

THE

# CANCER

RESEARCH  
EDUCATION  
CONTROL

# LETTER

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## **NUTRITION MAY GET AN EXTRA \$4 MILLION IN FY 1979; PROGRAM ANNOUNCEMENT DESCRIBES OPPORTUNITIES**

NCI will fund an additional \$4 million in nutrition related grants during the 1979 fiscal year, provided sufficient high quality applications come in to compete successfully for that amount. This will be in addition to the \$7 million committed in FY 1978 directly to the Diet, Nutrition & Cancer Program and a total of \$18 million in 1978 funds

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### In Brief

#### **NCI'S "CONSTANT DOLLAR" BUDGET FOR FY 1979 EQUAL TO 1975 AMOUNT; DECOSSE MOVES TO S-K**

AN NCI APPROPRIATION of \$1 billion would buy only \$560 million of Cancer Program support in 1970 dollars, according to Dept. of Labor inflation statistics. That would still be three times NCI's budget in 1970 (\$175 million) but not the seven or eight fold increase it appears to be. Since 1975, NCI's budget has not increased at all in terms of 1970 (or "constant") dollars. That year the actual appropriation was \$699 million, while in constant dollars it was \$523 million. The President's request for NCI for FY 1979 was \$878 million, worth \$475 million in constant dollars. The final appropriation will be in the neighborhood of \$920-930 million, which would put it almost at the 1975 constant dollar level. . . . JEROME DECOSSE, chairman of the Cancer Clinical Investigation Review Committee, has moved from the Medical College of Wisconsin to Memorial Sloan-Kettering Cancer Center where he is the new chief of surgery. . . . ST. JUDE Children's Hospital has been doing research involving nutrition and cancer since 1953, Donald Pinkel, now with the Midwest Children's Cancer Center, said, supporting Jay Freireich's blast at Sen. George McGovern and McGovern's campaign to support more nutrition research at the expense of treatment (*The Cancer Letter*, Sept. 15). "A lot of nutrition research is going on that doesn't show up in any budgets," Pinkel said. "Diet has always been the leading form of quackery in treating any disease." Pinkel also offered his candidates as the primary culprits in the high cost of health care: "Blue Cross-Blue Shield, and the health care economic system". . . . SAN ANTONIO Breast Cancer Symposium, sponsored by the Cancer Therapy & Research Foundation of South Texas, the American Cancer Society and the Univ. of Texas Health Science Center, will be held Nov. 11. Faculty will include Robert Goodman, Nathaniel Berlin, Bernard Fisher, Edwin Fisher, Stephen Carter, Stephen Jones, Olof Pearson, Marc Lippman, William McGuire, Charles Coltman Jr. and William Knight III. . . . PACIFIC ENDO-CURIETHERAPY Society will have its winter meeting Dec. 15-17 at the Wailea Beach Hotel, Maui, Hawaii. CME category 1 credit for 12 hours is offered. Contact Harvey Frey, society president, 5522 Sepulveda Blvd., Van Nuys, Calif. 91411, phone 213-997-1522.

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## NUTRITION PROGRAM "ADVICE" TO COME NOW IN FORM OF GRANT APPLICATIONS

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spent by all NCI programs on nutrition.

NCI Deputy Director Guy Newell, who has assumed management of the Nutrition Program, explained this week to the National Cancer Advisory Board how nutrition research now will be handled through each of the program divisions.

(A program announcement describing nutrition research opportunities suggested by each division follows, starting on page 4.)

The DNCP was started in 1974 following a congressional mandate in the renewal of the National Cancer Act. It was organized within the Div. of Cancer Cause & Prevention and headed by Gio Gori. At that time, the only funding mechanisms DCCP could use were contracts and cancer research emphasis grants.

Gori utilized the Diet, Nutrition & Cancer Program Advisory Committee and a series of workshops to develop ideas for research projects. He contended that committee members and workshop participants, made up of nongovernment scientists and experts in nutrition, for the most part, offered the best opportunity to get high quality advice from the scientific community.

Now that the program divisions can award traditional, investigator initiated grants, Newell feels that the best "advice" on "program development" will be in the form of grant applications from a broad segment of the scientific community.

Each of the program divisions had been supporting some nutrition research, mostly through contracts, and there were a handful of nutrition grants supported through the old Div. of Cancer Research Resources & Centers. They account for the difference between the \$7 million spent by DNCP (all through the Div. of Cancer Cause & Prevention) in 1978 and the \$18 million Newell said was being spent throughout NCI.

Newell told *The Cancer Letter* that the additional \$4 million was not assured and would not be earmarked in advance. "We'll have to wait until we see what kind of applications come in. If we get a lot of high quality nutrition grant applications, we might be able to compete for a chunk of the director's reserve." Director Arthur Upton sets aside 1% of the NCI appropriation for which program and division directors compete to support projects not funded through their budgets.

Newell told the Board that Upton's charge to him was to make DNCP institute wide, to strengthen it on a sound, scientific basis, "and to request whatever resources it might take to accomplish this. Implicit in his charge was an attempt to reconcile several operational definitions and several budget allocations, reset priorities for both program content and methods of

operations, develop an action plan that will insure steady and proper attention to nutrition, create a more 'corporate' responsibility for the program within NCI and be able to speak to and defend the program before the scientific community, the public and Congress."

Newell said he views his role as one of "management rather than direction. The direction will come from within the major NCI divisions"—etiology and prevention nutrition research in DCCP, treatment in the Div. of Cancer Treatment, and rehabilitation and professional education in the Div. of Cancer Control & Rehabilitation. Communication, planning, budget, legislation and resource development responsibilities will remain in the director's office.

The Cancer & Nutrition Scientific Review Committee, the group which reviewed nutrition contract proposals, has been moved along with other review groups to the new Div. of Extramural Affairs. This committee could be utilized to review grants, but most of those probably will go to the NIH Div. of Research Grants for study section review. DRG has a nutrition study section, and proposals closely related to one or another of the major disciplines probably will be referred to the appropriate study section.

Newell said DRG has agreed to add members to study sections if necessary to assure fair review, or to appoint ad hoc committees. He said DRG's cooperation was evidenced by agreement to postpone the deadline for the first round of grant applications coming out of the new program announcement. Normal deadline for the next round is Nov. 1, and DRG agreed to Dec. 1 to give investigators enough time to adequately prepare their proposals.

While assuring that all present contract commitments will be honored, Newell pointed out that the emphasis from now on will be on investigator initiated grants, including program projects, and on young investigator awards. Future contracts will be limited to support services, data acquisition, workshops, conferences, and in some instances the funding of special programs such as the group of nutritional status assessment studies currently being awarded.

"The establishment of nutrition research units at institutions around the country is a particularly important new initiative of the DNCP now in the planning stage. They will ensure the presence of expert nutritional consultative services in each region of the country. It is anticipated that most, if not all, of the research units will be located in institutions where a nucleus of researchers and clinicians working in nutrition already exists," Newell said.

Congress has been extremely critical of NCI for not spending more money on nutrition, with most congressional critics citing the budgets of DNCP. Upton attempted to answer by pointing out that this was only part of the nutrition research supported by NCI, but it was difficult to pin down a definite figure.

Newell said "The primary reason for the discre-

pancies among the figures is the differing definitions used in identifying nutrition activities. Since nutrition research is frequently combined with other disciplines such as biochemistry, physiology, toxicology, pathology and epidemiology, designation of a particular activity as nutrition depends upon the breadth or narrowness of the definition used."

The \$18 million (specifically, \$18.7 million) Newell cited "includes a wide range of activity, intramural and extramural, training and support activities," he said. "As I learn more about this area, I'm increasingly impressed at how varied and complex it is. Because of this I think it quite justifiable to accept a broad approach rather than a narrow one. No single classification of projects or dollars will ever satisfy all of the varied components of this area.

Newell discussed a number of theories on relation of diet and nutrition to carcinogenesis.

"Some of these theories are quite esoteric, others less so. Some lend themselves to possible dietary modifications far more easily than others. The identification and systematic review and evaluation of these theories is an important task for the DNCP.

"Fiber is the residue of plant cells after digestion. There is mounting epidemiologic evidence associating low fiber intake with a high incidence of colon cancer. This form of cancer is far more prevalent in westernized cultures consuming large amounts of refined sugar, animal protein and other low-fiber foods.

"Exactly how does fiber exert this anticarcinogenic effect? Several hypotheses have been advanced. First, by increasing fecal bulk, dietary fiber reduces the concentration of carcinogens in the intestinal tract, thus reducing carcinogenic exposure of the intestinal epithelium and possibly also reducing carcinogenic and precarcinogenic absorption. Since increased fecal bulk also decreases intestinal transit time, potential contact time of carcinogens with epithelial cells and absorptive surfaces is shortened. The metabolic processes and population of endogeneous microflora may also be affected in a way that diminishes chances of mutagenic or carcinogenic changes.

"Fats—numerous theories have been proposed:

"—Affect metabolic pathway leading to endogeneous hormone levels (breast and endocrine related cancers).

"—Stimulate bile acid production (suspected carcinogen).

"—Whether total fat, saturated fat or unsaturated fat is not known.

"—Some endogeneous contaminants introduced during processing of edible fats and oils may be carcinogens.

"—Cooking of food in unsaturated fats produces hazardous compounds.

"—Thus, fats may be a direct carcinogen, a cocarcinogen with other substances, a promoter, or vehicle for introduction of exogenous contaminants.

"Food additives—These are used extensively in food processing in this country, and the identification of carcinogenic substances in some of these additives has led to the removal of a few from the market. No comprehensive testing for possible carcinogenic qualities in all the additives has been conducted, and therefore no definitive statements can be made about their relative safety. However, as some researchers have pointed out, testing of substances in additives has been far more extensive than that of naturally occurring substances in food, which may also be potentially dangerous. While wholesale banning of additives is not warranted at this time, there is some logic to the argument that additives should be minimized.

"Aflatoxins—These are produced by fungi which normally grow on peanuts, soybeans, corn and certain other crops. They are the most potent hepatocarcinogen yet identified. Presumably, the molds which might be dangerous are removed prior to eating these foods and there is little real risk associated with their consumption, in this country.

"Artificial sweeteners—The possible carcinogenic property of artificial sweeteners has created considerable concern in this country, where they are consumed in large quantities. Cyclamates have already been banned and saccharin is undergoing rigorous investigation as a consequence of its association with bladder cancer in some animal studies and epidemiologic surveys. Additional investigation was thought necessary before imposing the ban on saccharin since existing evidence was considered inconclusive by many investigators. Indeed, it is the conclusion of NCI that this evidence does not establish a role for saccharin in the causation of human bladder cancer. The Food & Drug Administration and NCI are currently conducting a large-scale study which hopefully will resolve the debate.

"Alcohol—This is known to irritate the mucosal linings of the throat, esophagus and stomach. Whether this action, or other properties of alcohol, can induce cancer is not known. There is evidence to suggest that alcohol acts as a cocarcinogen or potentiator with tobacco to promote cancers of the throat and esophagus.

"Nitrates—Nitrosamines in relatively low doses have been shown to cause cancer in several species of animals. Whether these research findings hold true for humans as well has not yet been proven, but the possibility clearly exists.

"Nitrates and nitrites are substances which are transformed into nitrosamines, and their presence in food is therefore a matter of concern. Nitrates are naturally occurring chemicals in many vegetables which can be converted to nitrites by saliva. Nitrites are also added to processed meats and other products to preserve them and to give them a more appetizing color. Chemical reactions in the stomach form nitrosamines from the nitrites. Sodium nitrite in bacon

can be converted to nitrosamines in the frying process as well. Since nitrites are so important in preventing food poisoning, their outright ban would present problems for which solutions are not readily available. However, levels of sodium nitrite in bacon are being reduced as a result of a Dept. of Agriculture ruling.

"Cooking—The cooking process itself is a concern in the production of carcinogens. Benzpyrene, a known carcinogen, is created during the process of grilling some fat containing foods over a very hot heat source. The interaction of the dripping fat and the high temperature produces the benzpyrene which is then redeposited on the food in smoke.

"Mutagens which have not been fully identified are produced when fatty meats are broiled at extremely high temperatures. Pan frying of meats at lower temperatures produces other mutagens as a result of the reactions between fat, heat, and heated

trition that isn't well spent. I hope that scientific quality and opportunity will still play a crucial role in what you do."

Board member Bruce Ames, Univ. of California, commented that Nobelist Linus Pauling, an outspoken advocate of research with vitamins as a possible tool in cancer treatment and prevention, has not succeeded in getting NCI support.

"His application really wasn't a grant application," Schmidt said. "It was a request for funds. He wrote describing some research with vitamins in England and said if he had \$300,000 he could do some good work in that area. He was asked if he would put his request in the form of an application, and he said that he couldn't."

Upton said he had two sessions with Pauling. "I told him we were ready to support him and requested him to submit a grant application. He knows there is

ment that is the same as one concurrently being considered by any other NIH awarding unit.

Identify grant applications submitted in response to this announcement by writing at the top of the face sheet of the application: "Submitted in response to announcement on Diet, Nutrition & Cancer Program on nutritional aspects of cancer and its etiology/prevention, treatment, rehabilitation, and training."

#### **Etiology and Prevention of Cancer**

The Div. of Cancer Cause & Prevention of NCI encourages the submission of research grant applications in the broad areas of diet and nutrition, and these may be related to the (a) etiology of cancer and (b) prevention of cancer. Examples of studies judged to merit consideration are shown below. However, it is not the intent of this announcement to make or imply any delimitation relative to the nature or scope of the research which might be proposed. Examples:

Identification of mutagens/carcinogens in human food, body fluids, and feces.

Relationships between diet and excretion of mutagens/carcinogens.

Evaluation of methods of cooking/processing of human foods relative to the formation of mutagens/carcinogens.

Analysis of human foods for the presence of substances which inhibit the carcinogenesis process. Dietary/nutritional approaches to the inhibition of carcinogenesis.

Determination of whether individual vitamins, administered in excess of the maintenance dose, inhibit or promote the carcinogenesis process.

Studies on the role of dietary fiber in the carcinogenesis process.

Studies on the effect of diet/nutrition on tumor induction, tumor incidence, activation/inactivation of chemical carcinogens.

Relationships between diet and possible hormonal status, which may be related to cancer.

Questions concerning these grant-related activities of the Div. of Cancer Cause & Prevention should be addressed to:

Thaddeus Domanski  
NCI Rm 8C29, Landow Bldg.  
7910 Woodmont Ave.  
Bethesda, Md. 20014  
Phone 301-496-9448

#### **Treatment of Cancer**

The Div. of Cancer Treatment is responsible for the development and validation of treatment modalities for neoplastic diseases. There exists at this time an increasing awareness of the impact of malnutrition upon the quality of patient life, duration of survival, and responsiveness to antineoplastic therapy. For this reason, DCT is expanding its interest in the nutritional aspects of malignancy and its treatment.

Grant applications are invited for clinical and pre-clinical research in the general areas of anorexia,

cachexia metabolism (including etiology and pathogenesis), nutritional supplementation, and the nutritional complications of antineoplastic therapy.

End results in cancer management may well be enhanced by expanding our understanding of the mechanisms of malnutrition in cancer patients, and attempts at therapeutic intervention designed to interrupt these mechanisms and/or provide nutritional support. Specific research areas and suggested approaches are:

A. Anorexia—Specific etiologic factors are not fully understood. The role of possible altered taste sensation is unclear and deserves further investigation. Treatment-associated learned food aversions may contribute to the anorexia syndrome in cancer patients. Their role requires further clarification. Prevention of food aversions and/or their interruption with the use of behavior modification techniques are potential therapeutic maneuvers that deserve further study.

Pharmacologic treatment of anorexia through the use of appetite stimulants has received very little investigation but is a potentially important area. Adequate diets acceptable to anorectic patients need to be developed. One aspect of this problem might be the development of foods with increased acceptability for these patients.

B. Host-tumor competition—cachexia metabolism—Further work is required in the area of carbohydrate, lipid, protein, and overall energy metabolism of the cancer patient. Mechanisms of accelerated protein and fat depletion in these patients require further elucidation. Ineffective utilization of dietary carbohydrates with energy wasting metabolic pathways must be further clarified with the eventual aim being therapeutic intervention. Biochemical or dietary efforts to correct aberrant metabolic pathways might be useful in reversing or preventing malnutrition in patients with malignancy. Impact of enteral or parenteral dietary supplements upon aberrant metabolic pathways should be investigated to determine the most efficient source of calories for the cancer patient.

C. Consequences of nutritional deficiencies and the role of dietary supplementation—The role of enteral nutritional supplements in treatment of the cancer patient is not established. The clinical implications of dietary deficiencies and the potential efficacy of enteral supplements require further study in the following areas: (1) Maintenance of nutritional status of cancer outpatients; (2) Amelioration of the toxicities of antineoplastic therapy; (3) Potential enhancement of tumor responsiveness to antineoplastic therapies.

The role of parenteral nutrition in the management of the cancer patient requires further evaluation. The development and validation of techniques for efficacious, safe, and cost-effective outpatient parenteral nutrition is required, as are studies of less hypertonic

parenteral solutions containing lipids as a partial energy source with regard to efficacy and safety. Comparison with more conventional parenteral solutions would be an important aspect of these studies. Studies demonstrating nutritional efficacy of parenteral nutrition are also required (i.e., correction of abnormal body composition, reversal of glucose intolerance, and aberrant metabolic pathways). Prospective randomized studies of the effect of nutritional supplementation on the ultimate outcome of aggressive cancer therapy are also needed.

D. Complications of antineoplastic therapy—Both radiotherapy and chemotherapy have an impact upon the nutrition of the cancer patient when anorexia, mucositis, nausea, vomiting, and diarrhea occur. Abdominal radiation had been shown to cause a clinically apparent malabsorption syndrome. Preliminary studies are less convincing for malabsorption secondary to chemotherapy. In many clinical settings these are the dose limiting toxicities in antineoplastic therapy. Efforts aimed at further characterization, prevention, and correction of these complications of therapy might include the use of enteral or parenteral dietary supplementation, development of improved anti-emetic agents for concomitant use with antineoplastic therapy, and experiments with dose scheduling in combined modality treatments designed to reduce gastrointestinal toxicities.

E. Nutritional deficiencies as antineoplastic therapy—Preclinical in vivo laboratory studies have suggested that dietary exclusion of essential amino acids upon which the host's tumor can be shown to be dependent may inhibit tumor growth. Further work of this type with amino acids and other essential nutrients are required with the eventual goal being clinical evaluation of these modalities.

Questions concerning these grant-related activities for the DCT Diet, Nutrition & Cancer Program should be addressed to:

Daniel Kisner  
DCT—NCI Rm 8C08, Landow Bldg.  
7910 Woodmont Ave.  
Bethesda, Md. 20014  
Phone 301-496-2522

#### Rehabilitation

The Div. of Cancer Control & Rehabilitation is seeking investigators to develop specific nutritional regimens that affect the rehabilitation of cancer patients. In general, rehabilitation in cancer is concerned with prevention of impairment, maintenance of host strength and function, and the early restoration of functional loss as a result of cancer or its treatment.

The following examples are not meant to be inclusive, but only to illustrate some possible topics to be considered.

- A. Dietary counseling for pediatric patients and their families.
- B. Effectiveness of psychological support as an

appetite stimulant.

C. Consequences of malnutrition in host impairment and its relationship to patient rehabilitation.

Questions concerning these grant-related activities of DCCR should be addressed to:

Laurence Burke  
NCI Blair Bldg. Rm 617  
8300 Colesville Rd.  
Silver Spring, Md. 20910  
Phone 301-427-7477

#### Training in Diet/Nutrition Cancer Research

Programs are available for the training of individuals in the broad areas of diet and nutrition as these might relate to cancer. Two programs—"Individual Postdoctoral Fellowships" (F-32) and "Institutional Training Grants" (T-32) provide fulltime, longterm support to promising individuals and well qualified institutions through the National Research Service Act. Additionally, the "Cancer Research Career Development Program" (K04) provides support for individuals with demonstrated research potential who require additional experience in preparation for careers in independent research.

Questions concerning these NCI grant-related training programs should be address to:

Research Manpower Branch, NCI  
5333 Westbard Ave.  
Bethesda, Md. 20016  
Phone 301-496-7803

#### YARBRO RESIGNS, SAYS DISCORD MAKES MISSOURI CORE GRANT RENEWAL UNETHICAL

John Yarbrow, director of Missouri Cancer Programs Inc., a coalition of seven institutions developed as a regional cancer center, has informed NCI Centers Program Director William Terry that he will not apply for renewal of the center's \$300,000 a year core grant because "it will not be possible to fulfill the goals for this program that we established at the outset."

Yarbrow blamed failure to reach those goals on "institutional, regional, departmental and individual discord" among the center's participating institutions.

Yarbrow's statements were made in a letter to Terry, a copy of which was obtained by *The Cancer Letter* from a Washington source. Contacted by *The Cancer Letter*, Yarbrow confirmed his disappointment with lack of progress in his three years as head of the center and added that he had resigned as director, effective next February. He will remain at the Univ. of Missouri as professor of oncology and chairman of the department of oncology;

Yarbrow told Terry that his decision was a matter of integrity and concern for the Cancer Centers Program.

"Any new idea meets opposition," Yarbrow wrote. "Some people and some institutions are ready for

change, others are not. Proponents of change must skillfully and persuasively argue their cause. But, the most precious asset of those who advocate progress is integrity. We, who have supported the centers concept, should be the first to point out where we fall short of our goals. The statement of AACI on cancer centers made last year in Memphis, and the courage of the Core Grant Review Committee in its recent reviews, are all positive statements of our collective integrity.

[The Assn. of American Cancer Institutes approved a resolution calling on NCI to fund existing and new centers strictly based on the quality of their programs and priority scores in grant review without giving existing centers any extra consideration merely because they are there. The Core Grant Review Committee has recommended against continued funding for several centers during the past year.]

"But we must speak as individuals as well," Yarbrow's letter continued. "Those who are the most ardent center advocates, the most outspoken center critics, must set personal examples. They, least of all, should claim success when the facts are otherwise. As I enter the fourth academic year in Missouri, it is clear that it will not be possible to fulfill the goals for this program that we established at the outset. Institutional, regional, departmental and individual discord remain, despite all efforts. It is for this reason that I will not make application for a renewal of the core grant for Missouri Cancer Programs."

Yarbrow, an MD and PhD, headed the Cancer Centers Program at NCI for three years before he went to Missouri in 1975.

"In three years, we've accomplished what I thought we should have accomplished in three months," Yarbrow told *The Cancer Letter*. "I'm ashamed to go to NCI and ask for renewal of our grant. We have made some progress, but not enough. I have seen other center programs worse than this. We could put on a floor show and perhaps get renewed, but I feel too strongly about the centers program and I will just not do it.

"People here just do not want to work together. There have been too many picky roadblocks. It would not be ethical to try to cover it up."

Yarbrow said he hoped that "when the shock (of his decision) sinks in, it will result in a change of directions." If the organization does manage to put together a renewal application without Yarbrow, it is not likely that could be done by the November renewal deadline.

### **COMP CENTERS MUST GET CORE GRANTS IN TWO YEARS, SUBCOMMITTEE SUGGESTS**

Comprehensive cancer centers which lose their core grants should be given two years in which to regain them or forfeit their prized recognition as comprehensive, the National Cancer Advisory Board Subcommittee on Centers has recommended. The NCAB was scheduled to act on the recommendation

later.

The policy approved by the subcommittee this week was a result of the review of 18 comprehensive centers by the Board undertaken to determine how well the centers are meeting the Board's criteria for comprehensiveness. It was also spurred by the dilemma the Board found itself in when one comprehensive center—the Colorado Regional Cancer Center—lost its core grant earlier this year, and another, the Illinois Cancer Council, had not secured a core grant.

Implicit in the subcommittee's recommendation is the feeling that centers which cannot compete successfully for core grant funding against comprehensive and other centers cannot be considered as having met the tougher requirements for comprehensive designation.

The subcommittee recommendation said:

"If a comprehensive cancer center loses its core grant and chooses to continue to be recognized as comprehensive, the center can re-apply for a core grant within two years. If the center fails to obtain a funded core grant within this period, or if the center decides not to re-apply for a core grant within two years, the center shall automatically cease to be recognized as comprehensive by the director of NCI."

The subcommittee approved two other recommendations dealing with the continued recognition of comprehensive centers. The review of existing centers turned up a variety of deficiencies among some centers, with the speculation that those which appear to be weakest may be in danger of losing their comprehensive recognition (irrespective of whether or not they have core grants).

The mechanics of how a center would become "de-recognized" had never been adequately considered by the Board or NCI. The subcommittee recommended simply that "comprehensive cancer centers shall continue to be recognized by the director of the National Cancer Institute on recommendation of the National Cancer Advisory Board."

The subcommittee and Centers Program staff had agreed following presentation of the review of existing centers that at least two of them would undergo review again within two years. They also agreed that all would be subject to review for comprehensiveness again at some future date, but there had been some disagreement at the meeting of the full Board on the mechanism for review. There also were suggestions for modifying the 10 characteristics for comprehensive centers established by the Board.

The subcommittee approved a statement delaying decisions on the mechanism (such as whether the review should be combined with the core grant review) for perhaps a year:

"The mechanism of review for comprehensiveness shall be determined by the Cancer Centers Program staff in conjunction with the Subcommittee on Centers of the NCAB; a final report will be presented to the Board by September 1979."

## RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Their addresses, all followed by NIH, Bethesda, Md. 20014, are:

Biology & Diagnosis Section — Landow Building  
Viral Oncology & Field Studies Section — Landow Building  
Control & Rehabilitation Section — Blair Building  
Carcinogenesis Section — Blair Building  
Treatment Section — Blair Building  
Office of the Director Section — Blair Building  
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

### RFP NCI-CM-87214

**Title:** Isolation of antineoplastic agents from plants  
**Deadline:** Approximately Dec. 1

NCI's Div. of Cancer Treatment will make available to interested contractors a request for proposal for the fractionation and isolation of antineoplastic agents from plants. The organizations should have capabilities and facilities for (1) the fractionation and isolation of antineoplastic agents from plants; (2) the determination of chemical structures of the antineoplastic agent from plants.

The objectives of this project are (1) to prepare by isolation enough of each compound to test for anti-tumor activity, to identify chemically, and to prove the structure if necessary and (2) to prepare additional quantities, usually a few grams, of those compounds that require more biological testing to determine interest to NCI (3) to develop isolation procedures suitable for pilot plant scale up if necessary.

NCI will provide the plant materials and in vivo tumor bioassays. The contractor may or may not elect to use inhouse in vitro bioassays. The facility must have the capacity for grinding plant samples of 25-500 lbs., preparation of extracts from 50 lb. samples, for performing all types of organic chemistry necessary for isolation of active compounds, and for carrying out organic structure and identification work.

A well instrumented analysis laboratory and adequate library must be available. The principal investigator must be trained in organic natural products chemistry, preferably at the PhD level from an accredited school and must have extensive experience in isolating pure compounds from natural products and in organic chemical structure determination.

It is anticipated that the total project will require a minimum of 12-15 technical man-years of effort

per year. The government will consider multiple awards of 4 technical man-years (without inhouse in vitro bioassay capability) and five technical man-years (including inhouse in vitro bioassay capability). The proposal may be at either level of effort and should clearly indicate levels being proposed. The number of awards to be made and the level of effort of each will be at the discretion of the government.

### RFP NCI-CM-87215

**Title:** Production of investigational parenteral dosage forms

**Deadline:** Approximately Dec. 1

NCI's Div. of Cancer Treatment will make available to interested contractors a request for proposal for pharmaceutical manufacturers to produce parenteral dosage forms for investigative trial in man. Most production assignments will require prepreparation of sterile lyophilized products between 5,000 to 10,000 x 20 ml vials per batch.

Chemical, physical and biological testing on all finished dosage forms will be required. All products are to be prepared to NCI specifications and in accordance with current good manufacturing practices. Organizations must submit evidence of inhouse competence and resources.

### RFP NCI-CM-87237

**Title:** Production of investigational oral dosage forms

**Deadline:** Approximately Dec. 1

NCI's Div. of Cancer Treatment will make available to interested contractors a request for proposal for the production of solid oral dosage forms (tablets/capsules) for investigative trial in man.

Most production assignments will require preparation of 100,000 to 300,000 tablets per batch. Chemical and physical testing on all finished dosage forms will be required. All products must be prepared to NCI specifications or in accordance with current good manufacturing practices. Organizations must submit evidence of inhouse competence and resources.

**Contracting Officer for the**

above 3 RFPs: John Palmieri  
Cancer Treatment  
301-427-8125

### NCI CONTRACT AWARDS

**Title:** Pharmacologic studies of antitumor agents, continuation

**Contractor:** Univ. of Texas System Cancer Center, \$30,526.

## The Cancer Letter

—Editor JERRY D. BOYD

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