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FY 1990 Bypass Budget Of $2.345 Billion Approved By NCAB; Hammer's Effort Makes That Possible

The National Cancer Advisory Board last week approved a 1990 fiscal year bypass budget for NCI of $2.345 billion which, if Armand Hammer's ambitious matching fund challenge to Congress and the country succeeds, could be the first in nearly a decade to be close to what the Institute actually

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In Brief

Gallo, Montagnier, Four Others Share Japan Prize; RPMI, First Cancer Center, 90 Years Old

JAPAN PRIZE for 1988 was awarded to six scientists selected by the Science & Technology Foundation of Japan. Winners were Robert Gallo and Luc Montagnier, recognized for their research on AIDS; American virologist Donald Henderson, Iasao Arita of Japan and Frank Fenner of Australia, for their efforts in the eradication of smallpox; and Georges Vendryes of France, honored for his work in establishing fast breeder reactor technology. Vendryes was the sole winner in the energy technology category and received a cash award of 50 million yen (about $400,000); the others divided 50 million yen equally. . . . **ROSWELL PARK** Memorial Institute is observing its 90th anniversary this year as the world's first cancer center. It was founded in 1898 by Roswell Park, an internationally known surgeon who believed that the only way to conquer cancer was through organized research with the full resources that an institution can provide. Park and newspaper publisher Edward Butler persuaded the New York state government to establish a cancer research center asociated with the Univ. of Buffalo. Park, the first director, died in 1914. Thomas Tomasi is the eighth director. The May issue of "Cancer Research" featured RPMI and included a history of the institute written by Edwin Mirand, dean of the graduate school. . . . **ANOTHER WELL** known center has a new name. The former Univ. of Texas System Cancer Center/M.D. Anderson Hospital & Tumor Institute is now the Univ. of Texas M.D. Anderson Cancer Center. President Charles LeMaistre said "even our own employees have struggled to master an exceptionally complicated name. I think this (new) name will serve us very well in the years ahead". . . . **ROSE KUSHNER**, author, journalist, former member of the National Cancer Advisory Board and national patient rights activist, has received the American Cancer Society D.C. Div. Courage Award.

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Bypass Budget Would Fund 50 Percent Of Competing Grants, Add 10 Centers

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receives. NCI's appropriations have been running about a half billion dollars behind the bypass budget.

Hammer has initiated a campaign to raise $500 million from the private sector if Congress will match it with funds over and above NCI's regular appropriation. He has obtained commitments from congressional leaders to provide the matching money.

NCI Director Vincent DeVita has said that if the Hammer funds come through, they will be used as spelled out in the bypass budget. Here's what that would mean in the 1990 fiscal year, which will start Oct. 1, 1989:

*Research project grants (ROIs, POIs)--50% of competing grants would be funded at recommended levels. This year, about 35% will be funded, at an average of 90% of recommended levels.

*Cancer centers--Ten additional centers would be funded, and all core grants would be funded at recommended levels (91% of those levels are being funded this year), with the goal to increase the number of centers with core grants by 50% by 1994 (to about 90 centers). The centers bypass budget total of $141.7 million includes $17 million for the proposed new comprehensive center core grants.

*Cancer prevention and control--The bypass total of $121.5 million would be a 70% increase over the current level, and would include funds to double the number of Community Clinical Oncology Program awards (now at 58).

*Clinical cooperative groups--The $141.7 million in the bypass budget would get the groups started on toward the goal of doubling the number of patients now in clinical trials by 1992.

*Construction--The bypass total of $60 million would be used to initiate a comprehensive program to upgrade and develop cancer research facilities, including a five year plan for modernization of the Frederick Cancer Research Facility. Estimated for FCRF's needs over the five years is $47 million; $17 million of that is in the 1990 bypass budget.

Other elements of the new bypass budget includes support for 1,800 trainees through the NRSA program (the budget presented to the NCAB called for 1,600, but members of the Board's Planning & Budget Committee asked that the total be increased by 200); $10 million for small instrumentation needs of the extramural community (for instruments costing $100,000 or less); a special initiative for the upgrading and expansion of biomedical research computing capabilities ($75 million which, among other things, would pay for a second supercomputer); and two year obligating authority for funding construction projects.

NCI is the only NIH institute with authority (granted by the National Cancer Act) to develop, make public and submit directly to the President its own budget. It is an authority that probably is unique in the federal government. The budget, drawn up by staff with the advice of the NCAB, by law is intended to tell the President the amount required, based on scientific needs and opportunities, to carry out the National Cancer Program to the most optimal degree.

DeVita refers to the $500 million Hammer and matching funds as "catch up money," closing the gap between the regular appropriations and the optimal bypass budget. The understanding is that this is a two year commitment, and that after that, Congress will maintain the bypass level which increases about 10 percent a year.

Although some critics argue that biomedical research progress can't be obtained "by throwing money at it," DeVita points out that much of the progress made in the last 15 years is directly related to the surge of money following the National Cancer Act of 1971.

"The infusion of money in 1972 permitted expansion of NSABP's breast cancer clinical trials," he said at the NCAB Planning & Budget Committee meeting last week. "All that has come out since in breast cancer treatment has to do with that."

DeVita commented on remarks by Sen. Lowell Weicker at a recent meeting with members of the National Coalition for Cancer Research. Weicker said that most people don't realize how susceptible Congress is to the mail members receive.

"The agenda is being set now," DeVita said. He suggested that those interested in the Cancer Program ask candidates to state their positions on biomedical research. The bypass budget is an excellent document to give to candidates and present office holders, he noted.

"This is the year to do it. In 1971, the investment in research worked. Unfortunately, the forces at work in 1971 no longer exist. The Institute has been carrying too much of the load."

The bypass budget will be developed into a document which explains how the money would be spent and justifies the increases. It is tied to the Year 2000 goal of reducing cancer mortality by 50 percent, listing the steps needed to achieve that goal and the costs involved. That document will go to the White House in September, and will be available to those who request it at that time.

Comments by NCI staff and NCAB members related to the new bypass budget:

--Doubling patient accrual by 1992 "probably is too optimistic," DeVita said. "I'm not sure the group mechanism can do that. I'm not sure the patient population is there where the groups can gain access to it."

"We wouldn't want to spend that much extra money without restructuring and streamlining the groups," Div. of Cancer Treatment Director Bruce Chabner added.

Chabner startled the committee by pointing out the major metropolitan areas of the U.S. where access to clinical trials is limited. He mentioned Milwaukee, St. Louis, Phoenix and Dallas as cities which do not have either an NCI supported cancer center or institutional members of cooperative groups for adult malignancies, "only individual physicians who may be members of a group."

Some of those do have CCOPs, a program DeVita called "an unqualified success." He said that CCOPs now are putting 4,500 patients a year into clinical trials. Doubling the number of CCOPs would go a long way toward the goal of doubling the number of patients on clinical trials.

DeVita credited the dramatic increase in pediatric cancer survival to the fact that such a high percentage of those patients go into clinical trials, about 60 percent.

--Cancer control "is an area that has been suppressed," DeVita said, referring to the nearly flat amount over the last five years in the line item budget for cancer control. "Peter (Greenwald, Div. of Cancer Prevention & Control director) has done a fine job building an infrastructure for prevention trials." The 70 percent increase called for in the bypass budget for cancer control is needed to take advantage of that infrastructure and the new knowledge on chemoprevention and diet factors. "We couldn't have done chemoprevention clinical trials in the early 1980s. We can now."

--Funding 10 additional centers in FY 1990 "is realistic," DeVita said. "There are quite a number ready to submit grant applications. We won't have any problem finding 10 more." Committee members remained skeptical and suggested that five would be a more reasonable goal.

--The White House Office of Management & Budget opposes funding a high percentage of competing grants or a fixed number of grants because of the out year commitments they entail, DeVita said. "They see it as the road to oblivion. We see it as the road to solving a major national problem."

--The most crucial problem facing NCI at present, one which has almost reached a crisis stage, is the reduction in number of positions (full time equivalents, or FTEs, in the government jargon). "We are having a lot of trouble," DeVita said. "Our budget has increased 47 percent in four years, but our FTEs have decreased 13.3%. That is counting the positions we've been given for AIDS slots. Non AIDS FTEs have decreased by 16.8 percent."

The bypass budget calls for an increase of 450 FTEs, which would make up the 340 lost and add some to help take care of the growth.

--Although the panel of experts convened by NIH to make recommendations on construction needs specifically asked that individual institute construction authorities remain intact, "as of today, NIH is preparing a budget with $125 million for construction, with all of it to go to NIH," DeVita said. "They don't realize that NCI has the sole responsibility for construction at Frederick. If we don't put a nickel in there, not a nickel will be spent."

The $60 million in the bypass budget for construction is not large enough, Board member Enrico Mihich said. "There's so much need out there you could put down any figure."

--If the bypass figure is obtained, ROIs and program projects, for the first time in NCI's history, would exceed $1 billion, specifically, one billion, 43 million. That would fund an estimated 1,400 grants.

--Intramural research would rise to $370.6 million, compared to $274.4 million in the President's 1989 budget request. Again, Mihich suggested that that was not enough. "We are restricted by walls," DeVita said, meaning space, not barriers. "Also, by (the restricted number of) FTEs."

--R&D contracts is listed for $285 million in the bypass budget, up from $208 million in the President's 1989 budget request. Some of that is for AIDS contracts.

All figures listed above included an estimate of $153.5 million for AIDS, which compares to

the $125.3 million requested by the White House for NCI's share of AIDS funding in 1989. The 1990 estimate for AIDS "is soft," DeVita said. "We're still developing it."

Each bypass budget includes estimates for four additional years ahead, going up about 10 percent a year. The total would hit $3.5 billion in FY 1994. ROIs/POIs would have $1.8 billion that year, centers would get $227.6 million, cooperative groups $160.7 million, prevention and control $218 million, intramural research $448.6 million, construction $62 million and contracts $347.6 million.

NCAB Says Restrictions On Animals Would Threaten Cancer Research

The National Cancer Advisory Board and other members of the biomedical research community have become increasingly alarmed about proposed legislation that would severely restrict use of research animals.

Bills now pending in Congress that would restrict animal use include:

--Consumer Products Safe Testing Act, HR 1635, by Rep. Barbara Boxer (D-CA).

--Bills that would ban use of pound animals in research, S 1457, by Sen. Wendell Ford (D-KY), and HR 778, by Rep. Robert Mrazek (D-KY).

--Pet Theft Act of 1988, S 2353, by Ford.

--Information Dissemination and Research Accountability Act, HR 1708, by Robert Torricelli (D-NJ).

--Various amendments to the Animal Welfare Act.

"That is a sad, recurrent theme," Board Chairman David Korn said. "Organizations operating under animal rights labels are a real problem in the (San Francisco) Bay Area. They are very powerful. Congresswoman Boxer is from Marin County. I wouldn't underestimate the problem representatives from Northern California pose."

Korn suggested that the Board draft a resolution to be sent to members of Congress and others. "The issues are exceedingly serious. The amount of damage that can be done is incalculable."

The resolution, approved unanimously by the Board, follows:

"Whereas, progress in cancer research depends on the humane and scientifically appropriate use of animals for research; and

"Whereas, there is concern that the public is confused about the necessity to use animals in studying the causes, prevention, diagnosis and treatment of cancer; and

"Whereas, major advances in cancer research have depended on the use of animals, including the revelations of the most fundamental information about the development of cancer, and new treatments for many previously incurable cancers; and

"Whereas, the Board is aware of new research techniques that provide alternatives to the use of animals in specific circumstances, there are major areas of cancer research, including studies of causation, prevention and treatment, in which the continued use of animals is essential; and

"Whereas, the Board finds that effective implementation and adherence to federal statutes, regulations and policies can ensure the appropriate use of animals in biomedical research; and

"Whereas, the Board finds that misrepresentations endanger biomedical progress and blunt reactions to the illegal acts of vandalism, destruction of property and theft that have occured in many research institutions;

"Be it, therefore, resolved that the National Cancer Advisory Board calls upon national, state and local legislators, health professionals, scientists and others to support the humane use of animals in research to ensure continued progress against cancer. Furthermore, the Board affirms that further proscriptions or curtailment of the use of animals in research threatens to paralyze future progress against cancer."

New "JNCI" Proving To Be Popular Replacement For Journals It Replaced

"JNCI," the new journal with an old name, has been on the street for about five months. Early returns indicate that its brisk, fresh approach to reporting new results from all areas of cancer research has been well received and that it is a worthy successor to the two publications it replaced, the old "Journal of the National Cancer Institute" and "Cancer Treatment Reports."

At last report, 1,222 subscriptions had been sold to the new "JNCI," at $60 per year U.S. $75 foreign. In addition, 1,685 subscribers to the old "JNCI" and 3,093 "CTR" subscribers were switched to the new journal, with few if any objections. About 5,000 copies are being sent out free as samples and for other purposes, a number NCI intends to sharply reduce.

Perhaps a more telling indication of the

new "JNCI" popularity is the flood of manuscripts pouring in. Ten peer reviewed articles and reports were published in the most recent issue (May 18), survivors of about 50 which had been submitted (the rejection rate is running at 80 percent). This is for a twice monthly journal, which has placed great pressure on itself by announcing a goal of publishing no less than eight weeks after acceptance.

So far, that goal has been difficult to meet, understandable with the new format, schedule, and overall philosophy.

Crucial to the journal's avowed mission of rapid dissemination of new findings is the time in review. An all-NCI Editorial Board headed by Editor in Chief Robert Wittes is assisted by an extramural Editorial Advisory Board of about 100 experts. Additional reviewers are called upon as needed. Manuscripts are first screened by the Editorial Board. Those considered not of sufficient priority for publication are returned within two weeks. Those of high interest will be sent to selected members of the Advisory Board or other outside consultants for review, with authors notified of acceptance, rejection or need for revisions within about six weeks.

The major impediment now to fast turnaround on the review is the U.S. mail. On occasion, overnight express services are used, and the staff is exploring for future use the prospect of electronic transmission of manuscripts.

"JNCI" is printed in Virginia by a firm on contract with the Government Printing Office. The cost of printing will be approximately $300,000 a year.

NCI has not compiled (at least for the record) other cost figures for the journal. With a full time staff of 18 and other overhead costs, the total including printing probably approaches $1 million a year. That does not include the part time players. Wittes says that he spends at least half his time with the journal. The outside board members are unpaid volunteers.

Subscription income, unfortunately for NCI's balance sheet, goes directly to the U.S. Treasury, so the entire cost of the operation comes out of the Institute's appropriation.

So how is this expenditure of Cancer Program funds justified?

"In my view, a government publication needs to be unique," Wittes said. The old "JNC" and "CTR" were not, although they may have been when they were started. There are now many oncology journals, covering the various subspecialties and disciplines or the broad areas of basic and clinical research. "There are none that are organized like ours, covering the map, with fast publication."

Wittes said he does not think "JNCI" poses a threat to any of the existing journals. He will feel the new journal is here to stay when paid subscriptions reach 10,000, which he expects within six to eight months, "certainly within a year."

Meanwhile, a venerable journal, "Cancer Research," also switched to twice monthly publication during the past year and has experienced "phenomenal growth," in the words of Editor Peter Magee and Managing Editor Margaret Foti.

"Cancer Research," of course, is published by the American Assn. for Cancer Research. Foti is executive director of the association.

The editors reported that submissions rose six percent in 1987, with 2,124 manuscripts. "We are experiencing an 18 percent increase over the first four months of this year. From all indications this exponential rise in submissions will persist throughout this year."

The editors suggested that the greater frequency and speed of publication are major incentives to potential contributors. Also, "the temporary interruption in the publication of the 'Journal of the National Cancer Institute' during the year [while the new 'JNCI' was being organized] sent a number of its regular contributors to 'Cancer Research.' Also, its new format may not be conducive to the receipt of comprehensive papers. We suspect that an even more important factor may be the response to our editorial in 1987 encouraging epidemiologists to send their papers to 'Cancer Research.' A similar call for papers from clinicians will soon be issued as a further way to bring into better balance the various subdisciplines of the cancer field published in our widely read journal."

Magee and Foti noted that, in 1986, "for the fourth consecutive year, 'Cancer Research' was cited more frequently than any other cancer journal." The journal was ranked 22nd among 4,316 scientific journals ranked by the Institute for Scientific Information.

DCPC Board Approves Reissuance Of RFA For Chemoprevention Trials

The Div. of Cancer Prevention & Control's Chemoprevention Branch received concept

approval from the division's Board of Scientific Counselors at its recent meeting for three more issuances of the RFA for prevention clinical trials evaluating intermediate endpoints and their modulation by chemopreventive agents.

DCPC hopes to make three to five awards a year, each with estimated annual budgets of $200,000, for three to five years. The awards will be cooperative agreements.

This RFA was first issued in 1985, from which no awards were made. The next year, awards were made to Waun Hong, at the Univ. of Texas M.D. Anderson Cancer Center, and Lewis Kuller, Univ. of Pittsburgh.

In the 1987 competition, 18 proposals were reviewed, 16 approved and two came through with fundable scores. The awards, approved last week by the National Cancer Advisory Board, went to Baruch Blumberg, Fox Chase Cancer Center, and Ronald Yanagihara, Univ. of Texas (Tyler). Two others were in the range that could be funded, if NCI determines that exceptions should be made.

The RFA will be reissued again next year and in 1990 under the concept approved by the BSC.

Other concepts approved by the BSC included a new master agreement for contracts for production of commercially unavailable chemopreventive drugs; recompetition of a contract for a chemopreventive agent repository; recompetition of a contract for management and support services for the division; and recompetition of a master agreement for technical resources and support for chemoprevention research.

The concept statements and BSC discussion follow:

Prevention clinical trials evaluating intermediate endpoints and their modulation by chemopreventive agents. Three to five cooperative agreement awards are anticipated, at a total maximum estimated budget of $1 million. Awards will be for three to five years, with planned competing renewals.

The application of biological markers to clinical prevention trials might be highly significant in relation to ultimate cancer prevention. When neoplasia itself is used as an end point in studies of this type, very large numbers of subjects tested for long durations are often required. The major objective of this concept is to encourage cancer chemoprevention clinical trials which use biochemical and biological markers to identify populations at risk and/or to provide intermediate endpoints that may predict later reduction in cancer incidence rates.

The main emphasis should be on small, efficient studies aimed at improving future research designs of chemoprevention trials, providing biologic understanding of what is happening in the trials, or providing better, more quantitative and more efficient endpoints for these trials. New rationales for dietary intervention have emerged from epidemiological and animal model studies that warrant evaluation in human populations. In human subjects, however, it is difficult to determine whether putative dietary modifications or chemopreventive agents actually inhibit tumor development. However, intermediate endpoints or biomarkers that are directly associated with the evolution of neoplasia, and that develop with much higher frequency in abnormal cells of susceptible individuals than do the actual tumors, make it possible to carry out many studies on fewer subjects for shorter durations. If such biomarkers were found to be modified by a particular intervention regimen in short term studies, a rationale would be provided for carrying out long term studies.

The dollar estimates with each concept brought before the various boards of scientific counselors or other advisory groups are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended as guides for board members to help in determining the value of the projects in relation to the resources available to the entire program or division. In the case of RFAs, the amounts cited are the maximum that will be set aside to fund those particular grants, the final amount depending on NCI's budget and program priorities. Responses should be based on workscope and description of goals and methods included in the RFPs (contracts) or RFAs (grants and cooperative agreements). Availability of the RFPs and RFAs will be announced when NCI is ready to release them.

A number of compounds and/or dietary components have been associated with the inhibition of carcinogenesis in animal models, in vitro systems, and/or epidemiological studies. Results from animal studies suggest that a number of compounds and/or dietary components affect the several stages of carcinogenesis. A variety of parameters have become available and may be used to identify or evaluate risk modulation in selected target populations by chemopreventive agents. Examples include reversal of abnormal cytology, prevention or reversal of nuclear abberations (micronuclei), ornithine decarboxylase and/or prostaglandin synthetase inhibition, DNA ploidy alterations, changes in colonic mucosal proliferation (histology, tritiated thymidine labeling indices), decreases in fecal mutagens, and oncogene suppression tests. Markers of precancerous lesions may also be useful to define populations that may benefit from chemoprevention trials; however, more information is required concerning the ability of such markers to predict and/or modulate cancer incidence. The development of sensitive and accurate intermediate endpoints should greatly enhance the ability to design effective cancer risk reduction trials.

This RFA will support studies which are directed toward examining the role of various biological and/or biochemical markers in assessing risk modulation by chemopreventive agents. One or more intermediate endpoints might be evaluated initially to determine baseline parameters, and subsequently to serve as a followup after the administration of the chemopreventive agent in vivo and/or in vitro.

These studies can be developed in phases, including a pilot or developmental phase and a full scale intervention phase. If it is determined that an intervention successfully fulfilled the biological, biochemical and statistical criteria established in a pilot study, it then might be justified to consider expanded studies on more subjects for longer durations, measuring more advanced stages of neoplasia. This announcement solicits applications for pilot studies, which would be expected to last up to three years, full scale intervention studies, or a combination of the two. After successful completion of the pilot phase and a demonstrated modulation of

marker endpoints in a direction characteristic of lower risk of neoplasia, phase 3 clinical trials with a defined monitoring test system and a cancer incidence or mortality endpoint could be implemented.

Short term chemoprevention clinical trials that evaluate the effect of innovative biomedical monitoring tests in high risk populations are sought. These tests might be useful to determine an intermediate endpoint, serve as a basis to assess risk or response to chemopreventive agent, identify high risk groups, or increase the power to detect the risk or the response to chemoprevention. Modulation of effects by the chemopreventive agents on tests which are indicative of neoplastic progression may be an early indicator of efficacy. Biological fluids including urine, blood, sputum and feces would be obtained from participants for analysis. Examples of populations suitable for such interventions may include subjects with preneoplastic lesions, subjects previously exposed to an identified carcinogen, or those curatively treated for a malignancy who are at high risk for the development of a second malignancy.

Effects on tests by the chemopreventive agent might be highly significant in relation to ultimate cancer prevention. Priority for intermediate endpoint studies would be given to interventions which do not overlap or duplicate currently funded projects (e.g., betacarotene and nonmelanoma skin cancer).

"I think it will be remarkable if you can find three to five investigators who can carry out such a wide range of activities," Board member Mary-Claire King said. The concept was approved without dissension.

Organic synthesis, chemical analysis and experimental pharmaceutical formulation of commercially unavailable chemopreventive drugs. Master agreements, with an estimated five awards anticipated, each at an estimated $200,000 a year.

The Chemoprevention Branch already has in place rigorous screening and efficacy evaluation programs for drug evaluation and development. One program consists of preclinical screening and initial efficacy of potential agents. In this program gram to kilogram quantities of potential drugs are initially evaluated for chemopreventive positive activity in several in vitro and in vivo carcinogen model systems. Those most promising agents are further evaluated in chronic safety programs. These tests require several kilograms of prospective agent for completion. The last program focuses on kilogram quantity drug availability for clinical drug development. Information from efficacy tests, safety evaulation and clinical drug preparation are required by FDA for justified issuance of an IND.

In this RFP, support will be sought from laboratories capable of synthesizing drugs for short term in vitro and in vivo screening. Larger quantities of more promising chemopreventive agents may be synthesized for chronic efficacy and safety evaluation. Drug synthesis laboratories providing documentation of good manufacturing practices will be sought for larger scaleup work supporting clinical drug preparation. The latter may be required to formulate finished drugs and study chemical stability of final pharmaceutical products. The latter shall participate in a quality assurance/quality control program at the National Bureau of Standards sponsored by DCPC.

A major factor retarding the rate of entry of potential chemopreventive agents into clinical intervention trials is lack of agent availability and/or suitability and approval by FDA for chemoprevention trials. Chemopreventive agents under both preclinical and clinical testing worldwide are agents that either occur naturally in the diet or represent a number of already known pharmacologic classes with specific therapeutic uses. The development of agents that are active as chemopreventive drugs is an urgently needed program capability for supporting preclinical, short term clinical and larger scale human cancer prevention studies.

This RFP seeks the synthesis of chemopreventive agents not readily available in commerce. Chemical analysis of synthesized agents and experimental formulation for drug development will also be required. General categories of such agents may include (a) plant phenolics such as ellagic acid and dithiolthione drugs like oltipraz; (b) epidemiologically important compounds like lignans such as enterolactone which is formed in the human body by intestinal microbial enzymes; (c) certain components of foods like crocetin which is the water soluble yellow-orange carotenoid pigment in saffron; (d) garlic compounds such as ajoene which modulates prostaglandin synthesis; and (3) certain natural products such as thiorubrin A, an unusual acetylenic disulfide discovered in folkloric herbal medicines.

The offeror may respond to any of the tasks or part of a particular task such as drug formulation. Final specifications for synthesis, analysis, priority, and formulation will be set by the NCI project officer. The offeror shall propose cost effective synthetic routes for such synthesis using minimal number of parent starting materials and synthetic steps. The offeror shall in addition propose at least one alternative route of synthesis per agent. Final synthetic products shall be analyzed in a standard fashion for yield, purity and chemical constituency. A meticulously detailed final report covering all aspects of drug synthesis, isolation, purification and structural verification shall be required and used to support larger scale synthetic studies of that particular chemical agent for pharmaceutical development and further efficacy studies; establishment of a master drug file at FDA; and support for an application for an IND to conduct clinical trials. In addition, final reports may be shared with other interested investigators.

Board member John Ultmann asked "if you are more less in line with Div. of Cancer Treatment costs, which now has years of experience" in chemical synthesizing, formulating and analysis.

Board member Edward Bresnick said there was good interaction and costs were approximately the same. Frank Meyskens agreed, and added, "This is very important. They have been close to stopping trials because of a lack of drugs." The concept was approved unanimously.

Multidisciplinary technical resources and support for chemoprevention research. Recompetition of a master agreement. Five awards of five years each, with a total of five different tasks at an estimated cost of $190,000 for each task, are anticipated.

The overall goal of this concept is to provide a full range of technical support products required for the multidisciplinary research, analysis and planning activities in cancer chemoprevention. The major objectives include:

1. Provision of preclinical technical support products needed by program staff and by the Extramural Selection Committee and Intramural Decision Network Committee to advise on selection and prioritization of chemopreventive agents and implementation of preclinical studies. These products will provide:

A. Analysis and evaluation of comprehensive and specific data including efficacy, toxicology, epidemiology, cost, availability, etc. from published and unpublished resources.

B. Technical and procedural support for development and implementation of criteria for prioritization and selection of chemopreventive agents, based on the above criteria as well as criteria involving mechanisms of action and structure function analysis.

C. Compilation of specific and extensive data

required to design and perform the preclinical laboratory studies required by FDA for approval of performance of clinical trials of agents in human subjects.

2. Clinical technical support products needed by investigators, program review committees and program staff to implement phase 1 and phase 3 clinical chemoprevention trials including:

A. Critical review, analysis, and documentation of all relevant information required for IND applications on new agents intended for clinical trials.

B. Comprehensive monographs on high priority agents entering clinical trials, so that the investigator can be provided with a summary of all relevant data on an agent.

C. Expert, multidisciplinary analysis of critical information in specialized topics of interest in clinical chemoprevention for planning and implementing new research initiatives.

The concept was approved unanimously.

Chemopreventive agent repository and preclinical and clinical support activity. Recompetition of a contract now held by Evaluation Research Inc. The new award will be for five years, at an estimated total annual cost of $900,000 a year.

The Chemoprevention Branch currently sponsors 24 clinical intervention trials that are evaluating 15 different drugs and micronutrients. The clinical drug evaluation component utilizes $5 million in drugs annually. Selecting, obtaining and developing agents for clinical evaluation is a complex effort involving contractors and subcontractors, NCI staff, investigators, drug and chemical companies, food manufacturers and FDA.

The Chemoprevention Branch has also developed a rigorous preclinical evaluation program where currently 150 new agents are on test in 50 studies. Obtaining and formulating agents for preclinical studies is a complex process differing significantly from clinical drug evaluations utilizing finished pharmaceutical products.

For preclinical agents commercial references are consulted for sources, manufacturers, availability, material data sheets, chemical quality, bulk supply, custom synthesis, chemical stability, propensity for formulation, ease of handling, safety and cost. All of the information is made available to principal investigators so that decision on agent preparation and finishing can be made.

The movement of a clinical agent to a study site requires absolute access to agents and this in turn may require intermediate steps such as formulation, packaging, storing, shipping, tracking activity and inventory planning.

It is for these reasons a centralized clearinghouse for the above activities was established and its continuation is essential.

The contractor shall furnish all necessary services, qualified personnel and materials to establish a centralized chemoprevention agent repository and distribution facility. The project requires the receipt of agents from various suppliers as arranged by NCI; safe and stable storage until requested by the project officer; repackaging of agents to meet user needs; shipping agents to users with appropriate characterization data and handling instructions; when necessary, shipping agents to other NCI contractors for special formulation and/or packaging before shipment to final destination; limited quality assurance capability for checks on purity of bulk agents and shelf life; when necessary the use of other NCI contractors for more complete analyses; monitoring stock levels in storage and at user locations; an inventory control system to ensure timely reordering and shipping of materials; and maintenance of up to date records of acquisitions and shipments.

The concept was approved unanimously.

Management and support services for DCPC. Recompetition of a contract now held by Technassociates Inc. This is an 8A minority small business set aside. Technassociates has been purchased by a larger firm which does not qualify as a small business and thus will not be involved in the recompetition. The new contract will be awarded for five years, with total estimated cost ranging from $500,000 in FY 1989 to $610,000 in FY 1993.

Support services to be performed under this contract will include conference management support, report documentation and editing (including slide and graphics preparation), and support for data collection and analysis.

Project officer Damian Crane noted that the estimated cost is about $100,000 a year less than the present contract, due to a "slimmed down workscope." Meyskens commented that since it supports production of reports to extramural scientists, "I would like to see the budget increased if the mission includes providing information to the community."

DCPC Director Peter Greenwald said he thinks that can be done within the estimated budget. But Board member Donald Iverson said, "I would like to have that option" and offered a motion to add $100,000, if needed. The concept, with the extra money if needed, was approved unanimously.

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 Blair Building room number shown, National Cancer Institute, NIH, Bethesda, MD 20892. Proposals may be hand delivered to the Blair Building, 8300 Colesville Rd., Silver Spring, MD, but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-97570

Title: Single photon radiopharmaceuticals for function, metabolism and tissue localization

Deadline: July 29

The Diagnostic Imaging Branch of NCI's Div. of Cancer Treatment is seeking contractors with expertise to develop and evaluate potential radiopharmaceuticals labeled with technetium-99m and/or iodine-123 for the purpose of diagnostic imaging using single photon emission computed tomography (SPECT). The government estimates that three awards will be made. It is anticipated that the resulting contracts will be awarded on an incrementally funded basis for 36 months.

Contract Specialist: Odessa Henderson
RCB Blair Bldg Room 228
301/427-8737

The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams

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