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NCI FY 1986 BYPASS BUDGET ASKS $1.445 BILLION WITH MAJOR INCREASE TIED TO GOAL FOR YEAR 2000

The National Cancer Advisory Board this week approved the 1986 fiscal year bypass budget which departs from the more conservative bypass requests of recent years and asks for a 31 percent increase over the President's FY 1985 budget for NCI. The total request, which will be submitted directly to the White House under NCI's unique budget bypass authority, is $1.445 billion (one billion, 445 million) which Director Vincent DeVita said is based on the "resources we need to achieve our year 2000 goals," the reduction of cancer

(Continued to page 2)

In Brief

NCAB APPOINTMENTS: BOUTWELL STAYS ON; BROWN, ELION, STRONG, KORN NAMED; ONE VACANCY REMAINS

FIVE APPOINTMENTS to the National Cancer Advisory Board were announced by the White House Tuesday: **Roswell Boutwell,** professor of oncology at McArdle Laboratory for Cancer Research, who was reappointed to a full term (he had been named last year to fill out the unexpired term of Gerald Wogan, who had resigned); **Helene Brown,** codirector of cancer control at UCLA's Jonsson Comprehensive Cancer Center; **Gertrude Elion,** head of experimental therapeutics at Burroughs-Wellcome and recent past president of the American Assn. for Cancer Research; **David Korn,** professor and chairman of the Dept. of Pathology at Stanford Univ.; and **Louise Strong,** associate professor of pediatrics and medical genetics at the Univ. of Texas System Cancer Center/M.D. Anderson Hospital. A sixth vacancy is still to be filled, and the White House asked Irving Selikoff, whose term has expired, to stay on until a new appointment has been made. Three of the five new appointees are "graduates" of NCI's boards of scientific counselors—Korn served as chairman of the Div. of Cancer Biology & Diagnosis Board; Elion is completing a term on the Div. of Cancer Treatment Board; and Strong is still a member of the Div. of Cancer Etiology Board. There should be nothing but praise for President Reagan on this round of appointments. All are well known and highly respected in the cancer research community, and four are prestigious scientists, as requested by professional organizations and by NCI Director Vincent DeVita, who felt the NCAB had more practicing physicians and fewer basic scientists as members than it should. The fifth, Brown, is a long time leader in cancer control activities and in the American Cancer Society. Apparently this round of appointments was not as dependent on political considerations as the last one was said to be. Brown has been active in the Democratic party and Strong is the daughter of the late Texas Democratic Sen. Tom Connally.

BYPASS BUDGET FOR FY 1986 ASKS BIG INCREASE FOR NCI, TO $1.445 BILLION

(Continued from page 1)
mortality by 50 percent through stepped up efforts to apply present knowledge in prevention, detection, diagnosis, and treatment.

The bypass budget, DeVita said, "is a statement of what we can do and the resources required to do it."

"This is logical, reasonable, long range planning that makes sense," Board member Geza Jako said. "It shows leadership from the Institute."

The plan to achieve the year 2000 goal, which NCI estimates would save 288,000 lives a year by then, is based on having in place by 1990 all elements of a national network of comprehensive, clinical, and community centers along with vastly strengthened cooperative groups, stepped up screening and detection efforts, and intensified programs aimed at smoking reduction, diet modification and chemoprevention.

"The years between now and 1990 are critical," DeVita said. To get all those elements into place by then will require major increases starting in the FY 1986 budget. Areas of emphasis reflected in the bypass budget are:

—The number of cancer centers would be increased by five a year starting in 1986. This expansion will include consideration of geographic location and underserved populations. As a first step in that direction, the NCAB approved Monday a change in the core grant guidelines which would waive the $750,000 base in RO1 and PO1 grants an institution must have to qualify for a core grant. This permits NCI to proceed with a planning grant it hopes to award to a consortium of black medical schools which is intended to help minority institutions qualify for clinical center core grants.

—Funding of clinical cooperative groups will be increased to double their capacity and patient accrual by 1990. "I believe the reduction in mortality we are seeing now is largely due to the numbers of patients beeing seen by the cooperative groups," DeVita said.

—The number of Community Clinical Oncology Programs will be doubled, from 62 to 124, by 1990, doubling the number of patients in the community on protocol studies funded by NCI, from 8,000 to 16,000.

—Fund 40 percent of competing research project (RO1 and PO1) grants at recommended levels. Cooperative group and cancer center grants also would be funded at recommended levels.

—Construction and renovation grants would be funded at a $20-27 million level.

—Manpower development would be stepped up by increasing all of NCI's fellowship and training programs and by putting in place a new three year cancer control science associates program.

The bypass budget by major categories:

	1985 President's Budget	1986 Budget
Total NCI	$1,101.1	$1,445.0
Research Projects	496.8	650.9
Centers	78.0	93.0
Coop Groups	46.9	68.5
Cancer Control	63.8	96.0
Intramural Resrch	185.2	216.6
R & D Contracts	130.4	175.0
Construction	2.1	23.0
Training (NRSA)	23.8	28.0

ROSWELL PARK WINS COMPETITION FOR ORGAN SYSTEMS COORDINATING CENTER

Roswell Park Memorial Institute won out in the spirited competition for the Organ Systems Coordinating Center Tuesday when the National Cancer Advisory Board voted 8-2 with two abstentions in favor of RPMI over the Univ. of Texas Graduate School of Biomedical Sciences.

The Board's action came after heated discussion in closed session. The initial review group had scored the Texas application nine points better than RPMI's, 263-272. However, some Board members, as well as some of those involved in the review, felt that scores that close left the issue entirely up to the Board. There was also the feeling by some Board members that since both scores were well past this year's grant paylines in the 170s, the award should be recompeted.

Maureen Henderson and Roswell Boutwell cast the two votes against RPMI. Gale Katterhagen abstained, and Chairman Tim Lee Carter did not vote.

RPMI Director Gerald Murphy is the principal investigator for the program. Murphy headed the National Prostatic Cancer Project in the old Organ Site Program, a factor in the Board's decision. The RPMI award will total about $900,000 a year for five years to coordinate the activities of the five working groups in the new Organ Systems Program.

ASCO PRESIDENT CRITICIZES COOPERATIVE AGREEMENT USE FOR CLINICAL TRIALS

Overreaction by NCI to criticism by regulatory agencies, some members of Congress and the media has resulted in practices "which many members of ASCO believe serve as serious impediments to creative investigation," Philip Schein said in his presidential address at last week's 20th annual meeting of the American Society of Clinical Oncology in Toronto.

Schein, vice president of Smith, Kline & French

and former director of medical oncology at the Lombardi Cancer Research Center, said the criticism of NCI caused the Institute to initiate monitoring of the activities of extramural investigators which has placed "unnecessary impediments in the path of productive and innovative experimentation."

Schein said, "These concerns are focused on the heavy reliance on cooperative agreements for clinical research funding, in contrast to the traditional mechanism of the investigator initiated research grant. The grant mechanism was developed with the concept that science is driven by investigators who are interested in a specific problem, rather than by governmental direction. In this setting, there is freedom to experiment within the limits of medical science and ethics, while minimizing the weight of bureaucracy. The cooperative agreement mechanism, in operation, requires that each protocol be reviewed and approved by NCI staff before it can be activated. This has resulted, in some cases, in substantial delays, and more importantly, allows for considerably greater government control over science."

Schein, who is chairman of the Mid-Atlantic Oncology Program, a regional cooperative group, and former chairman of the Gastro-Intestinal Tumor Study Group, said NCI with its drug development program "has dual and perhaps conflicting responsibilities. First, it shares the usual obligations of a pharmaceutical company. It must ensure that clinical research, and in particular the testing of investigational agents under its sponsorship, is carried out with high ethical and scientific standards in accordance with regulatory agency requirements. To determine the relative efficacy and safety of the treatment, it must provide for clinical trials that are properly designed to address these questions. This has been an area of deficiency in the past when many small and inconclusive pilot studies were allowed to proliferate.

"But NCI also has an additional and equally important responsibility to the investigative process, as well as its public mandate to further science and the broad improvement of therapy. This must include the provision of clinical studies that constitute research rather than development. It is from the latter that new concepts for future drug design and application are derived. Implicit to this process is the delegation of science to entrusted investigators who are given the responsibility to create and who ultimately are held accountable through the peer review process.

"It must be remembered that the successes that we now record in patient response and survival found their origin in programs that were largely conducted in the 1960s and early 1970s. I believe that the spirit of exploration and innovation that characterized that period has been momentarily lost. Our colleagues at NCI have the difficult task of fulfilling FDA requirements without managing science to the extent of stifling creativity. In this context, it is appropriate to consider a partial decentralization of NCI's drug discovery and development process which would draw more heavily on the expertise of extramural investigators and institutions. The multidisciplinary comprehensive cancer centers, in particular, can be more effectively utilized."

NCI Director Vincent DeVita, responding to Schein's comments, told **The Cancer Letter**, "Phil is wrong about the cooperative agreement. The cooperative agreement is no different than the old cooperative group grants except that everything is in writing." Investigators should have no less incentive now than they ever had to develop innovative, creative protocols, he said. As for the protocol review required by the Div. of Cancer Treatment, DeVita denied that it imposes any undue delays. "We don't cause any delays. Sometimes protocols pile up at the institutions, but they aren't delayed at NCI."

In remarks later in the week at the meeting of the American Assn. for Cancer Research, DeVita mentioned the new program initiated by NCI establishing New Drug Discovery Groups which are intended to "decentralize" the drug discovery and development process, as suggested by Schein. The first of those groups will be funded soon, DeVita said.

Schein also referred in his presidential address to the Medicare reimbursement system based on diagnosis related groups which many investigators feel threatens clinical research. "It is unlikely that hospital administrators will allow their institutions to participate in clinical research if such activities are to be funded off of a fixed allocation based upon diagnosis," Schein said. "The impact on diagnostic and therapeutic research could be devastating. This places in jeopardy many of the National Cancer Institute's programs, including the recently initiated Community Clinical Oncology Program as well as the efforts of national and regional cooperative groups. The situation could become even more acute within two years when the Health Care Finance Administration reports to Congress on the advisability of paying physicians under the DRG system. Physicians undoubtedly will be rewarded for efficient and cost effective care, which may be in direct conflict with the needs of clinical investigation that in many cases involve more frequent and expensive testing, as well as extended hospital stays for patient treatment and observation... ASCO through its Public Issues and Clinical Practices Com-

mittees has a major responsibility to convince the federal government that cancer centers, both academic and community, need to be excluded from the constraints of the DRG system. In addition, the government must be made to acknowledge that for many tumors, investigational drugs represent the best form of treatment and that their use should not exclude a patient from standard health care benefits."

AACR MEMBERS UNANIMOUSLY BACK TOUGH FEDERAL ANTISMOKING LEGISLATION

Members of the American Assn. for Cancer Research unanimously approved a resolution on smoking and lung cancer calling for tough anti-smoking legislation, putting the prestige of the society solidly behind the drive to reduce the health toll exacted by tobacco.

The action was taken at the association's 75th annual meeting in Toronto last week after hearing a report from an AACR task force on smoking and lung cancer which leaves little doubt that cigarette smoking is the causitive agent in at least 85 percent of lung cancer cases. The report was presented by Lawrence Loeb, director of the Gottstein Memorial Cancer Research Laboratory at the Univ. of Washington, who headed the task force.

The position statement approved by the membership:

"The American Assn. for Cancer Research accepts the evidence gathered by cancer scientists as establishing that cigarette smoking is the major preventable cause of human lung cancer. We therefore go on record as advocating that the greatest cancer prevention measure that might be undertaken would be for people not to smoke. As interim steps towards this goal we recommend the following actions be taken by the government and members of our society to reduce cigarette smoking:

"1. Take legislative action to reduce 'image' advertising and other types of promotional efforts designed to attract people to the practice of cigarette smoking.

"2. Enact legislation designed to reduce the availability of cigarettes for children and young adults--particularly in school, military, and hospital settings. One measure would be to eliminate the tax free status on cigarette sales in government installations.

"3. Enact and enforce legislation that restricts smoking in public places.

"4. Increase taxes on cigarettes and other tobacco products and use the proceeds for research, education, and treatment of the resulting diseases.

"5. Eliminate federal support for the production and distribution of tobacco products.

"6. Increase the effectiveness of warning labels on tobacco products."

Summarizing the scientific findings of the task force, Loeb noted the following points:

*Tobacco smoking is the cause of 85 percent of the lung cancer cases, and about 30 percent of all cancer deaths in the U.S. Heavy smokers have more than a 40 times greater chance of developing lung cancer than nonsmokers.

*There is no effective treatment for most cases of cancer of the lung. The five year survival rate for lung cancer patients is less than 10 percent and has not changed in the past 30 years.

*Numerous carcinogens have been detected in cigarette smoke. When the smoke is fractionated into distinct components, each component contains multiple carcinogens. Removal of any one carcinogen from cigarette smoke would still leave many more; thus, the likelihood of developing a 'safe' cigarette seems remote.

*Economic costs of smoking related lung cancer amount to $7.3 billion. Estimated costs from all smoking related illness, including direct medical costs and productivity losses from sickness and premature mortality amount to $42 billion. Both productivity losses and medical costs, which are paid largely by government programs and other third party insurers, are burdens on general society, where nonsmokers are a large majority.

"In short," Loeb said, "there is overwhelming epidemiological evidence linking smoking and lung cancer; there is no cure; there is no safe cigarette; and smoking imposes enormous costs on society. Cancer from smoking is a preventable epidemic, and the most effective way of reducing cancer mortality is to discourage smoking."

Members of the AACR task force on smoking and lung cancer, and the portion of the position paper which each prepared, are:

John Laszlo, professor of medicine, Duke Univ. Medical Center, prepared the section on clinical aspects of lung cancer.

Virginia Ernster, associate professor of epidemiology, Univ. of California (San Francisco), prepared the section on epidemiology.

Kenneth Warner, professor and chairman, Dept. of Health Planning & Administration, Univ. of Michigan, prepared the section on economics of smoking and lung cancer.

Loeb and John Abbotts, research scientist at the Gottstein Laboratory, prepared the section on carcinogens in cigarette smoke and coordinated the preparation of the position paper.

MORE CONCEPT APPROVALS BY DCPC BOARD OF SCIENTIFIC COUNSELORS

Requests for grant applications (RFAs) given concept approval by the Board of Scientific

Counselors of NCI's Div. of Cancer Prevention & Control appeared in last week's issue of **The Cancer Letter.** An additional RFA approved by the board, along with concept approvals for new contract programs and recompetition of contracts, follow:

RFA Concept Approved

Title: Physiochemical effects of dietary fiber in humans. Estimated total annual budget, $840,000, three awards anticipated, each for four years to be funded by cooperative agreements.

Epidemiological observations show that the rate of colorectal cancer is inversely correlated to dietary fiber intake. Studies indicate that diets with a high intake of total fat and beef and a low intake of dietary fibers and certain vegetables are generally associated with an increased incidence of large bowel cancer in humans. In Finland where the dietary intake of fat is similar to that of many western countries but the fiber intake is much higher the incidence of colon cancer is lower than in all other western countries. In England a significant negative correlation between the intake of pentose containing dietary fiber and colon cancer was reported. These studies have led to the hypothesis that fiber is exerting a protective effect against colon cancer.

While the concept of fiber involvement in colon carcinogenesis is attractive, the data supporting it appears contradictory and sometimes confusing. One reason for this may be that evaluations of the biologic functions of dietary fiber have often lacked complete information on the nature of dietary fiber. Dietary fiber is a complex group of polymers with differing physical and chemical characteristics. The fiber components are usually grouped into major classes: polysaccharides and lignin. Polysaccharides include cellulose and noncellulose which comprise a number of substances, hemicellulose, pectic substances, mucilages and gums. The physiologic consequences of fiber ingestion are dependent on their chemical and also to some extent on their physical structure. This means that not only do different dietary fibers produce different physiological responses but that isolated fiber components may produce different responses from that of the intact plant.

Differences in fiber structure impart a broad range of physicochemical properties such as water holding capacity, cation exchange properties, and adsorptivity of organic molecules. In addition the mere physical presence of some fibers may increase fecal bulk. These properties might allow dietary fiber to play a protective role in the etiology of cancer by dilution and/or adsorption of fecal mutagens, cocarcinogens, promoters and yet to be identified carcinogens.

While most fibers are considered resistant to the action of human upper intestinal enzymes, passage through the ileocecal valve exposes fiber to bacterial enzymes that selectively degrade many of its components. In general fermentation of polysaccharides by bacteria varies from 30-90 percent, cellulose being the least digested whereas hemicellulose and pectic substances are almost completely digested. Lignin is practically nondigestible. Fermentation of fiber by bacteria lowers the pH of the feces and has major effects on colonic metabolism. Changes occur in the pH and oxidation/reduction conditions of the colon, which may also affect bacterial enzyme activity and alter the colonic metabolism of steroids, bile acids and other substances. A number of studies have shown a positive correlation between fecal bile acids (FBA) and colorectal cancer (Wynder and Reddy, 1978). While the exact role of FBA in carcinogenesis is far from settled, one hypothesis is that certain bile acids are converted to carcinogens or cocarcinogens by colonic microflora (Hill, et al, 1971). Fiber fermentation also produces short chain fatty acids (SCFA), of which butyrate has been shown in experimental studies to be antineoplastic (Leavitt et al, 1978).

Bruce et al (1977) were the first to show that feces of normal humans contain compounds that caused direct mutagenesis in the Ames assay. Because of the potential importance of fecal mutagens in the genesis of large bowel cancer, the fecal mutagenic activity of various population groups with distinctive dietary habits and varied colon cancer incidence has been investigated. In general, the fecal mutagenic activity is higher in the low fiber diets.

Increased fecal bulk which is produced by some fibers largely by virtue of their physical presence in the stools, can also be due to increased microbial growth from the utilization of digestible fibers (Stephen and Cummings, 1979). An increase in fecal output has generally correlated with an increase rate of passage of material through the intestine. This decrease in fecal transit time has been postulated to have a protective effect against colon cancer. The amount of time which materials spend in the gut is also important in determining colonic metabolism.

The mechanism of action of fiber has generally been considered as being limited to the interactions with some components of the gut contents, whether such contents be ingested food substances, physiological secretions, or bacterial flora. However, it is also possible that fiber per se or other substances such as bile salt derivataives interact directly by some mechanism with the mucosa to evoke a fundamental alteration in the biochemical or morphological properties of the intestinal tract (Cassidy et al, 1982).

In the past few years numerous studies on the physiological consequences of dietary fiber have been undertaken, and multiple mechanisms appear to be involved in producing the wide range of effects associated with enhanced intakes of dietary fiber. How any of these mechanisms protect against cancer of the bowel is far from settled. What is required now is that highly controlled and standardized experimental approaches be used to further evaluate the biologic actions of various dietary fibers, and their role if any in the prevention of carcinogenesis.

In order to elucidate the role of specific dietary fiber fractions in carcinogenesis, it is essential to have information on a broad range of physiochemical effects of various fiber fractions within the colon including, but not limited to, 1.) fecal mutagenic activity, 2.) fecal content of bile salts and bile acids, 3.) fecal pH and oxidation/reduction status, and 4.) colonic cell kinetics, morphology, and physiology. Different types of dietary fiber either as chemically pure substances or in foods containing a predominance of one or another fraction can be utilized. Investigators are encouraged to be creative and to explore novel physiochemical effects of dietary fiber components. All studies should have direct relevance to human carcinogenesis.

Elaine Lanza is project officer.

New contract concepts approved:

Prevention and cessation of smokeless tobacco use. Estimated total annual budget, $1.5 million for five awards, each for five years.

Smokeless tobacco includes both chewing tobacco (loose leaf, plug, twist) and snuff (moist or dry, fine cut). In the U.S., snuff is usually held in the mouth between the gum and lip, like a variant of chewing tobacco; in England, it is sniffed. Use of smokeless tobacco has been linked to oral and pharyngeal cancer, as well as oral leukoplakia and gum disease. In one study, the risk of developing oral or pharyngeal cancer was four times higher among users of snuff; among chronic users the increased risk factor approached 50.

As recently as 1975, only one to four percent of the U.S. population was estimated to use these products, but sales have been increasing steadily. The fastest growing sector is fine cut tobacco, used in snuff, which increased 188 percent between 1970 and 1979. Sales of moist snuff have continued to increase seven to eight percent per year in the 1980s. Market analyses indicate this growth is due to the creation of new markets that differ demographically from the traditional smokeless market. Products are being aggressively promoted in campaigns that target young adults and teenagers, and there are recent reports of increased use among youth. Industry reports claim increased social acceptance and use among white collar workers as well.

Very little is known about the patterns of use and factors influencing use of smokeless tobacco products within these new populations of users. Specifically, the relationship of use to cigarette smoking is unclear. Users often absorb as much nicotine as do smokers. Nicotine dependence can therefore be established and among the young, use of smokeless tobacco could serve as an introduction to cigarette smoking, which poses even greater health risks. Use of smokeless tobacco by populations that have previously not used it is a very recent phenomenon. We are therefore in a unique position to monitor this new trend in health risk behavior and to intervene at an early stage, thereby minimizing the potential health consequences for the nation.

The proposed studies will develop and evaluate intervention strategies to reduce the long term incidence and prevalence of smokeless tobacco use. The target populations for these interventions will be both adolescents and adults, for the reasons cited above. There will be an emphasis on interventions which are effective, durable, and easily replicable and which are also geographically representative of the different patterns and types of smokeless tobacco use in the U.S. A phased in approach to this research will be encouraged in which data describing the target population and its patterns and types of smokeless tobacco use are first obtained. Reasonable standardization of measures, definitions, and analyses among the studies to be supported must be achieved, and finally, the interventions should be carried out with a minimum one person followup. Each of these controlled intervention studies will be carefully monitored, not only to assess their long term effectiveness, but also to be alert to changes required in the intervention should those giving up smokeless tobacco use turn to cigarette smoking as an alternative. Finally, studies using existing resources (e.g., physicians, dentists, school nurses, media, athletic coaches) and aimed at high risk subgroups (e.g., athletes, certain occupational groups) will be encouraged.

Gayle Boyd is project officer.

Methodology and analysis of retinoids and carotenoids in selected foods. Estimated total annual budget, $300,000, one award, three years.

The goal of this procurement is to support the development of new and improved analytical procedures to measure vitamin A activity, including the naturally occurring retinoids and carotenoids in foods. Subsequently, the aim is to employ the procedures to analyze foods which are major contributors of these components in the U.S. diet. The major objectives include:

1. Improve and automate analytical methodology to separate and quantify vitamers of vitamin A retinoids and provitamin A active carotenoids, particularly alpha and beta and other major carotenoids as they commonly occur in foods.

2. Develop extraction and preparation procedures for different food matrices for detection of retinoids and carotenoids by analytical procedures.

3. Develop internal standards of these components for reliable instrument calibration.

4. Develop standard reference materials and control samples.

5. Sample and analyze selected foods as consumed in the U.S. food supply which contribute significant amounts of these nutrients.

Major tasks include:

A. Develop a reliable, instrumental method of choice for separation, identification and quantification of different forms of retinoids and carotenoids in foods.

B. Foods have variable matrices and contain different forms of retinoids and carotenoids. Methods of extraction of retinoids and carotenoids from the different food matrices need to be

developed which preserve the stable/unstable species and remove interfering compounds.

C. For analytical methods, internal standards will need to be secured and reference materials should be developed. Automation of the methods and automation of report generation should be accomplished.

D. Foods selected for analysis will comprise those which are important sources of retinoids and carotenoids in the diet of Americans, such as deep yellow colored fruits and vegetables, dark green leafy vegetables, and those of the cabbage family. To determine the most significant contributors of vitamin A activity to the U.S. diet, the latest analysis of the HANES Survey will be used to rank foods, considering frequency of consumption, portion size and previously reported vitamin A density. Approximately 30 foods currently account for 85 percent of the total vitamin A consumed in the U.S. In addition, ethnic foods such as papaya, mango, persimmon and bitter melon which are important sources of carotenoids for specific population groups will be included. Effects of processing and preparation on the various components before consumption will be assessed. Schemes of sampling of the selected foods for analysis need to be developed in order to ascertain a representative sample of food consumed throughout the U.S.

Elaine Lanza is the project officer.

Board member Virgil Loeb noted that the concept had been presented previously and sent back for refinement, with the suggestion that the U.S. Dept. of Agriculture might want to share in its cost. William DeWys, director of the DCPC Prevention Program, said USDA is offering "technical assistance" but no money. "They are interested in prevention of vitamin deficiency, but are less interested in the detailed breakdown of vitamin A and carotenoids," DeWys said.

Board member Harry Eagle said he had "no quarrel with the purpose" of the study but "I am concerned about the scope." Staff had requested a five year contract. "I think this will require much less than five years. You could get the answer in two years."

"My problem with it was if five years were enough time," Board member Jerome DeCosse said.

DeWys said the first year would be required for methodology development, "then we'll go on to analysis. If it looks like it could come to a conclusion in one more year, we can always terminate the contract then."

"It might never come to a conclusion," Eagle said. "This could go on and on, to other types of food."

"This is the function of the Dept. of Agriculture," Board member Lewis Kuller said. "None of us can collect precise data from individuals. It is vital that we learn the vitamin A and carotenoid content of foods if we are going to advise people what to eat to protect against cancer. The primary responsibility of NCI is to find out what type of foods are going to protect us from cancer."

"It's fine to say the Dept. of Agriculture should do this," Board member David Hegsted said. "But that doesn't get it done. There are a lot of things the Dept. of Agriculture should do but doesn't. This contract will provide information the epidemiologists need."

Board member Charles Smart said he agreed that the study did not need five years. Also, "I would be careful about the concept that cancer is a nutritional deficiency disease, until we are on firmer footing. That's been the war cry of the quacks for 30 years. There may be some truth to it, but we need to be on firmer ground."

"Agriculture ought to be pricked on this, but I doubt they'll bleed much," Board member Kaye Kilburn said. "If a proper data analysis center can be found, I feel confident we'll have the type of information we need."

Board member Barbara Hulka insisted that two years would be sufficient.

"This is mickey mouse," Kuller said. "Half the food in our diet is eaten in restaurants, and you never know what's in that. If the beta carotenine trials are negative, then we don't need this. If they are positive, then everyone will jump on the bandwagon. This is out of cycle for us."

The Board finally approved the concept, however, after the award period was reduced to three years.

Additional concepts approved by the DCPC Board will be published next week in **The Cancer Letter.**

RFA 84-CA-11
Title: Obesity and cancer risk in women
Application receipt date: July 27, 1984

The objective of this RFA is to stimulate research to elucidate the nature of the association between obesity and cancer risk in women, including the development of new research methods which may enhance the understanding of pertinent metabolic processes or improve the measurement of informative parameters. Research questions of interest include, but are not limited to, the following examples: (1) Is the association causal? If not, what other factors might explain the observed associations between obesity and increased risk of certain cancers? (2) Is the association with obesity related to certain forms of body fat distribution? (3) Is the association explained by the conversion of adrenal hormones to estrogen, or are more complex, metabolic, hormonal or enzymatic processes involved? (4) How do diet and physical activity relate to obesity and cancer risk? (5) What parameters are informative for studies of obesity and cancer risk and how can their measurement be improved? (6) Is the mobilization of fat associated with cancer risk (as by the release of substances stored in adipose cells) either in association with lactation, weight loss, or change in hormonal status? (7) How do individuals differ in the conversion of dietary constituents to adipose tissue and how do these differences relate to cancer risk?

Responses to this RFA may be analytic epidemiologic studies, biochemical epidemiologic investigations, experimental studies in humans, or pilot/feasibility studies.

The total project period for applications submitted in response to this RFA should not exceed five years. The intent is to fund about five individual research project grants, with total costs amounting to approximately $500,000 for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of NCI, the award of these grants is also contingent upon the availability of funds for this purpose.

Copies of the RFA may be obtained from Dr. Genrose Copley, Extramural Programs Branch, Epidemiology & Biostatistics Program, Div. of Cancer Etiology, NCI, Landow Bldg Rm 8C-16, Bethesda, Md. 20205, phone 301-496-9600.

RFPs AVAILABLE

Requests for proposal 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. 20205. 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 NIH-ES-84-20

Title: Quality assurance data audition, support resource.

Deadline: Approximately July 10

The National Institute of Environmental Health Sciences is soliciting proposals for support services for the National Toxicology Program. This will involve services primarily for the auditing of data submitted to the NTP archives or to various NTP components. These audits will determine the quality of data and will validate the technical reports and other publications prepared by NTP. This effort will encompass the following nine functions which will be carried out based on priorities established by NTP:

Function 1—Preaudit preparation. Function 2--Data audits. Function 3--Validation of reports. Function 4--Audit reports identifying problems. Function 5--Summary audit report and interpretation of impact. Function 6—File of audit reports. Function 7—Common data file for each testing laboratory. Function 8--Tracking of audits. Function 9--TDMS data audit procedures.

Offerors will be required to assemble audit teams. A single audit team will consist of: Toxicologists, one person year; analytical chemists, one person year; pathologists, one person year; pathology associate, one person year; histology technician, one person year; data clerks, one person year; clerical staff, one person year. It is anticipated that the total level of effort will be three audit teams or 22.5 person years for each of the three years of contract performance.

Each offeror may propose one, two or three audit teams, and one or more awards will be made to attain the total level of effort required. The major activities of the contract will take place at the NTP archives. For the period Nov. 1, 1984 through Dec. 31, 1984, it is anticipated that up to four contractor personnel will be required to work at the NTP archives presently located in Rockville, Md. After this period, the archives will be located within a 25 mile radius of NIEHS in Research Triangle Park, N.C., and office space will be provided for six-eight persons at the archives for the audit support contractor(s). Offerors must have or be willing to establish by the time of the award office facilities within a 50 mile radius of the NIEHS in Research Triangle Park. It will be essential that the personnel assigned to this contract are in no way associated with NTP contracts which have performed the testing from which the data were generated. This is not to say that those laboratories having other NTP contracts (except the pathology support service and quality assurance control) are disqualified from responding to this auditing support services contract; however, if such a laboratory does respond to this RFP it must explicitly explain how it will assure prevention of any conflict of interest or any appearance thereof.

The award of the archive contract and the audit support contract or the GLP monitoring support contract is not considered to represent a conflict. If personnel are proposed for this service contract who have previously been involved in NTP activities or have been employed by one of the NTP testing facilities or other service contracts, they must explicitly explain how they will make sure there will be no conflict of interest or any appearance thereof. No one will be allowed to audit his/her own data or use data generated by past activities on other NTP contracts.

National Institute of Environmental Health Sciences, Contract Management Office, OAM
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RFP NCI-CP-EBP-41022-60

Title: Support services for a mortality study of workers exposed to acrylonitrile.

This RFP, availability of which was announced in The Cancer Letter, Jan. 27, has been canceled.

The Cancer Letter _Editor Jerry D. Boyd

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