THE CANCER LETTER

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Congress Agrees On $1.989 Bil. FY92 NCI Budget, But Most Of Increase Not Available Till 1993

Congressional budget negotiators last week agreed on a Labor, HHS, Education Appropriations bill that gives NCI a $1.989 billion budget for fiscal year 1992, a 16 percent increase over the FY 1991 operating level of $1.713 billion. On the face of it, the $276 million increase is the largest for the Institute since 1976 and represents a major step in restoring NCI's budget to its pre-Reagan era level as measured in constant dollars. There is one important caveat: most of the increase,

(Continued to page 2)

In Brief

Donaldson, Wilson Lead ASTRO; Thomas To Hear Arguments In Cigarette Case; Doll, Peto Honored

SARAH DONALDSON, Stanford Univ., assumed the presidency of the American Society for Therapeutic Radiology & Oncology following the group's annual meeting this week in Washington. President-elect is **Frank Wilson.** Other officers for 1991-92 are **Rodney Million**, last year's president, became chairman of the Board of Chancellors; **Lester Peters** is secretary; and **David Hussey** is treasurer. ASTRO also gave gold medals, its highest honor to: **Rodney Withers,** UCLA, and **Seymour Levitt,** Univ. of Minnesota. . . . **CLARENCE THOMAS,** new Supreme Court justice, will cast the deciding vote in a case involving health warnings on cigarette labels sometime next year. The Court recently announced it will hear new arguements in the case, Cipollone v. Liggett Group Inc., to help it decide whether cigarette manufacturers may be sued for allegedly misrepresenting the dangers to smokers. The new arguments will be heard in January. The scheduling of new arguments suggested that the court was deadlocked 4-4 over the case. . . . **META-ANALYSIS** for randomized control trials will receive some attention with the award of a new prize worth about $700,000 to the two pioneers in the field, **Richard Peto** and **Richard Doll** both of Oxford Univ. The two will receive the Helmut Horten Research Award of one million Swiss francs later this month. Martin Spiess of Univ. of Basel also will receive a 400,000-franc incentive prize for research on biochemistry of cell membranes. . . . **AMERICAN NURSES** Assn. will move its headquarters from Kansas City to Washington, D.C., next March. The group currently has three small offices in D.C. which will be combined with the headquarters, to be located at 600 Maryland Ave. SW. ANA and its nonprofit arm American Nurses Foundation employ 190 people and have an operating budget of $17 million. About 80 percent of the staff opted not to move from Kansas City and will be replaced.

NCI FY92 Budget Nearly $2 Billion, Largest Single Increase Since 1976

(Continued from page 1)

$223.4 million, will not become available until the last day of the fiscal year. The Institute will be able to obligate the money, but it will not come out of the Treasury until 1993.

However, it remains to be seen whether the Administration will subtract the forward funding from its request for NCI's FY93 budget, an action that would negate the gains made.

Whatever happens in FY93, this year's budget negotiations came down to a battle over the principle of restoring NCI's purchasing power that it lost due to stingy budgets in decade of the 1980s.

Congressional testimony by cancer program advocates, especially by the National Coalition for Cancer Research and its member organizations, combined with recognition of the twentieth anniversary of the National Cancer Act of 1971, convinced individual congressmen of the need to restore NCI's budget to the level equivalent in constant dollars to its 1980 budget.

NCI's bypass budget requested a total of $2.6 billion for FY92. The Coalition asked Congress to at least give the Institute a minimum increase of $200 million above the President's 1992 request of $1.81 billion, to return the purchasing power of the Institute to its 1980 level.

Sen. Fritz Hollings (D-SC) introduced an amendment to the Senate appropriations bill that would give NCI a $185 million increase over the President's request. The "Hollings amendment," as it became known, was debated each week for the three weeks of the House-Senate budget conference, according to a source who followed the process.

Many members of the conference committee complained that NCI already has the largest budget of any of the other institutes in NIH. Others thought the best science, rather than research on specific diseases, should be funded.

Throughout the debate, Hollings refused to back down despite attempts to kill the measure, though he reduced the amount of the increase to $160 million. There was also an attempt to give the money to the NIH director for cancer and other life-threatening diseases. Hollings fought for changes in wording to that statement, and the issue finally came to a vote. In the end, the amendment provides $160 million to NCI which cannot be spent until Sept. 30, 1992, and which the NIH director can transfer to other institutes "as she deems appropriate for research directly relating to the prevention, treatment or cure of cancer."

The $160 million is included in the total $223.4 million in delayed funding.

Congressmen who supported Hollings were Slade Gorton (R-WA), Tom Harkin (D-IA) and Brock Adams (D-WA). On the House side, Rep. Joe Early (D-MA) was NCI's main advocate, sources said.

"I'm delighted we were able to secure such unprecedented funding for cancer research, but the numbers pale in comparison with the number of lives that will be saved by stepping up our research efforts in this critical area," Hollings said in a press release last week. "Cancer Institute funding has been slipping. Each year since 1977, the Cancer Institute has fallen behind the increases given to other medical research institutes and 10 cancer centers [have lost their center core grants]. With the adoption of my amendment, we have turned this downward trend around and will regain our leadership in cancer research."

Albert Owen, chairman of the National Coalition for Cancer Research, said, "This increase has been a long time in coming. Sen. Hollings' dedication to make cancer research a national priority has brought hope to many Americans."

The Labor, HHS, Education appropriations bill was the last domestic bill to come out of the conference committee. There still is the possibility that the President will veto the bill, however. The Bush Administration has objected to a provision that would permit health workers to discuss abortion with patients at federally-funded clinics. The bill also contains a total of $4 billion worth of "prefunding," or money appropriated but not authorized for spending until the next fiscal year. It is not clear what the White House reaction to the prefunding will be.

THE CANCER LETTER

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NCI FY 1992 Budget Development

1991 Operating Level	$1.713 bil.
1992 President's Budget	$1.81 bil.
House Mark	$1.83 bil.
Senate Mark	$2.01 bil.
Conference Agreement	$1.989 bil.

▸$223 mil. of conference amount will not become available to NCI until Sept. 30, 1992. Of that, the NIH director may transfer $160 million to other institutes for research directly relating to prevention, treatment or cure of cancer.

NIH Discusses Plans For Women's Health Study In Public Hearing

NIH officials took the unprecedented step last week of soliciting public comment on the proposed plan for the Women's Health Initiative, a massive, three-pronged program to study cancers and other major causes of morbidity and mortality in older women.

The initiative, announced in May by NIH Director Bernadine Healy, consists of three arms: three interlocking clinical trials of dietary interventions and hormone replacement therapy, an observational study, and a community-based trial to promote healthy behaviors.

The studies are designed to produce information that will fill gaps in knowledge about the effects of certain interventions on cardiovascular disease, breast and colon cancer, osteoporotic fractures, and diabetes.

"Women need not just a longer life but a healthier life," Healy told representatives from dozens of groups who attended the public hearing. "The scientific and medical point of view is that the time has come to close vast knowledge gaps about women, especially postmenopausal women."

The initiative calls for enrollment of a total of 160,000 women between the ages of 45 and 79, nearly one percent of all age-eligible women in the U.S. Studies would continue for up to nine years. "Our success depends on our ability to muster volunteers," Healy said. "It will be even more of a challenge to get women of different races, ethnic groups, and women underserved by the health care system."

Each year in the U.S., 500,000 women, most of whom are postmenopausal, die from cardiovascular disease, according to a synopsis of the initiative. In 1991, an estimated 175,000 women will be diagnosed with breast cancer, and 44,500 will die from the disease. Another 78,500 women will be diagnosed with colorectal cancer, and 31,000 will die from it.

Osteoporotic bone fractures are a major cause of morbidity and loss of mobility for women: after age 50, women have a 12 to 15 percent chance of being hospitalized with a hip fracture at some point.

William Harlan, NIH associate director of disease prevention and director of the initiative, said "there is a paucity of research on conditions and treatments unique to or of greater interest to women."

Although medical experts have recommended female hormone therapy and changes in diet to prevent these problems, few studies actually document the effect of diet on breast and colorectal cancer in women, or the efficacy of hormone replacement therapy in preventing coronary heart disease, stroke, and osteoporosis, Harlan said.

In addition, he said, "there is too little longitudinal data on predictors or markers of disease development in women. And everyone recognizes that a significant gap exists between the established value of healthy behaviors and the adoption of these behaviors by women; this is especially true among minorities and the medically underserved population."

Harlan said the medical community needs to measure all the benefits and risks of each intervention. Hormone replacement therapy, in particular, may decrease the risk of cardiovascular disease for postmenopausal women, but may increase their risk of breast or endometrial cancer.

"This means that the studies should be large enough and of sufficient duration to provide this benefit and risk data, and to the extent possible, give use the opportunity to look at particular risk subgroups," such as women with a family history of the diseases in questions, Harlan said.

In order to ensure that the findings of this massive undertaking are applicable to all women, he added, researchers must make an extra effort to include minorities and those normally underserved by the nation's health care system in the study populations.

Scientific staff from 10 institutes of NIH have worked on the plan for the initiative, which will be coordinated by the Office of Disease Prevention and the Office of Research on Women's Health, both of which operate under the Office of the Director.

The initiative will be funded through a contract mechanism; NIH officials expect to develop the final version of the initiative in the next few months and issue a series of requests for proposals for each facet of the initiative in 1992.

NIH is prepared to spend up to $500 million on the

study over 10 years. Healy said up to $25 million had been set aside for 1992 funding for the initiative.

Clinical Trials

In three interlocking clinical trials researchers at 50 clinical sites will assess whether hormone replacement therapy, a low-fat diet, and calcium and vitamin D supplements can reduce the incidence of certain cancers, cardiovascular disease, and osteoporosis in a total population of 70,000 postmenopausal women between the ages of 50 and 79.

Most of the women will be involved in at least two of the three intervention arms. A subset of women from both the control and intervention groups in the dietary study will also be randomized to one of the three arms in the hormone replacement study, and almost all women will be randomized to the control or treatment arm of the calcium/vitamin D portion.

Because some of the interventions assessed in the trial, especially the hormonal replacement therapy, can have some positive and some negative health effects, the trials will measure both, said NHLBI scientist Jacques Rossouw. However, at this point, he said, researchers believe that "for all the treatments the benefits exceed the risks."

The trial of hormone replacement therapy consists of three arms enrolling a total of 30,000 postmenopausal women between the ages of 50 and 79. For the six-year treatment period, 9,000 women will receive estrogen replacement therapy, 9,000 will receive estrogen-progesterone replacement, and 12,000 will receive a placebo.

Researchers will attempt to determine whether hormonal therapy reduces the incidence of cardiovascular disease, reduces the incidence of osteoporotic fractures, or increases the risk of breast or endometrial cancer.

Women with a history of breast cancer and endometrial cancer are excluded from all portions of the clinical trials. Elizabeth Travis, a professor in the experimental radiotherapy department at M.D. Anderson Cancer Center, questioned the exclusion of such women from the hormone therapy trial.

Travis pointed out that no controlled studies have assessed the risks and benefits of estrogen replacement therapy in women who have had these malignancies and have entered menopause prematurely as a result of systemic chemotherapy or abdominal irradiation.

She suggested that "because of the real potential for benefit by postmenopausal administration of estrogen and because of the lack of any available data regarding estrogen use in this setting, we suggest a prospective, randomized, controlled trial in the use of estrogen replacement therapy for women with a background of breast cancer who developed amenorrhea as a result of successful antineoplastic therapy."

In the dietary modification trial, 24,000 women will follow diets low in fat and high in fiber, fruits, vegetables, and complex carbohydrates for nine years; another 36,000 women will serve as a control group. The primary aim of this trial is to assess whether a low-fat diet reduces breast and colorectal cancer; it will also test whether this diet can reduce the incidence of coronary heart disease and diabetes mellitus.

The Women's Health Initiative marks one of the first attempts to assess the link between dietary fat and the development of certain cancers in a clinical study, said NCI Div. of Cancer Prevention & Control Director Peter Greenwald. "The most comprehensive reviews that we have to date suggest that roughly a third of all cancer is related to diet," he said.

He noted that a barrage of laboratory, epidemiological, and mechanistic studies in the area all pointed to a link between diet and breast cancer.

"Most of the evidence on dietary fat pertains to the 80 percent of breast cancer that occurs in women over 50," or mostly postmenopausal women. It is not clear, he said, whether these findings also pertain to premenopausal women.

In certain epidemiological studies, women on a high-fat diet had 1.6 times the level of colorectal cancer as those with a low-fat diet, Greenwald said.

Kay Dickersin, an epidemiologist at the Univ. of Maryland School of Medicine and member of the Breast Cancer Coalition, criticized the plan to exclude women with breast cancer from participation in the dietary intervention trial and outlined reasons in favor of their inclusion.

"First, women with breast cancer can be considered a high risk group because they are at high risk of reaching trial endpoints, that is recurrence and mortality," Dickersin said. In addition, "we assume that the theoretical underpinnings of the trial are to test a promoter rather than initiator role for diet in carcinogenesis. There is no reason to assume that promoter activity, such as that hypothesized for dietary fat, is limited to women who have not yet been diagnosed with breast cancer."

In the calcium/Vitamin D trial, 30,000 women will receive calcium and vitamin D for nine years, and another 30,000 will receive a placebo. Investigators will assess whether the supplements reduce the incidence of fractures and colorectal cancer.

Travis said that although earlier studies have indicated that "estrogen development can reduce or

prevent trabecular bone loss and the development of osteoporosis" none had shown that "calcium supplementation, exercise, and fluoride administration have been of benefit."

Observational data do indicate that women with higher calcium intake have denser bones and fewer fractures, Rossouw said, but only one small trial has indicated a reduction in fractures.

Because the women documented in observational studies who take calcium and vitamin D may be those who are more health conscious and therefore healthier to begin with, said Rossouw, a randomized, placebo controlled trial was necessary.

Beverly Zakarian, president of the Cancer Patients Action Alliance, expressed concerns about the general structure of all the trials. She noted that although the information to be gained from these trials would be significant, because "the earliest results of trials would not be forthcoming for nearly a decade, I would like to urge that some time be saved and additional information be gleaned by modifying the trials."

Zakarian first suggested that NIH eliminate placebo or "no intervention" groups from the trials and instead use historical controls as a basis for comparison.

"We know what happens in a control population: that's why we're here to talk about these protocols," she said. "Time is of the essence for each individual woman sitting here. There is no sense of urgency in this trial design."

But some NIH officials at the meeting stressed that because few clinical trials had been conducted on the link between diet and certain cancers in women, the medical community needed large, definitive clinical trials in which participants were randomly assigned to either the intervention or control arm.

In addition, Zakarian said, "although we are all interested in the late-emerging effects of diet, hormonal and environmental influences" on the diseases targeted by the initiative, "I fear that manifestation of disease is the delayed result of earlier effects. I suggest that a parallel study follow a younger group of women. It could offer critically needed insight into the causative factors of our fatal diseases."

Observational Study

The initiative will include a major observational study of women between the ages of 50 and 79. "There's a general recognition that there are too few mature women studied longitudinally," said Joan McGowan, a scientist from the National Institute of Arthritis and Musculoskeletal Diseases.

The observational study will serve two major goals: it will provide epidemiological data on a large group of women--data that may allow researchers to identify risk factors for the major diseases affecting older women. In addition, investigators will also identify biological markers of those diseases.

The observational study and the clinical trials "go hand in glove," said Salim Yusef, a scientist with the National Heart, Lung and Blood Institute. The same 50 clinical centers that conduct the clinical trials will enroll women excluded from or unwilling to participate in those trials into the observational study.

The observational study will take nine years and include 70,000 women; data on the 33,000 women in the control groups of the clinical trials will also be analyzed for the observational component.

Using questionnaires, physical examinations and laboratory tests, investigators for the observational study will develop risk factor analyses for cardiovascular disease, cancer, and osteoporosis. They will also track the incidence of deaths and hospital admissions for these diseases, as well as for strokes.

In addition, researchers will use the case-control approach to study the link between subclinical markers and clinical disease. In a subgroup of the enrolled women, investigators will document the physiological changes related to menopause.

Community Trial

The community trial is the first community-based collaborative study to evaluate how to get women to adopt a variety of health behaviors to reduce the risk of several major chronic diseases.

"The community trial will evaluate particular already known preventive regimens, will find out how to use what it is we already know will work," said Edward Sondik, deputy director of NCI's Div. of Cancer Prevention & Control. According to 1988 estimates, the diseases that are the focus of the trial represent 65 percent of all causes of mortality for women older than 45, Sondik said.

The five-year trial will involve 20 intervention sites and 20 control sites, with 500 women between age 45 and 75 at each site. Only communities with at least 30 percent minority or medically underserved women in the population will be included.

Investigators at the intervention sites will counsel women on adopting healthy behaviors, including: quitting smoking; changing fat, fiber, and calcium intake; increasing physical activity and maintaining a desirable weight. Women will be encouraged to undergo screening for breast and cervical cancer, and risk factors related to cardiovascular disease.

The trial must include control groups, said NIH officials, because the success of interventions can be evaluated only if contrasted with results of the sociological trends toward better health.

DCT Advisors OK Grant Program For Clinical Hematologic Studies

Advisors to NCI's Div. of Cancer Treatment gave concept approval to two new grant programs worth $2.4 million in first year costs, including another in a recent series of programs designed to increase opportunities for clinical investigators.

DCT's Board of Scientific Counselors agreed to set aside $2 million to fund 15 to 20 grants for clinical correlative studies in hematologic malignancies. The program would be similar to an RFA concept approved at the board's spring meeting on clinical correlative studies in solid tumors.

Another proposed RFA to set aside $800,000 for studies in imaging guided stereotactic tissue diagnosis for breast cancer was voted down. Board members indicated they did not think the concept merited set-aside funds; investigators interested in these studies could apply for regular research project grants.

A proposed program announcement on frameless stereotaxy for imaging guided stereotactic tissue diagnosis and tumor treatment also was not approved. The board asked NCI staff to revise the concept for consideration at a future meeting.

Following are the approved concept statements:

Clinical Correlative Studies in Hematologic Malignancies. New proposed RFA for cooperative agreements, $2 million proposed first year award, 15 to 20 awards, three years (board gave approval to extend to four years; this requires NCI Executive Committee approval). Applications would be reviewed by the CCIRC study section with supplementation of other experts.

This RFA is designed to promote collaborations and interactions between basic researchers and clinical investigators to advance research on clinical correlations that can improve therapeutic approaches. NCI is seeking to encourage correlative laboratory studies linked to large scale clinical trials. In many instances the laboratory investigators are already recipients of R01 or P01 support for their basic research. Likewise, many clinical investigators are supported through the CTCG mechanism (U01) for clinical research. This initiative proposes to link these peer approved activities and for a relatively small additional investment provide a mechanism to obtain definitive data on the relationship of biological features and the clinical behavior of the tumors.

Objective and approaches will be investigator-initiated, with participants funded via cooperative agreements. Several levels of coordination are anticipated. NCI staff will be involved in a coordinating committee that will set priorities for the most effective use of available specimens. By combining several studies to answer several questions at the same time, an economy of scale not possible with individual studies will be achieved. The Cancer Diagnosis Branch (DB) has been working closely with CTEP, under the aegis of the NCI Diagnosis Decision and Implementation Committee (DDIC), to assure that promising new approaches will be moved more rapidly into clinical practice. The charge to DDIC, created in 1989, is to identify assays ready for evaluation and to set priorities for large-scale clinical evaluations. The role of DDIC in the proposed cooperative agreements will be to assist in coordination of studies and to provide information regarding NCI priorities.

CTEP and CDB are seeking applications for research grants (U01) concerned with clinical correlative studies relevant to cancer treatment of clinical outcome in patients with hematologic malignancies. Hematologic malignancies that are relevant to this RFA include leukemias, lymphomas, myelomas, and myelodysplastic syndrome. The rarer forms of hematologic malignancies such as APL and myeloma will have priority. The therapeutic correlates must have a potential clinical application such as development of new treatment strategies or identification of patient subsets for specific treatment approaches. The laboratory assays must utilize tumor specimens from patients receiving defined treatments in large-scale multi-institutional clinical trials. These assays must have already been demonstrated to be applicable to tissue samples and/or body fluids. In order to obtain statistically valid data, applications are limited to investigators who have access to appropriate numbers of tumor specimens. All investigators are encouraged to work with multicenter organization in order to access statistically meaningful numbers of patients and adequate clinical information.

Some examples of therapeutic laboratory correlated studies may include but are not limited to: (1) phenotypic or genotypic alterations which appear to correlated with the development of therapy resistance; (2) loss or inactivation of tumor suppressor genes related to prognosis; (3) studies of chromosomal rearrangements or deletions that may be sued as prognostic indicators; (4) correlation of growth factor production or oncogene expression with response to therapies; (5) characterization of tumor-associated antigens that may lead to new immunotherapies; (6) evaluation of use of serum or tumor markers that correlate with disease progression; (7) analyses of expression of cellular receptors for growth factors or differentiating agents; (8) defining and targeting specific populations of cells for therapy; and (9) analysis of in vitro response of tumor cells to growth factors/differentiating agents.

Michael Friedman, director of the Cancer Therapy Evaluation Program, said this RFA is designed for the clinical cooperative groups and cancer centers. "Groups have no access to new money; their budgets are fixed," and may not have the resources to do these kinds of studies translating laboratory findings to the clinic. "These are not going to be easy grants to submit, or fund," he cautioned. "Applicants are going to have to demonstrate incredible lab skills and incredible clinical skills--the difference is, people will be paid to do it."

Board member David Martin objected to the term "correlative" in the concept's title. He said more appropriate would be "testing hypotheses."

The concept was approved unanimously.

International Cooperative Biodiversity Groups. New proposed RFA for cooperative agreements, $400,000 first year award, five years beginning in FY 1993. A workshop on Drug Development, Biological Diversity, and Economic Growth, held on March 13-14, 1991, was sponsored by the U.S. Agency for International Development, the National Science Foundation, the Fogarty International Center, and NCI in order to explore how these agencies might develop joint programs to help strengthen global efforts to protect biological and cultural diversity and thereby

assure a continuing supply of potential pharmaceutical products from natural products. Following the workshop, the agencies met and formulated plans for such a joint effort, utilizing as a prototype the National Cooperative Drug Discovery Group concept.

Tropical rainforests, found almost exclusively in developing countries, cover only a small percentage of the earth's surface, but are thought to contain at least one-half of all plant and animal species. As advances in technology expand our ability to exploit new discoveries more effectively, the raw material is being lost. Deforestation is proceeding at an alarming rate, resulting in the loss of species at rates far greater than background extinction.

The underlying causes of biodiversity loss are many and complex and involve interwoven social, economic, and political elements. In developing countries struggling to meet basic human needs, efforts to protect biological diversity will succeed only if implemented in the context of promoting economic growth.

It is proposed that cooperative agreements be established to form International Cooperative Biodiversity Groups (ICBGs) to promote biodiversity conservation, drug development, and economic growth. USAID, NSF, and the Fogarty International Center are cosponsoring this initiative; other agencies and institutes within NIH have been asked to participate as well.

This proposed RFA is designed to support broadly based, international interdisciplinary projects to meet the missions and objectives of each of the sponsoring agencies in four general areas: (1) collaboration in the discovery and development of drugs for diseases of concern to both developed and developing countries, (2) development of inventories of native species and indigenous knowledge, (3) training directed toward the needs of the individual country, and (4) improvements in the scientific infrastructure within the host country.

Each of the sponsoring agencies would fund those aspects relevant to its own mission. NCI would support anticancer drug discovery and development efforts, as well as possibly some of the training activities.

Each ICBG will be assembled by a principal investigator who will form the multidisciplinary and multi-institutional consortium of skills needed. Specialized components required in the ICBG could include, but would not be limited to, economists, sociologists, ecologists, ethnobiologists, medical chemists, pharmacologists, and a foreign government representative. The PI will be the conceptual focus of the ICBG and will organize the appropriate ICGB components regardless of their institutional or geographic location. ICBG components from the developing country as well as from the U.S. are encouraged.

Successfully competing ICBGs will be funded as cooperative agreements. The involvement of government staff may include assistance in research planning; suggestion of specific studies within the project scope; provision of information not otherwise available to the group; and participation in the design of experiments and analysis of results. Specifically for NCI, this relationship could also involve the provision of contract-generated resources. However, the applying group is expected to define its objectives in accord with its own interests and goals.

Board member Philip Crews said he collaborated with scientists in developing countries, but was not able to provide them support. This RFA would allow those scientists "to begin to do research" in parallel with colleagues in the U.S. In the long run, the money spent would pay off. "If we don't do this, then down the line we could be shut out of these countries because of no collaboration opportunities," he said.

Board member JoAnne Stubbe said the proposal contains "a huge amount of bureaucracy at the top," and does not address the fact that a major health problem in developing countries is not cancer but parasitic diseases.

The board approved the concept, with Stubbe opposed.

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.

Master Agreement Announcement (MAA) NCI-CM-27730-28
Title: Master agreement for chemical synthesis
Deadline: Approximately Nov. 15

The Drug Synthesis & Chemistry Branch, Developmental Therapeutics Program in NCI's Div. of Cancer Treatment is interested in proposals from, and establishing master agreements with offerors who have the capability to provide services for the synthesis of a variety of organic/inorganic compounds. This is a recompetition; current MA holders are Univ. of Alabama, H.G. Pars Pharmaceutical Laboratories, Research Triangle Institute, Ricera Inc., Southern Research Institute, Starks Associates, SRI International, and the Dept. of Scientific & Industrial Research.

Agreements negotiated as a result of this solicitation will be awarded for a five year period beginning Sept. 30, 1992.

The objective of this project is the resynthesis of known compounds of varying degrees of complexity for confirmatory testing, the synthesis of unique compounds with reported biologic activity, the resynthesis of compounds identified by in vitro anti cancer and anti-AIDS screens as candidates for secondary testing, and the synthesis of unique compounds in support of the NCI intramural program.

Contract Specialist: Carolyn Barker
RCB Executive Plaza South Rm 603
301/496-8620

RFP NCI-CM-27726-72
Title: Pathology and veterinary support for preclinical toxicology studies
Deadline: Dec. 15

The Developmental Therapeutics Program of NCI's Div. of Cancer Treatment seeks an organization to perform a variety of pathology and veterinary services to support the DTP preclinical toxicology program for anticancer and anti-AIDS drug development. Organizations must have the facilities and staff to carry out these efforts and the management expertise to respond to the diverse needs of this contract. As a minimum requirement, organizations must comply with the FDA current Good Laboratory Practice Regulations.

One contract will be awarded and will be administered on a task managed basis. Task orders will be issued under the funded cost reimbursement level of effort contract resulting from this solicitation. Specific task orders to be issued will involve: 1)

operation of a repository to hold the pathology materials generated in toxicology studies, 2) performance of an independent verification (quality assessment) of the pathological findings by the study pathologist, especially with respect to drug relatedness, nomenclature, and slide quality, 3) provision of a pathology support program to prepare blocks and slides and conduct histopathological evaluation of tissues, and conduct site visits to perform necropsies, slide preparation, or to assist the project office in project evaluation, 4) storage, maintenance, and shipment of government infusion equipment to other DTP contractors, 5) development and implementation of new surgical or other procedures for drug administration, instruction in these procedures, and performance of these procedures in actual animal studies, and 6) performance of site visits to the DTP toxicology contractor laboratories to evaluate animal care programs or to investigate animal care problems.

The principal investigator must be a board certified veterinary pathologist or veterinarian with at least three years experience with similar programs. This is a small business set aside.

Contract Specialist: Jacqueline Ballard
RCB Executive Plaza South Rm 603
301/496-8620

RFP NCI-CN-25403-41

Title: Surveillance, Epidemiology & End Results Expansion

Deadline: Approximately Dec. 2

NCI's Div. of Cancer Prevention & Control is soliciting proposals for an expansion of the SEER program. The thrust of this project is to 1) obtain within the geographic area of coverage, data on all newly diagnosed cases of cancer beginning Jan. 1, 1991 forward, 2) obtain cancer patient survival data on all cases diagnosed in 1991 forward, 3) monitor trends in the incidence of specific forms of cancer, particularly with respect to demographic and social characteristics of the populations, and 4) assess the completeness and accuracy of all data collected. It is anticipated that offerors must provide documentation of authority to collect data for their identified coverage area and be required to have a hispanic population of at least 300,000 in their coverage area.

Contracting Officer: Susan Hoffman
RCB Executive Plaza South Rm 635
301/496-8603

RFP NCI-CM-2772972

Title: Preclinical toxicology and pharmacology of drugs developed for cancer, AIDS and AIDS related illnesses (small business)

Deadline: Dec. 30

NCI's Developmental Therapeutics Program is seeking organizations to carry out pharmacology and toxicology studies, the data from which must be suitable for filing with the FDA as part of Investigational New Drug applications. Organizations must have the facilities and staff to carry out such studies and the management expertise to analyze and evaluate the data. As a minimum mandatory requirement, the contractor must perform all toxicology studies in accord with the FDA Good Laboratory Practice Regulations. Organizations must also indicate their willingness to sign a confidentiality of information statement. One contract will be awarded and administered on a task managed basis. Task orders will be issued under the funded cost reimbursement level of effort contract.

Assignments are estimated to involve two to four chemical agents annually per contract. Offerors are required to propose at both levels of effort (46,875 and 93,750 hours over a five year period). The objectives of the task orders to be issued are 1) validation of analytical methodology to quantitate drug plasma level in laboratory animals and to measure levels in rodents and dogs treated with the agent under study, 2) determination of bioavailability of drugs after parenteral and/or oral administration, if efficacious drug levels can be attained in plasma in vivo, and if the drug crosses the blood-brain barrier (AIDS drugs), 3) assessment of acute and subacute toxicity in rodents and dogs including determination of a maximum tolerated dose, of dose limiting toxicities, schedule dependent toxicity, or the reversibility of adverse effects and of a safe clinical starting dose, 4) the use of pharmacokinetic information to permit extrapolation of toxic effects across species by relating plasma drug levels to the time of appearance and severity of toxicity and to establish the safety of potentially efficacious doses.

The principal investigator must have a doctoral degree in pharmacology/toxicology plus at least three years experience in directing, implementing, and evaluating drug toxicity studies in experimental animals. The pathologist and analytical chemist must likewise have credentials that illustrate their competence and accomplishments in serving as critical team members in the conduct of such studies. This is a small business set aside. This effort is currently performed by Springborn Life Sciences Inc.

Contract Specialist: Jacqueline Ballard
RCB Executive Plaza South Rm 603
301/496-8620

RFA Available

RFA CA-92-01

Title: Clinical trials of cancer therapy with biological response modifiers

Letter of Intent Receipt Date: Nov. 20

Application Receipt Date: Jan. 22

The Biological Response Modifiers Program in NCI's Div. of Cancer Treatment announces an RFA to establish cooperative agreements for clinical trials of cancer therapy with BRMs. These cooperative agreements are designed to foster innovative clinical trials of BRMs by peer reviewed groups of highly experienced clinical and preclinical investigators. The "Research Goals and Scope" of this RFA will require a novel plan for early clinical development of a given new agent or agents, adequately supported by the applicant's own prior preclinical and, if available, clinical results. The application must describe how its objectives are in accord with the applicant's own interests and experience. The applicant must provide evidence of access to the agents proposed for study. A detailed protocol for an initial clinical trial must also be included. NCI will facilitate the institution of a peer reviewed, investigator initiated trial.

Each study group will be composed of a principal investigator, one or more laboratory programs, each headed by a program leader with the demonstrated expertise to design and carry out assays for the appropriate monitoring of patients on the study, one or more clinical programs, each headed by a program leader with demonstrated expertise in conducting clinical trials of BRMs, and the NCI program director. The application may include investigators from one or more academic, nonprofit, and/or commercial institutions. This RFA may provide an opportunity to develop agents identified in National Cooperative Drug Discovery Groups, program projects, or individual research grants.

Academic, nonprofit, for profit institutions, domestic and foreign, and governments and their agencies are eligible to apply.

Applicants may request no more than four years of support. The earliest possible starting date will be July 1, 1992. NCI plans to make up to five awards for periods of up to four years, and has set aside $1 million total costs for the initial year funding.

Copies of the complete RFA are available from Dr. Jon Holmlund, program director, Biological Resources Branch, Biological Response Modifiers Program, NCI, Bldg. 1052 Rm 253, Frederick, MD 21702-1201, phone 301/846-1098; fax 301/846-5429.