THE CANCER LETTER
RESEARCH EDUCATION CONTROL

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Vol. 1 No. 28

July 11, 1975

Subscription $100 per year

NCI NEARS CONFRONTATION OVER CONSTRUCTION AS OMB CONTINUES OBSTRUCTIONIST POLICIES

One year ago, this was the Administration lineup NCI had to deal with on major policy and fiscal matters:

Richard Nixon, President; Roy Ash, director of the Office of Management & Budget; Fred Malek, OMB deputy director; Paul O'Neill, OMB associate director for Human & Community Affairs; William Fischer, O'Neill's deputy; Victor Zafra, health chief under Fischer; Anne Stone, OMB examiner for NIH; Caspar Weinberger, HEW Secretary; Charles Edwards, HEW Asst. Secretary for Health; and Robert Stone (no relation to Anne), director of NIH.

The turnover in the last 12 months could hardly be more complete: Nixon, driven from office in disgrace; Ash, Malek, Weinberger, Edwards and Fischer, resigned; and Robert Stone, fired by Edwards. Anne

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In Brief

PITTSBURGH JOINS LIST OF COMPREHENSIVE CENTER PROSPECTS; FDA SCHEDULES MEETING ON CANCER DRUGS

UNIV. OF PITTSBURGH is coming on strong as a prospect for comprehensive cancer center status. Although not yet on the list for site visits by the National Cancer Advisory Board (*The Cancer Letter,* July 4), Pitt could make the schedule for site visits next year with comprehensive designation in 1977. When UCLA and NYU are named later this year, that will bring the total number of comprehensive centers to 19. The Office of Management & Budget is determined to hold the line at 20, so the pressure will be on NCAB and the NCI director next year to decide whether or not they should defy the Administration and follow the law as spelled out in the National Cancer Act. . . . **NORRIS COTTON,** who was named to NCAB earlier this year after retiring from the Senate, has resigned from the Board. Speculation is that in the stalemate over New Hampshire's disputed election, the governor will appoint Cotton to resume his Senate seat until the matter is resolved. . . . **SIX NCAB** terms, including those of some key members, will expire next March. Going off then will be Harold Amos, Irving London, Gerald Murphy and Philippe Shubik, as well as lay members Elmer Bobst and Donald Johnson. . . . **ADD TO JULY** meeting schedule: FDA's Oncologic Drugs Advisory Committee, July 31 and Aug. 1, at FDA's Parklawn Bldg in Rockville, Md. Agenda for the July 31 open session includes discussion of clinical guidelines for anticancer drugs, preclinical pharmacology guidelines, guidelines for selection of drugs for clinical testing, guidelines for testing of anticancer drugs for children and infants, and NDAs on mitomycin and bleomycin. The closed session Aug. 1 will include a summary of pending INDs and NDAs. . . . **AND CANCEL** the Cancer Control Intervention Programs Review Committee meeting scheduled July 11.

MORE THAN 40 INSTITUTIONS SEEK NEW CONSTRUCTION GRANTS

(Continued from page 1)

Stone is planning to leave in the near future.

Only O'Neill and Zafra remain. O'Neill moved up to become deputy director under new director, James Lynn. Zafra so far is remaining in place and is still the man at OMB most frequently in contact with NCI.

Under Nixon, OMB illegally impounded NCI funds; submitted unrealistically low budget requests for NCI to Congress; attempted but failed to get a statutory limit of 18 placed on the number of comprehensive cancer centers; imposed severe and damaging limits on NCI job positions; looked for loopholes in the National Cancer Act to limit grants, training programs and the number of consultants NCI could hire; cut NCI information activities and used the money to beef up HEW's propaganda mill; and established the policy that no federal funds would be awarded for construction of new cancer research facilities.

With the wholesale departure of most of the policy makers responsible for that unremarkable record, one would expect some policy changes. The fact is, the only changes have been those forced by Congress through legislation.

The new budget act prohibits the Administration from impounding money appropriated by Congress, and specific language added to the Cancer Act when it was renewed last year closed most of the loopholes and increased NCI's authority to act independently in a number of areas.

OMB has not given up the fight, however. O'Neill is still telling NCI Director Frank Rauscher that comprehensive centers will be limited to 20, and repeatedly has insisted that no money will be released for new construction. He was forced to back down on construction projects at UCLA, NYU, Harvard, Columbia and Salk, but on the last occasion he emphasized that that was it. He even intimated that OMB would order NCI to stop accepting applications for new construction grants.

Here's what Congress added to the National Cancer Act last year regarding construction:

Sec. 410 (a)—"The director of the National Cancer Institute (after consultation with the National Cancer Advisory Board), in carrying out his functions in administering the National Cancer Program and without regard to any other provision of this act, is authorized to (subparagraph 9) award grants for new construction as well as alterations and renovations for improvement of basic research laboratory facilities, including those related to biohazard control, as deemed necessary for the National Cancer Program."

Congress emphatically and repeatedly repudiated the cancer program obstructionist policies of the Nixon-Ash-Weinberger regime. Are O'Neill and Zafra being permitted to carry on the policies of their departed bosses? It appears so, and OMB is heading for a confrontation with Rauscher, NCAB and the President's Cancer Panel.

NCI has received or is expecting to receive grant applications involving new construction from 11 institutions in fiscal 1976 asking for a total of $29.6 million. The institutions are Univ. of Arkansas, $.2 million; Univ. of California (San Francisco), $1 million; Univ. of Delaware, $1 million; Univ. of Miami, $3 million; Mid-America Cancer Center, $3.5 million; Mountain States Tumor Institute, $.5 million; Ohio State Univ., $2.5 million; Univ. of Rochester, $4 million; Sidney Farber Cancer Center, $3 million; Stanford Univ., $5 million; and Wayne State Univ., $5.9 million.

The applications from Ohio State and Rochester are also asking money for alterations and renovations which OMB is not opposing.

NCI expects to receive construction applications this fiscal year from Univ. of California (Berkeley) and the Colorado Regional Cancer Center, but has no line yet on amounts to be requested.

NCI also has received letters of intent expressing needs for construction from 28 additional institutions, most of which will probably be for new construction. They are:

Augusta Radiation Center—Medical College of Georgia, Univ. of California (San Francisco) in addition to the application noted above, Charity Hospital of Louisiana at New Orleans, Community Cancer Program in Memphis, Downstate Medical Center of SUNY, East Tennessee Cancer Research center, Ellis Fischel State Cancer Hospital—Cancer Research Center, Emory Univ. School of Medicine, Hahnemann Medical College and Hospital of Philadelphia, Illinois Cancer Council, Univ. of Illinois, Memorial Hospital of Phoenix, Mount Sinai School of Medicine, Univ. of North Carolina, Univ. of Pennsylvania, Univ. of Puerto Rico, Univ. of Texas at Houston, Thomas Jefferson Univ., Univ. of Utah, Virginia Commonwealth Univ.—Medical College of Virginia, Washington D.C. Area Cancer Coordinating Council, American Health Foundation, Medical Univ. of South Carolina, Hershey Medical Center, St. Louis Univ., Univ. of Oklahoma Health Sciences Center, Univ. of Texas Medical Branch (Galveston), and Univ. of Louisville.

NCAB Chairman Jonathan Rhoads has flatly stated that the Board will not heed any Administration order to stop accepting or reviewing new construction applications. Once the Board has completed final approval of a grant, the pressure will be on Rauscher to go ahead and make the award.

The Administration then would have several options—back down and release the money; refuse to release it; fire Rauscher and replace him with someone who would not make any more new construction awards.

That last option would bring on another "Saturday Night Massacre," and it isn't likely President Ford would risk it.

If the awards are made and the Administration refuses to release funds for them, the applicants would have solid legal grounds for court action. The intent of Congress is clear, and the successful suits overturning Nixon's illegal impoundments proved that the courts can read the law even if the President and OMB cannot.

RESEARCH OPPORTUNITIES IN DIET, NUTRITION PROGRAM OUTLINED

Basic and applied research, from cellular nutrition to "a rational understanding of normalcy ranges for human diet," will be supported by NCI's new Diet, Nutrition & Cancer Program.

Gio Gori, deputy director of the Div. of Cancer Cause & Prevention is program director for the new effort, mandated by Congress in the Cancer Act renewal last year.

Gori reported to the National Cancer Advisory Board progress in getting the program off the ground. A literature search is under way "to provide an initial and a continuing evaluation of current scientific knowledge and future developments," Gori said. And two workshops have been held to assess the state of the art.

One of the problems in understanding dietary effects on cellular nutrition is that the "depth of knowledge available today runs in the opposite direction" from the nutritional process of dietary intake, digestion and metabolization of food to the release of cellular nutrients in the general circulation, Gori said.

"There are history and methodologic reasons for this trend. Namely, it has been easiest, less costly and more convenient to study cellular nutrition in a laboratory setting. The study of metabolism and digestive processes at the animal level was somehow less easy, but still affordable.

"And least easy, popular and doable for the individual scientist was the approach to the rather complex logistic and design constraints that dietary and epidemiologic surveys require," Gori said.

"The same can be stated for the processes of digestion and transformation of nutrients—before their release in circulation—and cellular uptake. . . .

"But dietary understanding is where knowledge is most wanting, and where intensive and at the same time basic and elementary approaches are needed."

Research areas required include, Gori said:

- **Clarification of differential nutritional requirements of specialized cells and the toxic, carcinogenic or otherwise negative effects of unbalanced nutrient availability.**
- **Additional information on the impact of digestive disorders and imbalances on the final availability of cellular nutrients, and eventually on cellular normalcy and stability.**

A solid, scientific understanding of what is normal human diet is not available, Gori said, rendering irrelevent talk of dietary excesses and deficiencies.

"Too many times normalcy has been assumed or fabricated on the basis of traditional eating habits and values, cultural trends, food availability and agricultural realities, if not on marketing grounds alone," Gori said.

"The analysis of nutritional sequence in animals indicates that the cellular requirements are fairly stable among higher species. Namely, cells from different animals appear to all have a similar palate for a rather uniform set of nutrient building blocks.

"Where animal species differ markedly is in their ability to produce these building blocks from their dietary intakes, in their digestive processes and in their selection of food intake.

"It is also clear that dietary intake and digestive differences have an evolutionary background, and that the evolutionary record of man must be consulted if an idea of the range of normal human dietary intake is to be secured.

"From an evolutionary point of view, modern man is still outfitted with a body that evolved over millions of years to fit stone age conditions, where the food basket available was much different from our modern diet, and the caloric consumption was likely to far exceed the demands of our sedentary habits.

"A study of the adaptive mechanisms that have determined the present anatomy and digestive metabolism and cellular nutrition in man would help define the range of dietary intake that man did evolve to consider as 'normal.' Obviously this knowledge will have to be carefully interpreted, but it is a necessary first step."

NCI's need for a study of the anthropologic record of man does not mean it is ready "to sponsor safaris and expeditions to New Guinea or Central Tibet," Gori said. "This information is largely available in scattered different formats and only needs to be assembled and coordinated with this specific purpose in mind. Comparative evolutionary studies in different species will also help understand the current situation in man.

"Once a rational understanding of normalcy ranges for human diet is available, then it may be significant to talk of excesses and deficiencies and of accidental or intentional contaminants.

"This information, coupled with epidemiological studies, dietary surveys and exploratory studies in animals, can help define the epidemiological significance and eventually the carcinogenic potential of altered dietary intake in man—the impact of diet on hormonal balance, internal secretions, the composition and substrates available to the enteric flora, and the carcinogenic and toxic stimuli that may intervene on cellular and genetic stability, the immune status, the detoxification and reproductive competence of the individual."

Knowledge of nutrition in cancer therapy is at a

similar state of development, Gori said. "But the opportunities to be of immediate help to the cancer patient are very promising, as our workshops have indicated.

The intelligent modification of nutrition in the cancer patient requires some basic knowledge that laboratory and human studies can help to obtain. These include:

- **The host and its tumor must be viewed as competitors for the same available nutrients. Knowledge in this field would help clarify the precursors of cachexia, taste impairment, depression of appetite, toxic effects and nutrient depletion.**
- **Studies also will be needed to determine whether selective nutrient requirements of host and tumor can be exploited to starve the tumor and feed the host differentially.**
- **Causes of impaired food intake need to be investigated, those associated with toxic tumor effects, or digestive and anatomical alterations produced by surgery, chemotherapy, and radiotherapy.**
- **Nutrient depletion by therapy and synergistic or antagonist phenomenon between diet and therapy need to be investigated.**
- **Further development of artificial hyperalimentation techniques are necessary to define the formulation of nutrient solutions and to reduce their cost, to improve the hardware, to reduce the chances of sepsis and to devise portable infusion units for the use of ambulatory patients, that could be mass produced at reasonable cost.**

"All this will require clinical trials to establish the benefits of these techniques in the various forms of therapy available today, and it appears that a number of competent scientists stand ready to initiate these studies," Gori said.

Gori said that "hyperalimentation is today a major center of interest, where rapid advances are likely to occur under a coordinated and intensive effort. It is well known that the majority of cancer patients lose interest in food largely, we believe, because of a deterioration in taste perception.

"For the patient with a functioning gastrointestinal tract and not yet severely debilitated, a behavorial approach to hyperalimentation appears desirable.

"This would require a better knowledge of taste physiology and its modification in the cancer patient, a deeper understanding of food technology and flavoring, and of psychological or hypnotic techniques that may induce the patient to increase food intake.

"For the patient with impaired gastrointestinal functions—the head and neck patient, the stomach surgery patient, the patient with severe radiation enteritis—artificial intravenous hyperalimentation is the preferred approach.

"The pioneer work of Dr. Rhoads and his associates in Philadelphia, and the current work of Dr. Dudrick and his associates in Houston and other distinguished scientists throughout the country have established the feasibility of artificial hyperalimentation techniques."

Another significant activity of the program will be to compile and distribute dietary information helpful in the prevention and in the therapy of cancer, Gori said. An example is a pamphlet, produced by NCI's public information office and the Div. of Cancer Control & Rehabilitation, dealing with the problems of feeding young cancer patients. It will be followed by similar publications dealing with the specialized needs of other cancer patients, Gori said.

Selection of priorities for the Diet, Nutrition & Cancer Program will require a major effort, Gori said, because of the danger of diffusion considering the variety and vastness of nutrition interest.

The selection process will include recommendations of the newly-chartered Diet, Nutrition & Cancer Advisory Committee; input from the NCI divisions; interaction with specific consultants and workshops the program will sponsor.

"The program will coordinate with other NIH institutes and other federal and local agencies," Gori said. "But rather than become an all-encompassing nutrition study, it will focus on cancer-related problems and will attempt to stimulate other organizations to produce information relevant to nutrition at large."

The DNCP budget for fiscal 1976 depends on NCI's total appropriation, still a long way from final determination. NCI tentatively has the program budgeted for $5-6 million, including $2 million in Cancer Research Emphasis Grants.

Gori will present some suggested CREG projects to the advisory committee at its first meeting, scheduled for Aug. 19-20. "The DNCP will have a unique opportunity to test the viability of a unified program utilizing both the contract and grant mechanisms," Gori said.

CREG projects recommended by the committee and approved by NCI could be included in the next round of CREG announcements planned for September.

The rest of DNCP's budget will go into contracts. The first RFP is already out, for development, management and support services (RFP NO1-CP-55710-68, ***The Cancer Letter***, June 13). Deadline for proposals is Aug. 4.

A pre-proposal conference was held last week, with about a dozen organizations represented. Gori said he expects no more than five proposals from those organizations, although others not at the meeting could still enter the competition.

There probably will be no more DNCP RFPs until the end of the year or early 1976. Gori plans to ask the committee to convene a series of small workshops, each with 10-12 individuals with particular expertise, to work on developing specific proposals. These workshops will be held through the Fall.

Chairman of the program's advisory committee is Gerald Wogan, professor of food toxicology at MIT. Other members are William Darby, president of the Nutrition Foundation, NYC; Stanley Dudrick, director of the Univ. of Texas School of Surgery (Houston); Peggy Fry, assistant professor, Dept. of Pediatrics, Univ. of Texas (Dallas); Larry Garfinkel, assistant vice president for epidemiology, American Cancer Society, NYC; Willis Gortner, staff scientist, Human Nutrition & Family Living, U.S. Dept. of Agriculture; Joseph Kirsner, professor of medicine, Univ. of Chicago; Harold Sandstead, director, Human Nutrition Laboratory, USDA; Athanasios Theologides, professor of medicine, Univ. of Minnesota Medical School; William Thurman, provost, Univ. of Oklahoma Health Sciences Center; Myron Winick, director, Institute of Human Nutrition, Columbia Univ.; and Ernst Wynder, president, American Health Foundation.

Harold Amos, member of the National Cancer Advisory Board, is the Board's liaison with the committee. NCAB Chairman Jonathan Rhoads is an ex-officio member.

Gori said the committee reflects a cross section of scientific expertise, epidemiology, experimental carcinogenesis, animal nutrition, human clinical nutrition, biochemistry of nutrition, and clinical oncology. Also represented are the federal government, the academic community, industry, the American Cancer Society and other interested groups.

Gori noted that since the National Cancer Program deals continuously with emerging promising ideas, "the nutrition program will have to compete for attention. In the final analysis, the recommendations of the advisory committee and the inventiveness of the program will determine its level of funding relative to other important and timely efforts."

NIH EXPANDS MINORITY BIOMEDICAL RESEARCH TRAINING PROGRAMS

Two-year colleges, native American Indian tribes, and institutions with significant enrollment from ethnic minority groups are now eligible for research support under the Minority Biomedical Support Program of NIH.

The regulations, published June 30 in the *Federal Register,* broaden eligibility for the program, which is designed to encourage greater participation by minority group members in biomedical research. Under the original provisions of the program, grants were awarded for this purpose to predominantly minority colleges.

When the program was started in 1972, only four-year academic institutions with a student enrollment of at least 50% from ethnic minority groups were eligible for grants. The program, administered by NIH's Div. of Research Resources, now funds 69 grants involving 75 such institutions.

In addition to four-year colleges with 50% or more minority student enrollment, eligibility will now be extended to include:

– Two-year colleges with a traditionally high (more than 50%) minority student enrollment.

– Institutions with a significant student enrollment (but not necessarily more than 50%) which is derived from ethnic minorities.

– An Indian tribe which has a recognized governing body and which performs substantial governmental functions, or an Alaska Regional Corp. as defined in the Alaska Native Claims Settlement Act.

SMOKING & HEALTH CONTRACTORS MEETING AT ATLANTIC CITY, NOT HOT SPRINGS

The meeting of NCI's Smoking & Health Program contractors July 17-18 was announced as scheduled for Hot Springs, Va. (*The Cancer Letter,* June 27). The announcement was in error; the meeting will be held in the Haddon Hall hotel, Atlantic City, on those same dates.

The meeting will start at 9:30 a.m. both days and is open.

BIOMEDICAL PANEL TO HEAR PUBLIC ON ISSUES AT SEPTEMBER MEETING

The President's Biomedical Research Panel will be open for presentation by members of the public who wish to address issues relating to NIH and the Alcohol, Drug Abuse & Mental Health Administration at the Panel's meeting Sept. 30.

The meeting will be held at NIH, Bldg 31 Conference Room 6, starting at 9 a.m. The first day of the meeting, Sept. 29, is also open but will be taken up with other discussion.

Those intending to participate in the Sept. 30 meeting must send a notice of intent to the Panel by July 28. A detailed summary must be submitted by Sept. 1. Oral presentation will be limited to 10 minutes for each participant.

Requests to participate should be sent to Richard Louttit, Staff Director, President's Biomedical Research Panel, Suite 3100, 2401 E. St N.W., Washington, D.C. 20506.

The panel has been meeting monthly to carry out its congressional mandate to investigate and report on federally-funded biomedical research.

Contract Awards

LITTON BIONETICS' NEW FREDERICK CONTRACT DOWN FROM LAST YEAR

The biggest contract in the history of NIH won't be quite so big this year, although the scientific output it is generating and its cancer research support work are still gathering momentum.

Litton Bionetics' contract with NCI for the operation of the Frederick Cancer Research Center topped $25 million in the year just completed. Including obligations incurred for expenditures overlapping

into subsequent contract years, the total will be more than $28 million.

Under the recently negotiated renewal of the contract for the year starting June 26, Litton Bionetics will receive $17.6 million for management, operation and maintenance, plus an estimated $3 million for construction and another $3.8 million for interagency agreements, a total of more than $24 million. With operlapping obligations, NCI estimates the total will be $26.8 million.

The decline in expenditures is due to the fact that construction—including alterations and renovations—is tapering off as the contractor completes the job of converting the former Army biological warfare facilities to cancer research labs. Operations funding will increase more than $3 million, from last year's $14.2 million. Construction last year was $7.4 million.

NCI still has not decided whether or not to recompete the Frederick contract next year. After Litton Bionetics won out in spirited competition over an impressive list of organizations for the original contract, renewals were automatic. If the contract is not thrown open to competition for next year, it certainly will be the following year.

The work at Frederick was apportioned among 18 tasks last year. Three more have been added—biochemical markers, as task 19; research in colon cancer, task 20; and development of diagnostic animal labs, task 21. Other tasks are (1 through 18):

Virus production, developmental research, preparation of viral diagnostic test reagents, environmental control, NCI Office of Biohazard & Environmental Control, basic research program studies on selected bacterial species, large-scale bioassay, preparation & characterization of carcinogens, in vitro bioassay for potential carcinogens, animal holding, animal farm, basic research in viral oncology, special histopathology, safety of chemical carcinogens, basic research in chemical carcinogenesis, biochemical fermentation, and general support studies for the National Institute of Neurological Diseases & Stroke.

Michael Hanna, who runs the basic research program at Frederick, is trying to recruit two scientific directors for his staff—one for viral oncology and the other for chemical carcinogenesis. Hanna said they will develop their own basic research programs as well as work on the NCI tasks.

Other contract awards announced by NCI during the past week:

Title: Continuation of a primary breast cancer therapy group study
Contractor: Univ. of Pittsburgh, $494,000.

Title: Continued studies of the biochemical means by which receptor molecules bind to mammary cell surfaces and influence cellular biochemistry
Contractor: Mount Sinai School of Medicine, $60,500.

Title: Continued comparative study of xeromammography versus film mammography
Contractor: Univ. of Texas System Cancer Center, $55,900.

Title: Continue comparative study of xeromammography versus film mammography
Contractor: Duke Univ., $60,000.

Title: Investigation of possible correlations between morphological and epidemiological characteristics of breast cancer
Contractor: Univ. of Texas System Cancer Center, $38,750.

Title: Continuation of study of mammary gland responsiveness to multiple hormones
Contractor: Univ. of California (Berkeley), $94,400.

Title: Studies on human dihydrofolate reductases
Contractor: Univ. of Chicago, $25,854.

Title: Continuation of cultivation of normal and malignant human mammary cells: hormone dependent susceptibility of mammary tissue to transformation
Contractor: Pennsylvania State Univ., $67,400.

Title: Continuation of isolation of prolactin cells from the human and rat adenohypophysis: a new approach to the study of control of prolactin secretion in relation to mammary tumors
Contractor: Pennsylvania State Univ., $61,500.

Title: Continued biochemical and physiological investigations based on familial genetic patterns
Contractor: Montefiore Hospital & Medical Center, $191,900.

Title: Continue study of protein nucleic acid interactions in transcriptional controls of normal and malignant cells
Contractor: Duke Univ., $45,000.

Title: Therapy of patients with pancreatic carcinoma
Contractors: Yale Univ., $188,014; Sidney Farber Cancer Center, $181,208.

Title: Therapy of patients with brain tumors
Contractors: UCLA, $674,172; Memorial Hospital, NYC, $605,835; St. Louis Univ., $615,278; and Univ. of Tennessee, $541,453.

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Published fifty times a year by The Cancer Letter, Inc., 1411 Aldenham Ln., Reston, Va. 22090.