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MAJOR DECISIONS ON HOW NCI WILL SPEND EXTRA MONEY WON'T BE MADE FOR THREE-FOUR MONTHS

Major decisions on how NCI will spend whatever portion of the extra money given it by Congress for the 1984 fiscal year probably will not be made before January or February, Director Vincent DeVita told *The Cancer Letter*.

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In Brief

TWENTY-NINE PERCENT OF APPROVED ORGAN SYSTEMS APPLICATIONS FUNDED IN FEBRUARY, MAY CYCLES

ORGAN SYSTEMS Program grantees have not been doing too badly since their review was moved to NIH if the February and May rounds are taken into consideration, the dismal (so far) results of the October round notwithstanding (*The Cancer Letter*, Oct. 21). Since the NIH Div. of Research Grants assumed review from the old Organ Site Program Working Cadre groups, 62 applications from the OSP bladder, bowel, pancreas and prostate grantees have been approved, and 18 of those were funded. That rate of 29 percent is not far from the 33 percent average for NCI in all grant categories. Those figures do not include the October round, with the final results there still to come. Only three of 30 approved applications scored 175 or better and are thus assured of funding. However, several more were within 10 points of 175 and some of those might be picked up, either as exceptions or if the payline is raised. . . . ASCO, AACI both urged the Health Care Financing Administration to modify Diagnosis Related Group reimbursement regulations to permit more exceptions. In a letter from David Prager, chairman of ASCO's DRG Study Committee, the association asked that all NCI recognized comprehensive centers, clinical cancer centers, funded Community Clinical Oncology Programs, and any hospital entering 50 or more patients a year on NCI approved protocols qualify for exceptions. AACI, in a letter from President John Durant, asked exceptions for comprehensive and clinical centers; that for centers which are part of larger institutions, regulations be developed similar to those covering psychiatric and rehabilitation units; that the requirement that 80 percent of a hospital's discharges have cancer as the primary diagnosis be changed to 50 percent and for both primary and secondary diagnosis; and that there be no cutoff date for qualifying for exceptions. The proposed rule says no institution not qualified by last April 1 will be eligible.

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DEVITA THINKS NONEARMARKED EXTRA MONEY WILL BE LESS THAN $20 MILLION

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DeVita does not agree with The Cancer Letter's estimate that at least $20 million of the nearly $90 million above the Administration's request which NCI will get was not earmarked by Congress. "I think it will be somewhat less than that," he said. Much of the additional money will go into funding grants at recommended levels and full funding of indirect costs, Congress insisted. Lesser amounts were directed into training programs, and $7 million was earmarked for additional contract supported research and development.

Neither House nor Senate committee reports spelled out what contract supported programs would benefit. DeVita said it probably was intended for epidemiology and drug development, both almost entirely funded through contracts. Drug development has been cut by 30 percent over the last three to four years, as NCI struggled to cope with the budget squeeze.

The program which has suffered the most through the lean years was construction. NCI requested as much as $20 million a year for construction and renovation grants but has been getting only $1 million. Before any substantial sums can be added, specific concurrence of the Office of Management & Budget will be required—unless, as Congress once did in the early 1970s, language is written into the appropriations bill directing that a certain amount be spent for construction. That was not done this year.

NCI executives and senior staff members will make the major decisions on the 1984 allocations at their semiannual retreat, to be held in January or February. DeVita will discuss the budget with the National Cancer Advisory Board in November.

DCBD BOARD REJECTS BREAST CANCER MULTIPLE MARKERS CONCEPT PROPOSAL

A cautious Board of Scientific Counselors of NCI's Div. of Cancer Biology & Diagnosis rejected the only concept presented to it at its Oct. 20 meeting but went along with the staff's request for a "reorganization" of the division's diagnosis program.

The reorganization consisted primarily of establishing a Board committee on diagnosis, a suggestion Board members accepted somewhat reluctantly. Susan Zolla-Pazner was concerned that some members not on the committee might have ideas to contribute, and Bernard Amos felt an emphasis on diagnosis might lead to shifting some funds from basic to applied research.

Brian Kimes, who is acting chief of the Biology Branch, replacing Robert McIntire, who retired last summer, said he needed "help in prioritizing ideas. I don't think our staff alone is capable of doing that. We need a focus."

Kimes said there is no intent to shift basic research funds to applied diagnostic research. "We need a broader base of advice, to take advantage of new technologies."

Board Chairman Peter Nowell named himself, Nelson Fausto, Zolla-Pazner, and John Stobo to the committee.

In the reorganization of the Diagnosis Branch, Kimes will continue as acting chief until a permanent chief has been selected. He also will continue in his permanent position as chief of the Cancer Biology Branch.

Within the Diagnosis Branch, Bernice Radovich heads the Immunodiagnosis Section, Bill Bunnag heads the Pathology/Cytology Section, and Sheila Taube, newly recruited from the National Science Foundation and NIH Grants Associates Program, heads the Biochemical Diagnosis Section.

The Board rejected by a 7-2 vote a concept recommended by the Breast Cancer Task Force to study use of multiple markers in breast cancer diagnosis. The project would have involved award of three contracts for two years, at a total estimated cost of $465,000. Each of the competitively selected labs would have performed three or more diagnostic assays on coded sera from breast cancer patients, benign disease patients, and controls, testing selected putative breast cancer markers.

The staff's justification for the project noted that none of the single markers tested for breast cancer "has survived the test of time or evaluation by a blinded test." However, "there are preliminary data suggesting that several of the known assays for markers when used simultaneously and analyzed using multivariate discrimination techniques may overcome some of the problems of nonspecificity of a single marker."

Stobo was not convinced. "If one doesn't work, what evidence is there that multiple markers will?" he asked.

Ihor Masnyk, director of the division's Extramural Research Program, cited a number of studies supporting that contention.

DCBD Director Alan Rabson commented that

in the 1960s "I asked Tom Frei and Jay Freireich that since one drug didn't seem to work in treating cancer, what made them think that three together would?"

"Then what happened?" Stobo asked, eliciting laughter with the sarcasm.

Stobo remained unconvinced. "We're asked to support something for which there already are substantial data. Multiple markers have been around for years. If there was a glint of usefullness indicated, it would be apparent."

Only Amos and Irwin Freedberg voted for the concept, with Stobo, Kenneth Olden, Robert Perlman, Stewart Sell, Zolla-Pazner, Sondra Schlesinger, and Barbara Hamkalo opposed.

CONSENSUS: NEVI CAN BE MELANOMA PERCURSORS; MANAGEMENT SUGGESTIONS

Dysplastic nevi are both markers and precursors for familial melanoma, and melanoma also may develop in congenital nevi, an NIH consensus conference concluded this week.

The conferees agreed that strategies for treatment and followup should be formulated individually, on the basis of the risk of melanoma to each patient. Patients with dysplastic nevi and a family history of melanoma should be followed frequently, with documentation of lesions and excision of changing nevi. The relatives of patients with melanomas should be examined for dysplastic nevi and melanoma in view of the familial aggregation of both lesions. Patients with congenital nevi should be followed periodically for changes. Need for education in examination of lesions by patients, relatives, and health professionals is emphasized. The paucity of existing information on precursors of melanoma coupled with its increasing incidence indicate a continuing need for research, the conference draft statement said.

The statement noted that the accurate diagnosis of dysplastic nevus depends upon histologic confirmation. Typical histopathologic features are superimposed on those of a compound nevus and include:

1. Basilar melanocytic hyperplasia with elongation of rete ridges.

2. Cytologic atypia with enlarged hyperchromatic melanocytic nuclei, often present but not essential for diagnosis.

3. Melanocytes, spindle shaped and arranged horizontally, or occasionally epitheliod, aggregating in nests of variable size and fusing with adjacent rete ridges to produce bridging.

4. Lamellar and concentric dermal fibroplasia.

5. Lymphocytes in patchy or diffuse superficial dermal infiltrate. These changes may appear focally in any given lesion and may not be evident unless multiple histopathologic sections are studied. These microscopic findings of dysplastic nevus are distinct from those of malignant melanoma in situ.

A congenital nevus is a melanocytic nevus that is present at birth. Some lesions first become apparent during infancy, and when they do, it is assumed that preexisting nevus cells were present. This assumption is based on clinical, histopathological, and biological data. Not all pigmented lesions present at birth represent melanocytic nevi.

Addressing the question, "Are nevi precursors to melanoma?" the conferees reported:

"In the general population, the lifetime risk of developing cutaneous melanoma is approximately 1 percent. Among patients with dysplasatic nevi, who constitute a heterogenous group, the overall lifetime risk has been estimated at 10 percent. The risk is greater for those having one relative with melanoma than for those with no such relative.

"The lifetime risk of melanoma may approach 100 percent for those people with dysplastic nevi who are from melanoma prone families, i.e. families with two or more first degree relatives having cutaneous melanomas. Melanomas in people from these families may arise within the dysplastic nevi or de nova in ostensibly normal skin."

Conferees agreed on these recommendations for management:

Diagnosis—A patient suspected of having one or more dysplastic nevi should have the entire integument examined closely in good light. This should include a careful examination of the scalp and eyes. At least one of the more atypical appearing dysplastic nevi should be subjected to excisional biopsy. The family history should be obtained with special attention given to such items as moles, skin conditions, skin cancer, and melanoma.

Familial screening—If the family history suggests melanoma, an effort should be made to examine all first degree relatives. If a melanoma is found in any of these family members, all blood relatives should be examined to determine the extent of the risk of melanoma in the kindred.

Treatment and followup—In patients with dysplastic nevi and any family history of melanoma, the indication for excising additional dysplastic nevi is the suspicion of early melanoma. In such lesions, the decision will be influenced by variation in color, size of the lesion relative to the patient's other nevi, or progression. Follow-up should be conducted every three to six months.

In patients with dysplastic nevi and no family history of melanoma, the risk of melanoma is uncertain. Extant lesions should be followed for evidence of progression.

Education—All patients with a dysplastic nevus should be educated about their need for followup. They should be taught self examination to detect changes in existing nevi and the emergence of new nevi. Finally, as with other people at risk for melanoma, they would be prudent to avoid excessive sun exposure and use sun screens.

Congenital nevi—Management depends primarily on their size and the perceived risk of development of melanoma. Large congenital nevi are rare, and their management is complex. The management of patients with large congenital nevi should be individualized to accommodate such factors as technical difficulty and cosmetic consequences of surgical removal as well as the risk of melanoma.

Future research needs—Lack of information and increasing incidence of melanoma suggest a need for epidemiological, clinical and laboratory studies of populations known to be at increased risk as well as of general populations. Prospective studies are needed to collect data aimed at determining patterns of inheritance in melanoma; improving the accuracy and reproducibility of diagnosis; establishing the incidence and prevalence of melanoma associated with each specific precursor lesion; describing the natural history of these precursors; identifying other potential risk factors; quantifying the incidence, if any, of excess nonmelanocytic neoplasms in these patients.

Pilot studies should be initiated to evaluate the feasibility of and methodology for large scale prospective studies. The feasibility and effectiveness of proposed interventions also should be determined. Laboratory studies should be directed toward understanding how pigment cells in precursor lesions undergo transformation.

Ruth Freinkel, professor of dermatology at Northwestern, chaired the conference panel.

DRCCA BOARD OKs CONTRACT CONCEPTS, GETS TOUGH ON CHEMOPREVENTION PLANS

The Board of Scientific Counselors of NCI's Div. of Resources, Centers & Community Activities gave concept approval to contract supported projects worth an estimated $3.2 million in first year awards at the Board's recent meeting. Concepts involving grants and cooperative agreements acted upon at the meeting were reported last week in The Cancer Letter.

The contract supported concepts included recompetition of the Centers for Radiological Physics Program, the much acclaimed effort which is credited with improving standards and quality of therapeutic and diagnostic radiology around the country.

The other contracts involve chemoprevention and nutrition studies.

The Board also approved concepts for five noncompetitive contract efforts with estimated first year costs of $1.5 million.

Concepts approved were:

Centers for Radiological Physics. Five to seven awards anticipated, estimated annual budget, $280,000 each, three years. Present contractors are Memorial Hospital, New York City; Alleghenny Singer Research, Pittsburgh; Univ. of Wisconsin, Madison; M.D. Anderson Hospital, Houston; Univ. of Washington, Seattle; West Coast Cancer Foundation, San Francisco; and American Assn. of Physicists in Medicine, Philadelphia, the coordinating center. Staff description and justification:

The Cancer Detection Branch is requesting permission to continue to provide for a number of regional centers for radiological physics and their coordination. The primary objective of these contracts is to ensure uniformly high quality of radiological physics services in diagnostic and therapeutic radiology. Approximately six centers would be funded to provide a regional resource for review, consultations, and education. The contractors will be required to coordinate with other centers to ensure interregional uniformity and to evaluate the impact of the CRPs on the national control efforts.

The impact of the performance of the CRPs over the present contract period has been primarily in the area of the practice of radiological physics as it applies to radiation oncology and diagnostic radiology. The major accomplishments have been an increased accuracy in the delivery of radiation doses to cancer patients; a reduction of patient doses especially in mammography; and the development of a variety of regional calibration and training activities. Periodic in depth reviews have been made of the dosimetry practices employed at all radiation diagnostic and therapy facilities affiliated with DRCCA

screening and treatment groups.

Since 1974, six centers for radiological physics have carried out physics reviews at clinical facilities receiving support from DRCCA for activities in therapeutic and/or diagnostic radiology. Each CRP is assigned a geographic region under an individual contract. Over the same period of time, the American Assn. of Physicists in Medicine has coordinated the activities of the CRPs, ensuring that standardized procedures, measurement protocols, and appropriate instrumentation were used and intercalibrated. In addition, uniform report formats have been developed and utilized.

Over 260 community facilities presently are reviewed and monitored on a routine basis by the CRPs. This will increase to well over 400 facilities during the proposed period which will commence in February 1985.

As the conceptual aspects of radiation dosimetry are advanced, and physical data and measuring instruments are improved, it is important to adopt these improvements in order to reduce the uncertainty in the dose for radiation therapy practices. The purpose of these projects is to develop the methods, and provide the reviews, that will permit the radiological community to not only determine, but also maintain, the delivery of absorbed dose more accurately than has heretofore been possible.

A continuity of CRP activities is most important in that new or expanded programs involving a large number of additional community clinical facilities will be coming on stream within a relatively brief period of time.

With implementation of the Community Clinical Oncology Program there will be the need for a smooth and rapid incorporation of additional clinical facilities into the CRP review process. The implementation of cancer research clinical trials at these community facilities is a major undertaking which will require initial review and monitoring of radiation producing equipment, radiation sources, and measuring equipment for treatment planning procedures. Mechanisms will also have to be established for the transfer of dosimetry and other data to appropriate research groups for matching and evaluation with patient treatment data.

In addition, several cooperative groups have been added to the DRCCA program requiring the incorporation of these clinical programs into the CRP review system. There are also other activities, such as a new high energy photon and electron beam protocol which is being implemented that will require considerable training and monitoring.

The development and standardization of physics protocols, the correlation of physics data with patient data and the coordination of review visits is an important activity which is essential to the cancer control effort.

Winfred Malone is the project officer.

In vitro evaluation of chemopreventive agents. Multiple three year awards are anticipated, with a total annual budget of $800,000 in FY 1985, $850,000 in 1986, and $900,000 in 1987. Description:

The proposed project would evaluate the activity of chemopreventive agents in various in vitro assays of cell transformation for potential application in the prevention of cancer in humans.

Both in vivo and in vitro experimental model systems have historically been of fundamental importance in understanding the carcinogenic process. These data have led to the successful design of preclinical prevention and therapy studies often having direct relevance and immediate application for use in clinical trials.

Recent progress in the in vitro systems has led to the development of defined cell lines and techniques which make possible an evaluation of the effects of various substances on cell transformation. These systems will allow an evaluation of the efficacy of chemopreventive agents against a variety of initiating and/or promoting substances. The end points measured in the routine assays are either direct transformation (anchorage independent growth, foci of morphologically altered cells, tumor formation in nude mice) or parameters highly correlated with transformation (production of messenger RNA encoded by oncogenes, measurement of transforming proteins, clonogenicity of cells).

Defined reagents available include: 1) cloned cells transformed by various oncogenes and expressing specific transcribed messenger RNA and translated proteins which can be examined for modulation by chemopreventive agents. The transformed phenotype of such cells can be observed directly and is correlated with the levels of these substances which are measured respectively by labeled DNA probes and specific immunological reagents; 2) cell lines of fibroblastic or epithelial origin are available which are promotable to the transformed phenotype. Chemopreventive agents can be evaluated for their ability to directly inhibit the transformation; 3) cell lines having defined quantities of epidermal growth factor and tumor growth factor receptors are useful substrates for evaluating analogs which might block, inhibit or compete with the growth factors.

The potential chemopreventive agents which can be examined by these techniques run the gamut from all of the retinoid compounds, the antioxidants, growth factor analogs, inhibitors of promotion, antibodies to promoters, to synthetic viral polypeptide vaccines.

Advances in various in vitro techniques now make it possible to screen even large numbers of potential chemopreventive agents for efficacy. These evaluations can be done in a relatively rapid time frame and relatively inexpensively as compared to alternative means of evaluation. The resolving power of these techniques are such that data highly relevant to the carcinogenic process and its prevention in man is anticipated. The correlation of certain in vitro transformation parameters with tumorgenesis is now well established, and results from the in vitro techniques and studies will allow a focusing on the most promising agents for more exhaustive and lengthy in vivo efficacy and toxicology evaluation.

Gary Kelloff is the project officer.

"This is a very sophisticated approach," Board member Harry Eagle commented. "I wonder about the desirability of a contract rather than a grant."

DRCCA Prevention Program Director William DeWys said "A large element of direction will be required--which agents, which systems to

use. Individual investigators can apply for grants to study specific agents. We think there is a backlog of agents available which need to be considered."

"The central problem is the issue of direction by staff," Eagle said. "To say that NCI staff will say which agents are to be investigated is the wrong approach."

"Contracts are used to bridge the gap between research and clinical trials," DRCCA Director Peter Greenwald said.

"You're talking about a breakthrough, but this project is looking for compounds," Eagle said.

"We need to take 500 or so compounds and assess their activity," Greenwald said.

"This (proposed concept) doesn't say that," Eagle insisted. "This says screen for new compounds. I agree, you do need a contract to do the tedious work of looking at specific compounds. If you would announce this as an RFA (for grants) to look for new compounds, you would get a lot of good people working on this."

"To some extent, what you're asking for is already being done by the Div. of Cancer Cause & Prevention," Greenwald said. "We're taking it further, to application."

"We're losing sight of the fact that this is a program," Board member Robert Cooper commented. "A program necessarily involves multiple steps. Whether it is an RFP or RFA depends on the staff's view of how to get the program moving. If a program is worth doing, we ought not nit pick, and let staff proceed."

"I don't see how we can expect Bill (DeWys) to move ahead without the resources to do the job," Board member Charles Cobau said.

"Something was just said that is not entirely correct," Eagle said. "That the basic work has been done and now is the time to proceed with the application. There is a lot of basic work still to be done. To go ahead without an understanding of the transforming mechanism is wrong."

Thirteen members voted for the concept, none against, although seven abstained.

Evaluation of chemopreventive agents by in vivo screening assays. Two three year awards are anticipated, with estimated total annual budget of $800,000 in FY 1985, $850,000 in 1986, and $900,000 in 1987. Description:

The proposed project would evaluate the activity of chemopreventive agents in in vivo assays which measure inhibition of tumorigenesis. The results of these initial screening assays will be used to select the agents that will be further evaluated in a larger panel of animal models for efficacy.

Several scientific disciplines have elucidated the cellular processes that result in the transformed phenotype in vitro, and extensive knowledge exists about the correlation of measurable parameters of these in vitro transformed cells with in vivo tumorigenesis and malignancy. These in vitro parameters include anchorage independent growth, clonogenicity, morphologic alteration as well as biochemical markers such as calcium sensitivity, rate of glucose uptake, etc. Even though these assays allow tumorigenic potential to be predictable with some certainty, there are limitations to using in vitro criteria to predict tumorigenicity. There are many obvious reasons that account for this, including the differences in the nutritional milieu between in vitro and in vivo as well as the hormonal and immunologic influences that exist in vivo which can act to inhibit or enhance tumor growth. In addition, the potential inactivation of the chemopreventive agent when administered in vivo provides a further requirement that these methods of evaluation be included in early screening assays.

From these observations it can be concluded that early screening of potential agents for chemopreventive activity should include evaluation by both in vitro and in vivo techniques. A battery of three to four proven in vivo tumor model systems will be selected to evaluate potential chemoprentive agents. These will include rapid in vivo tumor induction systems involving different mechanisms of carcinogenesis. A variety of histologic types of tumors and target sites will be evaluated as appropriate.

The expected lack of complete correlation between in vitro transformation and in vivo tumorigenesis and the potential of inactivation of chemopreventive agents administered in vivo require the evaluation of chemopreventive agents by in vivo screening assays. These initial screening evaluations can be done in a relatively rapid time frame and relatively inexpensively by the in vitro techniques. Any agents showing activity by the in vitro techniques or having known chemopreventive activity from previous studies found in the published literature will be evaluated by these rapid in vivo assays. These techniques will provide a preliminary screening mechanism for selecting chemopreventive agents for longer term, more costly, and time consuming in vivo animal model studies, toxicology and eventually clinical trials.

Kelloff is the project officer.

"Which models have been found to be good predictors for which agents?" Cooper asked.

"For retinoids, mammalian and skin systems," Kelloff answered. "But we will be looking at a gamut of agents besides retinoids."

Procurement of chemopreventive agents through indefinite delivery contracts. Two to five contracts are anticipated, with an approximate annual budget of $100,000 each. The description:

The purpose of this procurement mechanism is to secure, from pharmaceutical manufacturers, special formulations of chemopreventive agents necessary to support specific human intervention studies.

The major pharmaceutical manufacturers have been most cooperative in providing investigational agents for human intervention studies in chemoprevention at no cost to NCI. As a general policy they will provide existing formulations or the bulk substance for formulation through NCI resources. In some instances they have been willing to provide special formulations, but this engenders some specific costs due to special filings with FDA, interruption or fitting into standard production schedules, etc., for relatively small production batches. Recently, it has been requested that NCI reimburse for the added costs of meeting these special requests. These special costs are minimal compared to the overall value received. For example, the test agent, analytic procedures, composition data for FDA and special techniques used in handling are provided at no cost to NCI.

As one example, the standard formulation of a marketed betacarotene capsule is 30 mg. This dose given daily results in a small but definite incidence of carotenodermia that could jeopardize compliance or the blinding of a study. The provision of a 15 mg capsule of betacarotene avoids these problems. The manufacturer will prepare special batches of a 15 mg formulation of betacarotene and corresponding placebo in return for payment of added encapsulation costs. Cost estimates for two recently awarded studies are:

Bowen, adenomatous colon polyps, 131,000 active, 131,000 placebo, cost estimate, $21,000.

Safai, basal cell carcinoma, 58,000 active, 29,000 placebo, cost estimate, $7,000.

The costs to NCI of doing the formulation, analytical and IND submission work necessary using bulk product would greatly exceed these estimates.

A second example is a special formulation of vitamin C and vitamin E into a single tablet for two separate chemoprevention studies. This special formulation permits a single placebo tablet so that both the administration of the study medications and subject compliance are enhanced. The expense of these special formulations have been borne by the manufacturer thus far, but the special costs will need to be covered by NCI in the future. Estimates for a typical study are:

Vitamin C/E, 234,000 tablets, $21,400, with a similar amount for 234,000 placebo tablets.

An indefinite delivery contract is a procurement contract device that is used when the requirements can be estimated but the exact time of delivery over the life of the contract cannot be precisely determined. The Div. of Cancer Treatment uses such contracts for purposes of securing agents needed for special chemotherapy studies. Under such a contract the time frame, generally one year, and the dollar amounts are specified. The money need not be spent, and the total cannot be exceeded without additional contract actions.

Donald Buell is the project officer.

The Board gave DeWys a bad time over four other chemoprevention/nutrition concepts, but ended up approving two of them while disapproving another on a tie vote and tabling the fourth until January. The disapproval, of a contract to perform search and analysis of the scientific literature for identification and characterization of chemopreventive agents, led DeWys to threaten to withdraw the other two because "you're not giving us the tools to do the job." He cooled off, however, and presented the concepts, which were approved but not without more criticism.

International food data system. One award, four years, estimated annual budget is $300,000 in FY 1984, $500,000 in 1985, $500,000 in 1986, and $300,000 in 1987.

The goal of this procurement is the development of a data system which will encompass all available certified data on the nutrient composition of foods. Such a data system would facilitate international research involving nutrient consumption and would enhance the completeness of the food data base within each country. The major objectives of this procurement include 1) a review and certification of analytic methods; 2) the compilation of an inventory and description of available data bases on nutrient composition; 3) development of a thesaurus of food items; 4) completion of a survey of potential users of this system; 5) development of a data base management plan; and 6) activation of a functioning data system.

This data system would clarify interpretation of studies involving comparisons between countries, would facilitate collaborations between scientists in different countries and would enhance the data base available for use within each country. An international data system exists for animal feeds and this has facilitated international research.

Tasks required of the contractor will be:

a. Review and certification of analytic methods of nutrient and nonnutrient composition of foods. At the present time different laboratories in different countries use different methods to assay for a given substance with little effort to standardize the methods between laboratories. Obviously, before data can be combined, the comparability of data must be known.

b. Compilation of an inventory and description of available data bases on nutrient composition. Every effort should be made to make this international system as comprehensive as possible. Each description should include data on sampling procedures, analytic methods and data format.

c. Development of a thesaurus of food items. Laboratories in different countries currently classify and name foods differently. For example, in one country American cheese and cheddar cheese are lumped together as processed cheese while in another country several varieties of each are analyzed separately. A standardized nomenclature will be needed for an international system.

d. Survey of users and uses of the data system. The uses of the system may be important for the organization of the data base management system.

e. Development of a data base management plan. Based on items a-d above, a plan must be developed to receive and organize the data into a usable format.

f. Activation of a functioning data system. This system should be responsive to the needs of its sponsors and contributors on a no charge and first priority basis. Other users will be expected to pay for use and will be assigned second priority.

Ritva Butrum is the project officer.

Board member Lewis Kuller said, "It is objectionable to see NCI establish another government data base," referring to similar efforts by the National Heart, Lung & Blood Institute and the U.S. Dept. of Agriculture. "I would be supportive, but with a strong caveat that this be linked with the NHLBI data base."

DeWys said it would be developed with the help of an advisory group with representation from those agencies and possibly others.

"Do you propose to create another data base, yes or no?" Kuller demanded. "We had assurances that NIH would not create another data base."

DeWys said the two would be linked.

"There must be 15 such data bases around the country," Board member David Hegsted said. "None of which gives you the same answer."

The vote to approve the concept was 15-1, with Kuller dissenting.

Methodology and analysis of fiber and fiber components in foods. Two awards are anticipated, for four years, with the total annual budget estimated at $500,000 in FY 1985 and $400,000 each of the next three years.

The goal of this procurement is to support development of new and improved analytical procedures to measure total dietary fiber and individual fiber constituents in foods. Subsequently, the aims are to employ the procedures to analyze foods which are the major contributors of these components in the U.S. diet; and to provide a representative data matrix.

The major objectives include a. Improve the present analytical methodology to quantitate the total dietary fiber and fiber components including cellulose, hemicellulose, lignin, pectins, gums, mucilages and modified celluloses as they commonly occur in foods; b. develop extraction and sample preparation procedures for different matrices for the detection by analytic procedures; c. develop internal standards of these components for instrument calibration; d. develop standard reference materials and control samples; e. sample and analyze foods in the U.S. which contribute significant amounts of these components.

Dietary fiber behaves within the GI tract as a polymer matrix with variable physicochemical properties, including susceptibility to bacterial fermentation, water holding capacity, cation exchange and adsorptive functions. These properties determine the physiological actions of fiber and are dependent on the physical and chemical composition of the fiber.

Lack of knowledge about dietary fiber and its components in foods have inhibited the elucidation of the often hypothesized beneficial effects of the total dietary fiber or its fractions to health. Until now studies related to fiber have almost exclusively relied on crude fiber figures as an index of the dietary fiber. The crude fiber analysis is a highly empirical chemical procedure that defines fiber as the residue remaining after extraction with dilute acid and alkali. Presently we define dietary fiber to include cellulose, hemicellulose, lignin, pectins, gums, mucilages, and modified celluloses. Crude fiber bears no consistent quantitative or qualitative relationship to dietary fiber. Data on total dietary fiber in the U.S. is severely lacking. There are no food composition data on the quantity of dietary fiber fractions in our food supply. Other analytical methods have emerged during the past few years: acid detergent fiber (ADF) which measures cellulose and lignin and neutral detergent fiber (NDF) which gives higher estimations of crude fiber because of improved recoveries for cellulose, hemicellulose, and lignin. Neither method includes the newer components which have been encompassed by the term dietary fiber. Better analytical methods and analysis of foods are needed to provide a data base to elucidate the significance of these dietary components to the incidence of cancer. Data on fiber and fiber fractions in foods is of great importance to cancer prevention studies. Studies with animals have shown that different fiber fractions have specific effect on intestinal transit time, lipid absorption and metabolism, e.g. gelling fibers inhibit fat absorption and particularly cell accumulation of lipid, and intestinal cytokinetics and mucin production resulting in morphological change in the intestine.

It is proposed that a technical advisory group would convene with the contractors to review and advise in regard to techniques and procedures.

Butrum is the project officer.

Eagle objected because he said there were not enough details in the presentation on the budget. He asked that in the future, concept proposals include more budget information.

Board members were divided on the proposal. Hegsted commented, "We've got to get some idea that dietary components do what we attribute to them. It is pure speculation that these methodologies will measure what we want to know."

"Is $2 million going to get us any closer to understanding prevention of cancer?" Kuller asked. "I don't think so. Our priority should be to look and see what things affect the biology of human cancer."

Laurence Kolonel disagreed with Kuller. "You can measure individual diets. This is an important concept."

Jerome DeCosse said that "this is a first step toward wisdom."

The Board tabled, by a 15-1 vote, a concept for a project to perform methodology and analysis of vitamin A and carotenoids in foods. That project would have involved two contracts for five years at an estimated cost of $900,000 the first year and $600,000 over each of the next four years.

Charles Smart suggested that five years was longer than the study would require; Eagle and other members objected to lack of budget details. But Saxon Graham commented, "We approved $15 million for the outreach program without much budget information. We trusted the people involved. I think we have to trust the study sections to look at the budgets." Graham cast the only vote against the motion to table the concept until the Board's meeting in January.

Board members objected to the concept for a literature search for chemopreventive agents after Kolonel commented, "Most of us impoverished investigators have to do literature searches ourselves. I don't seen why you need a half million dollars to do one. Why not do it in house?"

Other members supported the concept, but a motion to disapprove ended in an 8-8 tie. Chairman Lester Breslow refrained from breaking the tie and ruled that since the concept did not receive a majority supporting it, it was disapproved.

The Cancer Letter _Editor Jerry D. Boyd

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