pool, now $14.8 million after the budget sequestration, in the FY 1990 NIH appropriation. Funds were taken from each of the Institutes; NCI had to provide $3.5 million for the pool.

Most of the money in the pool--$10 million--is to be used for construction of a mouse production facility intended to replace the Jackson Laboratory facility that was destroyed in a fire last year. Of the remainder, NCI will get $2 million and $2.8 million will be competed NIH-wide for other construction projects.

NIH recently released the RFAs for the mouse production facility and for other projects (text of the RFAs begin on page 7).

NIH Acting Director William Raub made public the $2 million allocation to NCI last week at a Senate budget hearing. Previously, he had said all of the money that was left from the mouse facility probably would be competed NIH-wide. However, at the recent National Cancer Advisory Board meeting, Raub referred to cancer construction projects that were already reviewed and approved, noting that NCI has "some high quality, high performance aircraft already on the runway lacking only fuel." (**The Cancer Letter,** Feb. 16).

Asked what might have caused NIH to make the $2 million commitment to cancer center construction, Broder said, "I think our construction projects spoke for themselves. The logic and priority of these construction projects carried they day."

It will be the first time since 1987 that NCI has had funding for extramural construction. That year, the Institute received $2.5 million, which went primarily for repairs at the Frederick Cancer Research Facility. Prior to 1987, NCI had not received construction funding since 1985, when $5.5 million was available.

Broder said NCI would use the funds to "try to match appropriate peer review levels" for the two projects. "I'm very, very pleased that we are able to provide support for construction projects," Broder said. He noted that although the money would fund only two projects, "all of the construction grants in our portfolio are very meritorious."

The projects that miss out on the $2 million appropriation are still eligible for the RFA for $2.8 million. The RFA states that applications that have been peer reviewed and unfunded will automatically be considered for the RFA without the submission of a new application. A new application is required if the plans for construction "differ markedly" from the application that was approved.

"We are going to advise every group that has an application in to compete for the RFA," Broder said. He said NCI will advise principal investigators to review their applications and consider making changes, if necessary.

At the hearing, before the Senate Labor, HHS, Education Appropriations Subcommittee, Sen. Arlen Specter (R-PA) took issue with Raub about opening up competition for the $2.8 million "when you have projects waiting in the wings." He indicated that Congressional intent was for all $4.8 million of that left from the mouse facility to go toward cancer center construction. "I'm just a little disappointed," Specter said.

Raub responded that NIH "took into account the legislative history" of the creation of the $15 million fund. He said he made the $2 million available to NCI because the top cancer center construction projects "were nearly flawless in their technical" merit.

Broder testified before the subcommittee on the President's FY 1991 budget request for NCI of $1.694 billion. The overall request for NIH is $7.929 billion.

Sen. Tom Harkin (D-IA), subcommittee chairman, asked what progress had been made since the enactment of the National Cancer Act of 1971. Broder cited statistics showing decreasing death rates in common cancers for Americans under age 65, but increasing death rates in some cancers for those over age 65 and for minorities. He noted that the death rate for women over age 65 from lung cancer is up 100 percent since 1973, as a result of increased smoking among women in the last 30 years.

"Cigarettes are one of the few things that are

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lawful and lethal when used as intended," Broder said. Tobacco companies are targeting young women "for initiation into smoking practices," he said.

"Something about that is really offensive to me," said Sen. Dale Bumpers (D-AR). Harkin called for more childhood education on the dangers of tobacco.

Broder pointed out that as a result of the recent changes in criteria for NCI-designated comprehensive cancer centers, centers must perform community service and outreach. He suggested this could have an impact on smoking practices.

Harkin also asked about the incidence of cancer in rural areas. Broder said NCI has established a task force on rural health and is expanding the Surveillance, Epidemiology & End Results program in rural areas this fiscal year.

On the overall NIH budget, Harkin said he was "disappointed" that the Administration's request "does not even keep up with the biomedical inflation rate." He said he was pleased to see an increase in funding for research grants in the 1991 budget, allowing for funding of 25 percent of approved grants. However, he was concerned that NIH is approving an increasing percentage of grants, about 95 percent in FY 1989. "Would it be desireable for NIH to be more selective on the front end?" Harkin asked.

Raub said the high approval rate is a consequence of increased competition, especially as grants are recompeted. "It is the hardier souls who are staying in the competition," he said. Being more selective "would not be very effective" since that might subvert the peer review process.

Harkin and Bumpers also pressed NIH to increase stipends for postdoctoral trainees, which now range from $20,000-$30,000 a year. They also spoke in favor of increasing salaries for senior scientists.

"Our priorities in this country are so screwed up," Bumpers said, commenting that he had just come from a hearing on the Defense Department budget. "If there is going to be a 'peace dividend,' Congress is going to have to carve it out. I feel strongly that we should get the (NIH grant) award rate up to 30 percent minimum and pay your scientists more."

CTEP To Start New Effort To Bring Minorities Into Clinical Trials

NCI has set aside $1 million to start a new therapeutic initiative for minorities which will involve cooperative groups, minority institutions, and the Div. of Cancer Treatment's Cancer Therapy Evaluation Program.

The minority initiative will be supported through groups' existing cooperative agreements. The $1 million set aside in FY 1990 funds is about one third of what CTEP Director Michael Friedman projected the program would need when fully implemented.

Cooperative groups will be involved by pairing their respective institutions with minority institutions. Groups' individual expertise and statistical offices will be utilized. In appropriate situations, funding will be on a payment by case basis.

Friedman described the initiative recently to the DCT Board of Scientific Counselors:

"The primary purpose of this initiative will be to improve the clinical investigation of therapies for minority patients with all types of malignancy. Two areas of emphasis will be:

▸Major killers. Lung, breast, colon, prostate, and cervix cancer affect all populations, but their treatment is associated with poorer outcome in minorities. This may be due to biologic differences, differences in access to care, or a combination of factors.

▸Disease of higher relative incidence. Myeloma, esophageal, gastric, and cervical cancer are examples of problems of special importance for minorities.

"Unfortunately, there is inadequate information as to why minorities have different epidemiologic, response, and survival characteristics. There are not even enough data to generate meaningful hypotheses for testing, much less permit firm conclusions to be drawn. What we lack is a biologic basis for understanding these observed clinical findings. In order to remedy this situation, CTEP proposes a program of three specific parts.

"1. Attempt to understand the problem using the current clinical trial mechanisms.

"This would involve increasing the information currently being generated by cooperative groups and phase 2 and 3 contractors."

Friedman estimated this part of the program would cost $300,000 a year, if all 10 major cooperative groups participated at an average of $30,000 each.

"Currently, incomplete racial, ethnic, and/or socioeconomic information is available from the roughly 20,000 to 25,000 new patients studied on therapeutic trials each year. CTEP can require these grantees and contractors to routinely collect racial data and perform comparative analyses on outcome and toxicity. Retrospective data can in some cases be reconstructed, but certainly contemporary data on those newly recruited to clinical studies can be gathered.

"What are the implications of this proposal? Care must be exercised so that minorities do not feel

'singled out for experimentation.' Clinical trial methodology considerations also apply. There are statistical considerations that must be taken into account if ethnic comparisons are to be made. There may be informed consent implications as well.

"2. Attempt to increase access to state of the art cancer care and increase the number of minority patients accrued to clinical studies."

Friedman estimated this would cost $900,000 a year, if six groups participated, at $150,000 each. He suggested the six groups which would initially participate might be North Central Cancer Treatment Group, Southwest Oncology, Eastern Cooperative Oncology Group, Cancer & Leukemia Group B, Gynecologic Oncology Group, and Radiation Therapy Oncology Group.

Friedman pointed out that CTEP currently is funding four minority satellite grantees through supplements to group awards, to assist their recruitment of minority patients. This will amount to about $400,000 in FY 1990, which he said would be folded into the new program.

The existing minority satellite supplements have not been very successful, Friedman said. "Despite these efforts, relatively few minority patients have been entered on studies and CTEP believes this is not the most effective or efficient means to achieve this goal. For FY 1991, we propose a different approach.

"This approach would stress direct linkage between a minority academic center or major institution and the headquarters center of a cooperative group. For example, Dr. [Charles] Moertel [NCCTG chairman] has expressed his commitment to link the Mayo Clinic/NCCTG with such a minority institution. The goal would be to ultimately bring the institution into NCCTG as a full member. The methods employed would include exchange of investigators, statisticians, and data managers. A full panoply of clinical protocols would be made available (via NCCTG, high priority trials, and intergroup studies). This institution would gain the requisite experience in multiple disciplines simultaneously.

"In the past, the performance of predominantly minority institutions in formal studies has been disappointing. Lacking the resources and the expertise, some type of special individual attention might prove more successful. We would initially suggest forming links with academic centers like Morehouse, Meharry, Drew, Howard, and the Univ. of Puerto Rico. We would attempt to build an institutional expertise and commitment to high quality clinical trials methodology.

"There are many potential benefits of this activity. It could influence the care of all cancer patients treated at that institution (not just study patients). Diffusion of new data to the practice community, upgrading or establishing multidisciplinary tumor boards and conferences, attracting students and house staff to oncology careers, etc. In order to effectively influence the long term prospects of minority patients, more minority physicians and institutions must be actively engaged in cancer care. Such an effort must be supported with consistent funding for a long term effort. It will be moderately expensive, but we suggest a mixture of frontloading and capitation support will permit responsible and responsive management by CTEP.

"3. New efforts to elucidate possible biologic determinants of disease outcome in minorities."

This would involve about 40 specific correlative studies averaging $50,000 each, for a total of $2 million a year, Friedman said.

"In order to capitalize on the burgeoning insights into the molecular biology of neoplasia and to establish a scientific frame of reference for cancers in minorities, more lab/clinical correlative studies must be supported. Currently, there is considerable activity in the cooperative groups to characterize various descriptive and prognostic features of patients and tumors. If minority patients have special biologic mechanism of metastasis or unique sensitivity/resistance to therapies, only these carefully performed, large comparative studies will demonstrate them. It may be possible to tailor therapies for specific subgroups.

"This proposal may have the least immediate impact on mortality, but it is likely to have the most relevance in the long run. It is conceivable that laboratory scientists at minority institutions will benefit from this interaction.

"These proposals represent an integrated, achievable set of activities which are consistent with DCT's mission. Such efforts will not dramatically drive down cancer mortality in minorities immediately. There are many complex social and economic obstacles which relate to prevention (lifestyle modification) and access to medical care. A major concern is that many of these patients are not able to be entered onto clinical trials because of poor insurance coverage for treatment or laboratory and radiographic testing. This problem was observed in the minority satellite program and was one obstacle to accrual.

"Interaction with several other programs would be ideal. CTEP has not proposed to directly incorporate the cancer centers as a unique mechanism. All centers are members of the cooperative group system, and well designed protocols for the diseases of interest

already exist in the group portfolios. However, the cancer centers are integral to the overall success of this initiative. Moreover, the new minority CCOP effort should be recognized as a relevant instrument to be considered. Finally, the VA and PHS hospitals see large minority populations of patients and have not been directly included in these plans."

Friedman pointed out that since the existing cooperative agreements with the groups have undergone peer review, "I am comfortable with CTEP staff management and the NCI Executive Committee approval [of additional funds for participating groups] since the groups are receiving only 64 to 85 percent of their recommended funding." However, he added that "because of the magnitude of the total project, it might be necessary to engage the Clinical Cancer Investigations Review Committee [which reviews the cooperative groups] to review some aspects.

"This proposal would attempt to engage the leaders of the minority medical community in identifying and implementing solutions to these vexing problems. In addition to directly offering quality care, and fostering better understanding of the molecular bases of their disease, those recruited to clinical studies would benefit all patients."

The Board of Scientific Counselors was not asked to approve the initiative; NCI Director Samuel Broder and the Executive Committee had already determined that it would be included in the institute's efforts to address the problem of higher cancer incidence and mortality among minority populations. Board members generally were supportive.

"There ought to be some effort to direct funds to centers, to study some of the biological questions," BSC Chairman John Niederhuber said. Friedman responded that the minority CCOPs and centers will carry out correlative studies.

Board member John Mendelsohn suggested that the program may require social workers to go into homes for followup.

Radiosensitizer Screen Concept OK'd, BSC Delays On Acoustic Microscopy

The Div. of Cancer Treatment Board of Scientific Counselors gave concept approval at its recent meeting to a new contract to screen compounds as radiosensitizers using a colorimetric assay. The contract would cost an estimated $750,000 a year for three years.

Approval was not unanimous; Chairman John Niederhuber and Ronald Levy voted against it.

The board was less impressed by a concept proposal for a $4 million, five year contract to develop tissue imaging through in vivo acoustic microscopy. Members voted unanimously to delay action until the next meeting, in June, when the Radiation Research Program will present a new proposal which incorporates concerns expressed in the discussion.

The Radiation Research Program also submitted the concept for a screening effort for radiosensitizers:

> The field of radiosensitizers is losing momentum due to the paucity of new active compounds. Current methodology, a clonogenic assay, for screening compounds for radiosensitization activity is time consuming and only a limited number of compounds (200)300 per year) can be screened. A high volume, automated, colorimetric assay system such as that being developed by DCT's Developmental Therapeutics Program for screening anticancer drugs offers a solution to the problem of screening radiosensitizers. This assay can screen a large number of compounds in a relatively short time using human tumor cell lines.
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> The consensus of a workshop held last year to discuss this possible approach to the problem was that the tetrazolium colorimetric assay was a realistic approach to screening a large number of compounds. A protocol was outlined for screening, the details of which will require initial development to optimize certain aspects (i.e., radiation timing, radiation dose, drug concentrations, cell lines, etc.). It was the consensus of the workshop that considerable savings in time and money could be realized if the radiosensitizer screening could be integrated in an effective and appropriate way with the screening program for chemotherapeutic drugs being developed by DTP.
>
> The high volume, automated, colorimetric assay represents a major advance in screening a large number of compounds as radiosensitizers. RRP is proposing a contract supported effort to do screening on a small scale (2,000-3,000 compounds per year) as compared with the anticancer drug effort. The capacity of the screen is expected to be multifold greater than the clonogenic assay currently being used. The first year of the contract will develop the parameters for the drugs, radiation, and cell lines to be used in the assay. The remaining years will be devoted to testing compounds as radiosensitizers.

NCI staff was not in total agreement on this proposal. Michael Boyd, director of the Developmental Therapeutics Program, said that "a screening assay does not make a drug discovery effort. This is not enough money. I think a national drug discovery group for this might be worthwhile."

"I have a lot of reservations about this," board Chairman John Niederhuber said. "It looks like a 'I wish we could do this proposal' without being well organized.

RRP Director John Antoine pointed out it is "a new approach to screening. We already have a screening effort. This recommendation was developed with the help of extramural investigators."

Board member John Mendelsohn said he thought Boyd's comments involved "a lot of wisdom. I like the idea of a national drug discovery group approach,

rather than a contract. I would like to put a lot of money into this. It is a very important area.."

James Mitchell, a member of the Radiation Research Branch in DCT's Clinical Oncology Program, defended the concept, although saying that he agreed with Boyd. "Things rarely are as simple as they seem. But in radiosensitizers, there are not hundreds of cell lines in a drug screen, only a few."

Board member Ralph Weichselbaum also defended the concept. "There are many good prospects for radiosensitizers. This proposal seems reasonable, and it is a worthwhile thing to do."

Board member Yung-chi Cheng said he supported the proposal for a contract, "but this is so important that I think we should have another concept for drug discovery group in this area."

DCT Director Bruce Chabner said he felt that in the next five years, most of the progress in cancer treatment will involve combinations of chemotherapy and radiotherapy. "Screening is the most direct way to find new leads for drugs that interact with radiation," Chabner said. In response to a suggestion that this screening could be added to DTP's screening effort, located at the Frederick Cancer Research Facility, Chabner said that would require more personnel with different expertise. "I would be in favor of doing it at Frederick if we could get the people and the space."

"We've put enough into Frederick not to use this facility," Niederhuber said. "For three and a half million dollars [estimated five year cost of the project], you could put a lot of resources there."

Antoine said that Boyd had been very helpful in developing the proposal and that his advice was good. He added that the proposal was not intended "entirely as a new contract but to beef up the old one," although it would have to be competed.

The present contract is with Stanford Univ., with Martin Brown as the principal investigator. That contract costs about $450,000 a year.

Levy, who is professor of medicine at Stanford, drew some laughs when he said "I had no idea I was speaking against a colleague [in opposing the concept]. I think we should alter his contract and let him do this."

Boyd said he agreed that the proposed screen is much simpler than the anticancer drug screens. But "I still would prefer that it be done with a cooperative agreement, although the contract is feasible. It could be coordinated with the DTP screen. It is workable."

Charles Balch's motion to approve was passed, with Niederhuber and Levy voting against it.

Tissue imaging: In vivo acoustic microscopy. Five years, estimated first year cost of the contract, $800,000.

State of the art radiologic imaging has the ability to resolve large and small (approximating 2 to 5 mm in diameter) tumors. Operative localization of these small tumors for the purpose of obtaining an excisional biopsy is technically difficult. Additionally, a surgical biopsy involves significant financial cost and the risk of patient morbidity and mortality. Currently, fluoroscopic imaging using triangulation or three dimensional imaging provides tumor localization and facilitates subsequent image documented needle aspirational biopsies from the tumor site. Thus, both the patient and the medical community receive an improved standard of care. However, even when the aspirational biopsy sample is obtained following imaging localization, it is frequently necessary to obtain numerous samples and occasionally terminate the percutaneous biopsy procedure without obtaining a conclusive pathologic diagnosis. Cytopathologic examination of aspirated cells is professionally difficult, with significant intra and interobserver variance. Tissues with rapid mitoses and pathologic processes promoting an inflammatory response make the cytopathologic examination less reliable.

Acoustic microscopy was first suggested by Sokolov in 1949. He noted that the wavelength of sound in water at a frequency of 3 GHz was 0.5um, and he predicted the possibility of building an acoustic microscope with resolution comparable to that of the optical microscope. It was not until the early 1970s, when techniques for producing high frequency sound waves were readily available, that Sokolov's proposition was taken seriously.

In 1979, R.A. Lemons and C. Quate, PhDs at Stanford Univ.'s Dept. of Applied Physics & Engineering, described a scanning acoustic microscope. Currently, Leitz and Olympus manufacture a scanning acoustic microscope.

The desired micron resolution for histopathologic interpretation requires a very high frequency ultrasound beam that has a low penetration approximating 2 to 3 mm. Current imaging technologies combined with available needle and catheter techniques allow placement of a biopsy needle into almost any anatomic location with low patient risk. Thus, the acquisition avenue for in vivo tissue acoustic microscopy imaging is available; however, the integrated probe, signal transfer, and image processing for obtaining a tissue specific diagnosis are not currently under development. The invasive requirement, technologic miniaturization, and interdisciplinary requirements (radiology and pathology) have kept this concept from being widely supported. Additionally, industry has not identified this application as a high priority and is not supporting research in this area at the present time. Current utilization of acoustic microscopy is only in industrial product quality assurance areas.

Why should the "gold standard" of formaldehyde fixed and H&E stained tissue provide an examination superior to the physiologic in vivo state? Currently, ultrasound microscopy is achieving resolution on thin section tissue (6 micron) approximating that of the optical microscope. This resolution if achieved in vivo presents the potential of in vivo histopathologic diagnosis. A recent meeting of ultrasound basic scientists concluded that current ultrasound physics and technology are sufficiently understood to allow the development of a small caliber (18 gauge needle) transducer. This size transducer would make possible percutaneous placement into pathologic tissue. The Olympus acoustic microscope demonstrates acoustic microscopy is possible on thin section in vitro tissue specimens. This same group of scientists felt that signal transfer from the transducer to an image processor with time gaging and scanning of a high frequency ultrasound beam are possible within the present state of technology. The system when developed, integrated and evaluated should achieve in vivo acoustic microscopy.

"If these goals are achieved, it could have a major impact on surgery, radiology, and pathology," Antoine said. "I can see a broad use, such as with catheters and endoscopes. Our goal is to be able to make the final determination, benign or malignant, with this technology."

Robert Holden, who is working at NCI for a year under an IPA with Indiana Univ., said that breast examination is a good example of how the system would be used. "If we could go from seeing the mammogram to acoustic examination and determine if there is malignancy, that would be great. I don't feel that you can make a definitive decision, benign or malignant, from mammography."

"To make an in situ diagnosis does not turn me on," Board member James Cox said. "But to pursue at the biological level is something else."

Board member William Hryniuk asked if acoustic microscopy could reach the level of cytologic definition. Antoine said it could, "down to the level of intracellular definition."

Board member Paul Carbone was not impressed. "I don't see this getting us to where we want to go," he said. "Just look at a cell will not necessarily help."

"I'm concerned that we will just create another instrument the patient has to pay for," Niederhuber commented. "You will still need surgical or needle biopsy."

"The goal is to not need them," Antoine insisted.

"There is enough doubt expressed here to not commit $4 million," Mendelsohn said. "You need more R&D first."

"In the context of the millions we are spending on the drug screen [approved earlier in the board meeting, **The Cancer Letter,** Feb. 26], I would not want to throw this out," Cox said.

Board member Emil Frei commented, "If there is something to this, industry would be all over it."

"No, industry feels there is not a broad market for it," Holden said. "It needs a lot of basic research, biology, miniaturization. Industry is not able to handle that."

"I'm not against the proposal, it is exciting," Hryniuk said. "But we need to be sure there are no barriers that need to be overcome."

"I would like to see this focus more on the biology that can be studied with this instrument," Cox said.

William Hendee's motion that staff address the board's concerns at the June meeting was approved unanimously.

The board approved without dissent a request by UCLA for permission to exceed the limit of $6,500 per patient in its neutron therapy contract with DCT.

Robert Parker, chief of the Dept. of Radiology at UCLA, said, "I'm not an advocate of fast neutron treatment. I am an advocate of finding out if it is any damn good."

UCLA, Univ. of Washington, and M.D. Anderson are carrying out NCI sponsored clinical trials with fast neutrons. UCLA found that it could not possibly hold costs to $6,500 per patient, and in fact that the cost is closer to $15,000.

The additional money will come from unexpended 1989 money in the contract and funds already budgeted for this year.

RFAs Available

RFA OD-90-01

Title: Extramural research facilities construction projects
Letter of Intent Receipt Date: March 23
Application Receipt Date: May 7

The HHS Appropriations Act for FY 1990 states that the Secretary shall transfer $14.8 million from "appropriations available to each of the Institutes which shall be available for extramural facilities construction grants if authorized in law and if awarded competitively including such amount as he may deem appropriate for research animal production facilities." As stated, the appropriations are available for grant awards under current construction grant authority. Conference language accompanying the Act further states that such construction projects be "identified by the Director of NIH as being of urgent national importance." Subsequently, NIH is authorized to award a contract to "a public or nonprofit, private entity for constructing facilities for the purpose of the development and breeding of specialized strains of mice (including inbred and mutant mice) for use in biomedical research." NIH intends to award a grant for this purpose either under its existing authority or pursuant to an amendment of Public Law 101-190 to authorize a grant award.

Given the breadth of activities that may be appropriate for support in response to these Congressional actions, NIH is issuing two concurrent RFAs to solicit construction proposals. RFA OD-90-01 will be limited to applications for the construction of facilities for biomedical research and/or services to support such research (which may include an laboratory animal component). RFA OD-90-02 will be limited to applications for construction of a large scale, specialized, mouse production facility. The main objective of each is to facilitate the conduct of biomedical research by providing funds for construction of new facilities and for the purchase of fixed equipment essential for the operation of these facilities.

The purpose of this RFA is to invite grant applications for the construction of research/research support facilities.

Support may be requested for the construction of new facilities and additions or renovations to existing facilities to meet the biomedical research or biomedical research support needs of an institution, or of a research group at that institution or elsewhere that utilizes the resources of that institution. The purpose of the proposed facility must be within the scope of one of the statutes authorizing the awards. Those statutes authorize construction grants which would benefit the fields of cancer, vision and heart, lung and blood research. Associated fixed equipment necessary for operation of these facilities also may be requested as part of the application.

Any domestic non-Federal institution, organization or association which conducts or supports biomedical research is eligible to apply. Construction grant applications from non-Federal institutions, organizations or associations, previously submitted to and peer reviewed by NIH but which currently remain unfunded, will automatically be considered under this RFA without the submission of a new applications if they are responsive to the objectives described above. Up to $2 million of the $4.8 million available under this RFA has been identified for funding of the highest rated of the applications in this category. The remainder of these applications will be considered along with the applications submitted in response to this RFA. However, if the design or plans for construction differ markedly from that which was peer reviewed, a new application will be required. These applicants are strongly encouraged to request a copy of the complete RFA and special instructions for completion of the application to determine their need to submit additional assurances and certifications, as well as other information they may feel relevant to their proposal in relation to the RFA.

NIH staff will verify application and award eligibility. Those judged to be unresponsive or ineligible will be returned to the investigator.

The award mechanism will be the construction grant award. This one time solicitation based on the FY 1990 appropriation will make available $2.8 million for this initiative. Up to 75 percent of the allowable costs of a project may be provided, not to exceed $2.8 million. Prior to a grant award, the applicant must provide an assurance of the required matching funds and that other funds have been secured to meet any projected costs in excess of the award amount. Requests of less than $500,000 will not be accepted. No indirect costs or continuation costs will be awarded.

For additional information and a copy of the complete RFA and application materials, contact Kenneth Brow, Chief, Research Facilities Branch, Div. of Cancer Biology, Diagnosis & Centers, NCI, Executive Plaza North Rm 300, Bethesda, MD 20892, phone 301/496-8534.

RFA OD-90-02

Title: Construction of a mouse production facility
Letter of Intent Receipt Date: March 23
Application Receipt Date: May 7

The purpose of this RFA is to invite grant applications for the construction of a mouse production facility.

Support may be requested for the construction of new facilities and additions or renovations to existing facilities which will be dedicated to the breeding and production of specialized strains of mice, including inbred and mutant mice, necessary to meet the nation's needs in conducting biomedical research on a broad range of topics. Associated fixed equipment necessary for operation of these facilities also may be requested as part of the application.

Any domestic, non-Federal public or nonprofit private institution, organization or associations which conducts or supports biomedical research is eligible to apply. NIH staff will verify application and award eligibility. Those judged to be unresponsive or ineligible will be returned to the investigator. The award mechanism will be the construction grant award.

This one time solicitation based on the FY 1990 appropriation will make available $10 million for this initiative. Final amount to be determined based on the peer review evaluation. Up to 75 percent of the allowable costs of a project may be provided, not to exceed $10 million. Prior to a grant award, the applicant must provide an assurance of required matching funds and that other funds have been secured to meet any projected costs in excess of the award amount. Requests of less than $500,000 will not be accepted. No indirect costs or continuation costs will be awarded.

For additional information and a copy of the complete RFA and application materials, contact Kenneth Brow, Chief, Research Facilities Branch, Div. of Cancer Biology, Diagnosis & Centers, NCI, Executive Plaza North Rm 300, Bethesda, MD 20892, phone 301/496-8534.

RFA 90-CA-09

Title: New approaches to understanding transformation by SV40 virus, polyomaviruses and adenoviruses
Letter of Intent Receipt Date: June 15
Application Receipt Date: Aug. 24

The goal of this RFA is to stimulate research leading to an understanding of SV40, polyomavirus and adenovirus transformation of cells in terms of the cellular processes which are altered by viral oncoproteins. The scope of this RFA includes studies of SV40, polyomaviruses (including BK virus and JC virus) and adenoviruses. Functional studies of viral oncoprotein-cellular protein complexes will be encouraged. Studies on the Rb, p53 and c-src interactions with oncoproteins should not be the focus of the proposed studies since they are already being studied extensively. Where appropriate, some experiments dealing with these cellular proteins may be included for comparisons or to extend mechanistic ideas involving several cellular proteins.

Examples of the research objectives that may be supported under this RFA are: 1) investigations of the impact of viral oncoprotein/cellular protein complexes on elements of cellular regulation related to transformation such as, but not limited to, second messenger regulation, cell cycle control, transactivation of cellular protein synthesis and alteration of plasma membrane properties; 2) development and application of new approaches to understand the regulatory activities of pertinent cellular proteins and second messenger molecules and assessment of the role of these processes in cellular transformation; 3) functional and structural characterization of cellular proteins that bind to viral oncoproteins; 4) development and application of new techniques and reagents to identify and characterize additional cellular proteins that bind to viral oncoproteins.

Where appropriate, collaborative arrangements to facilitate the achievement of research goals should be considered.

This RFA will use the traditional NIH research project grant (RO1). Responsibility for the planning, direction and execution of the proposed project will be solely that of the applicant.

Approximately $750,000 in total costs per year for five years will be committed to specifically fund applications which are submitted in response to this RFA. The funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. The total project period for applications submitted should not exceed five years. The earliest feasible start date for the initial awards will be April 1, 1991. Although this program is provided for in the financial plans of NCI, award of grants is contingent upon the availability of funds. Nonprofit and for profit institutions, foreign and domestic, are eligible to apply.

This RFA is a one time solicitation. Generally, future unsolicited completing renewal applications will compete as research project applications with all other investigator initiated applications and be reviewed in a standing Div. of Research Grants study section. However, should NCI determine that there is a sufficient continuing program need, NCI may announce a request for renewal applications.

Inquiries concerning the objectives and scope of this RFA are encouraged and should be directed to Dr. Susan Spring, Program Director, DNA Virus Studies I, Biological Carcinogenesis Branch, Div. of Cancer Etiology, NCI, Executive Plaza North, Rm 540, Bethesda, MD 20892, phone 301/496-4533.