THE CANCER LETTER

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DCT TO FUND 11 SURGICAL ONCOLOGY GRANTS, CONSIDER SWITCHING $700,000 TO PROGRAM PROJECT RENEWALS

NCI's Div. of Cancer Treatment will fund 11 of the new surgical oncology grants at a cost of $900,000 for the first year, leaving $700,000 budgeted for the program which DCT probably will transfer to clinical program project grants where additional funds are desperately needed to avoid a devastating cutback in competing renewals.

Twelve program project grants were approved for renewal by the Clinical Cancer Program Project Review Committee. With the money

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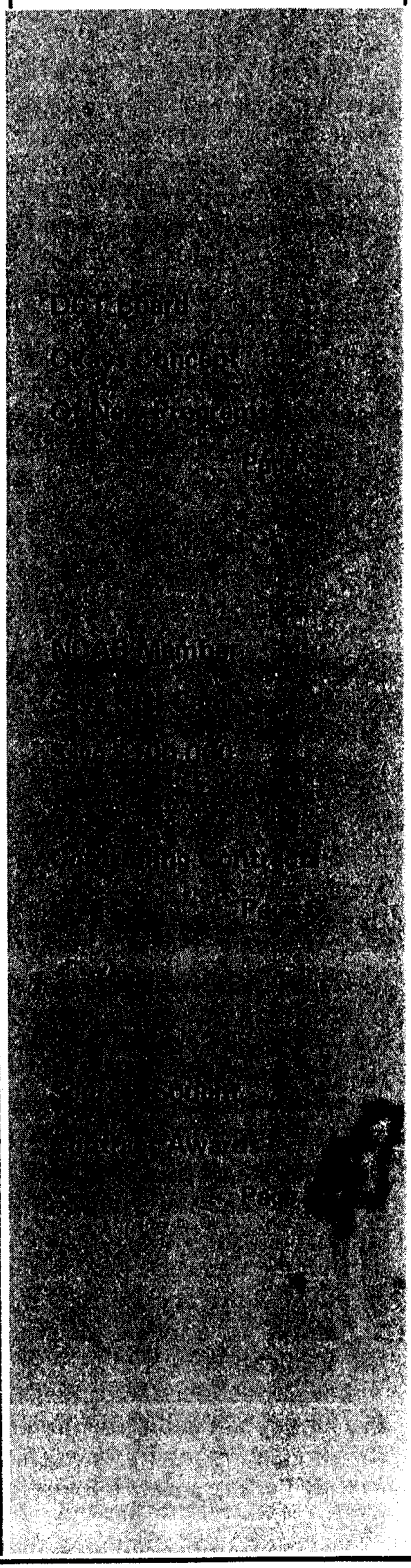
In Brief

NCI STILL UNDECIDED OVER SMALL HOSPITAL SEGMENT OF CHOP; MULTIHOSPITAL PROPOSAL REVIEW NOV. 14-15

FATE OF SMALL community hospital segment of NCI's new Community Hospital Oncology Program (***The Cancer Letter,*** Sept. 21) still is to be determined. The Div. of Cancer Control & Rehabilitation had hoped to award up to 10 contracts in each of three categories—multihospital, large single hospital, and small or rural hospital. Only three small hospital proposals were received; even if all are funded, that would leave as much as $700,000 a year which could be (a) held while an effort is made to generate more proposals; (b) used to fund more than 10 contracts in the other two categories; (c) reprogrammed into other areas. Donald Buell, program director, said no staff discussions have been held yet on the situation. There were 33 multihospital proposals, 23 large single hospital. Buell did not offer encouragement to those who would like to see the extra money support more contracts in those categories. "We developed the program on the basis that 10 in each group would provide satisfactory demonstration. It might be difficult to convince others now that we ought to fund more than 10, just because we have the money," Buell said. Review of the multihospital proposals will be conducted Nov. 14-15 and of the others in January. . . . **"UNRESOLVED QUESTIONS** in Oncology," a conference sponsored by the Children's Cancer Research Institute of San Francisco, will be held Nov. 12-13 in the Golden Gate Holiday Inn. The conference will focus on leukemia, lymphoma and bone and soft tissue sarcomas. Conference chairman is Jordan Wilbur, director of the institute, who may be contacted at CCRI, 2351 Clay St., Suite 512, San Francisco 94115, phone 415-563-8777. . . . **ST. JUDE CHILDREN'S** Hospital will hold its 14th annual Clinical Symposium Feb. 22-23. Current results in treatment of pediatric cancer patients will be presented, with emphasis on diagnosis and treatment for primary disease as well as the care of complications. The symposium is open to physicians, with a limit of 200, no registration fees. Register by writing to Associate Director for Clinical Research, St. Jude Children's Research Hospital, Box 318, Memphis 28101.



LAWRENCE OUTRAGED BY STUDY SECTION SCORING OF SURGICAL ONCOLOGY GRANTS

(Continued from page 1)

presently estimated as available for program projects and after funding the noncompeting renewals, NCI would be able to support only two of the competing renewals. The $700,000 reprogrammed from surgical oncology grants would fund two more, leaving eight unfunded unless DCT is able to switch over more money during the year.

The DCT Board of Scientific Counselors had recommended establishing the new initiatives in surgical oncology grants program last year. DCT budgeted $1.6 million for it, and 52 applications were received in response to the RFA.

DCT Director Vincent DeVita told the Board this week that the special ad hoc study section set up by the NIH Div. of Research Grants to review the applications had approved 26, with priority scores ranging from 208 to 417. If the entire $1.6 million were used for the program, the top 14 or 15 would be funded, through a priority score of about 322.

That would be a considerably higher payline than will prevail anywhere else at NCI, where the average cutoff will be at 247. DeVita said a heated debate has been raging within DCT over using the entire allocation for surgery grants or moving part of it to program projects or elsewhere.

"We did take the initiative to encourage funding of surgical oncology research," said Board Chairman John Ultmann. "We received a substantial number of applications. The Board has always spoken to excellence and a balanced program. DCT is asking the Board to give advice to staff on the matter."

"I always speak for excellence," said Board member Charles Heidelberger. "We should not take the actual numbers too literally. This was the first time this study section met. I suggest we go to (a priority score of) 288. That would fund 10 grants."

John MacDonald, director of DCT's Cancer Therapy Evaluation Program, later determined that funding to a score of 288 would include 11 grants and require $900,000.

"You are very generous, Charlie, in terms of the inexperience of the study section," commented Board member Enrico Mihich. "If they were primarily people who understand surgical oncology, then the intimation they did not understand the subject is negated. It could be they were inexperienced in grading, or the applications were poor. The issue may be, should we educate the study section, or educate the applicants."

Board member James Holland suggested that if all the money allocated for the grants is not spent now for surgical oncology, the remainder be "held in escrow" while a new RFA is issued to generate more applications.

DeVita pointed out that that probably would not be possible. Grants submitted as the result of a new RFA could not be funded in time to use FY 1980 money, and it could not be carried over to 1981.

Board member Walter Lawrence, director of the cancer center at the Medical College of Virginia and chairman of the department of surgery there, is also the current president of the Society of Surgical Oncology. He is now the DCT Board's chief spokesman on matters relating to surgery; he was outraged by the study section's scoring of the applications. (Lawrence was not an applicant himself.)

"We're looking at an artificial procedure," Lawrence said. The list of surgical oncologists which had been submitted to NIH as prospective members of the study section included many who had developed proposals for the grants and thus were not allowed to serve on it. "That left in the pool of reviewers some of the most naive people who had not participated in the review process before," Lawrence said. ". . . This is a funny system. I was offended that I was not permitted to participate in the review."

DRG had asked Lawrence to serve on the study section, but a previous commitment made him unavailable at the time selected, and DRG declined to change the days to accommodate him.

Arguing that persons not familiar with the NIH priority scoring system would not have an appropriate feel of how scores are assigned, Lawrence said, "When you say there is excellence at this number and not at that, you're smoking pot."

DeVita said that "excluding the most knowledgeable people. . . is part of the process. The surgical pool is small, and I don't know how to get around it." But he noted that his staff had looked over all the applications and had agreed that there was "a natural break" at the 288 score, above which the applications diminished significantly in quality.

"I think there was definitely a range of quality and it was reflected in the priority scores," MacDonald said. "And I think 288 is a reasonable break."

A motion to recommend paying the surgical oncology grants to the 288 level was approved.

Board member Philip DiSaia pointed out that in comparing the funding of approved grants throughout NCI, 11 of 26 (42%) was not bad. NCI will be able to fund only 30-35% of competing R01 grants this year.

Board member Carlos Perez said "the more important issue concerns sustained support for surgical oncology."

"Those grants will be funded for more than one year," Ultmann pointed out.

"But they are few," Perez said. "We need 10 more next year, and 20 the following year."

Holland's motion, "that it is the sense of this Board that surgical oncology research be encouraged and that the director of the division be asked to pursue with whatever method he feels best," was approved unanimously.

DCT BOARD APPROVES CONCEPT OF NEW PROGRAMS, INCLUDING "TASK ORDER"

The Div. of Cancer Treatment Board of Scientific Counselors, after "concept review" of proposed new initiatives, approved 11 new contract supported projects including pediatric phase 1 and 2 studies and a $1 million a year effort to determine if human tumor cell cloning assays can be used for drug screening.

The pediatric phase 1 and 2 studies will make use of a little used mechanism, the "task order" contract. The estimated first year cost of the five year awards is $250,000. DCT's description of the project:

"There is a large body of clinical evidence which demonstrates that childhood malignancies differ remarkably from adult malignancies in biology and response to therapy. In addition, children tolerate chemotherapeutic agents to a greater or lesser extent when compared to adults making the direct application of adult phase 1 data unreliable. Lack of accurate phase 1 data in children may lead to unevaluable phase 2 studies if less than maximally tolerated doses are employed, or may lead to serious side effects if the MTD is inappropriately high. The scarcity of investigational patients with these diseases makes accurate toxicologic and therapeutic studies mandatory.

"Pediatric phase 1 studies are currently being conducted on an ad hoc basis by members of the Pediatric Subcommittee of the Phase 1 Working Group, at the discretion of the investigators and without reimbursement. There is no mechanism by which new agents of theoretical interest can be assigned for evaluation in young humans. Phase 2 studies are conducted by the pediatric cooperative groups and by cancer centers, but not all new agents developed by NCI are entered into phase 2 trials in children, often because adult data are not encouraging. NCI thus proposes to collect a pool of investigators to be funded by a contract retainer who could do studies on a task order basis when the need arises. Such studies would be generated and completed in a short time."

DCT's definition of a task order contract:

"The purpose is to make available several contractors who have the capability of performing specific project requirements as designated by the government. This type of mechanism provides the capability of a quick response to a specified requirement, makes accessible a pool of contractors with varied expertise to deal with changing requirements, isolates costs for each project, provides flexibility for funding (funds are committed only as needed), and avoids prolonged contract competitions once the master contracts have been competed and awarded."

Board member James Holland, who is chairman of Cancer and Leukemia Group B, argued unsuccessfully to direct the project into the two cooperative groups which now include a major portion of the country's pediatric oncologists—the Children's Cancer Study Group and the Southwest Oncology Group.

DCT staff members pointed out that members of the groups could compete for the contracts, but Holland argued, "That's wasteful. You have virtually all the pediatric oncologists in two groups, and now you're not dealing with them."

Holland's motion to table the proposal died for lack of a second, and the Board approved it with no further dissent.

The proposal for application of the human stem cell cloning assay to drug screening would cost an estimated $1 million for the first year of a three year program, and staff said it would result in three to four contract awards. The program was described:

"The aim is to examine the feasibility of using human tumor cell cloning assays for drug screening. Fundamental studies have indicated that renewal cells arise from subpopulations of stem cells, themselves capable of reproducing and of maturing as well. Conceptually, then, a tumor stem cell is one which may reproduce or may give rise to tumor specific progeny cells. Thus, human tumor stem cell assays may provide models for drug screening with greater clinical predictive value for treatment of specific human cancers.

"DCT, cognizant of the potential value of human tumor screening models, has developed and used human tumor xenografts in mice. While results in no way negate the proposition that human tumors are effective screens, in vivo human tumor screening at a moderately high level has imposed logistical problems related primarily to the need to breed large numbers of immune deficient mice and maintain them disease free for long periods. Costs have limited the spectrum of xenograft models to three, each representative of an entire tumor type. In an attempt to shorten the test duration, Program is placing greater emphasis on the subrenal capsule (SRC) models which are less expensive and less time consuming. This will permit a reasonably rapid dissolution of the backlog of drugs for panel xenograft screening and could accommodate a wider spectrum of human tumors. Despite these advantages; the use of SRC models will still be limited by dependence on mice and conceptual projection of use for an initial screen is not feasible.

"Recent advances have overcome the major hindrance to in vitro colony formation from human tumor explants, i.e., creating conditions that give cells a proliferative advantage over normal cells. An impressive number of human tumor stem cells have been successfully grown in conditional soft agar and used to quantify antitumor drug activity. The use of such assays for prioritizing drugs in development to clinical trials is feasible at this time. The objective of this project is to determine the feasibility of using current in vitro human stem cell models to relatively large scale screening. We anticipate the testing of

about 1,000 materials per year against 10 cell types, no more than four of the same type. Activity against one cell will impel testing against five or more tumors of that type. Compounds selected will become candidates for development to clinical trial. In the long range, success of this project will indicate that the models may be useful in earlier screening steps.

Board member Sydney Salmon, who with colleagues at the Univ. of Arizona has been instrumental in developing the tumor cell cloning method and is using it clinically to select drugs for cancer patients, was not enthusiastic about some aspects of the Developmental Therapeutics Program's plan for the project. After he left the room (because of his potential involvement in the competition), Board member Alexander Fefer said, "The vibrations I got from Syd is that the time is not right for this now, that a lot of questions are in the process of being answered."

"Don't allow your interpretion of Syd's feelings to guide you," DCT Director Vincent DeVita said. "That's why we asked him to step out of the room."

"The time is right," Board member Charles Heidelberger said. "We've always had this question, that there may be compounds not active in mouse screens that are active against human tumors. Let's get this question answered now."

"It's an area where grant supported research would be good, but also an area where the Cancer Institute needs to direct the work with a top notch project manager," Holland said.

Board member Sharon Murphy asked that the pilot study results be communicated to the Board at every meeting, and the project was approved unanimously.

Other projects approved were:

• Hydroponic cultivation of plants, $100,000 first year of three years, multiple awards possible.

"This project is for the production under hydroponic conditions (growing plants in chemical solutions) of plant materials of interest to NCI as sources of potential anticancer agents. Such plants must be produced in a period of 4-6 months in quantities sufficient for isolation of active compounds to meet NCI needs for toxicology and clinical studies. This will require development of hydroponic growth conditions for a variety of plants, optimization of such conditions, sampling plants for the presence of the desired compounds, and growing the plants in quantities sufficient to provide enough active material for NCI needs. Several medicinal plants have been grown commercially by using the method of hydroponics: Dioscorea, which produces a composition used as an intermediate in producing cortisone; Rauwolfia, which produces reserpine, and Colchicum which produces colchicine. In addition, the following have been grown hydroponically for commercial use: beans, chrysanthemums, cucumbers, green peppers and lettuce.

This would allow NCI to be independent in obtaining plants of interest from foreign countries regardless of political problems, e.g., Brucea from Ethiopia. In addition, the plant can be made to grow quicker and precursors may be found which would increase the yield of plant product desired. If plants for large collections can be grown hydroponically, adverse weather and soil conditions and environmental problems could be avoided.

"Three materials have been quite difficult for NCI to obtain, bruceantin, homoharringtonine and tripdiolide. The plants producing these materials have not been successfully produced by plant cell fermentation. In addition, difficulty in obtaining the plants has been a major problem and these three plants would be the prime candidates for hydroponic evaluation."

• Provision of animal facilities and performance of routine experiments and tests, $415,000 first year of five years, multiple awards possible.

"The major objective of this contract is to provide a well equipped animal facility for various laboratories in the Developmental Therapeutics Program. The contractor should have a well equipped animal facility for the maintenance of standard laboratory animals, including mice, rabbits, guinea pigs, rats, goats, and subhuman primates. The contractor should provide essential veterinary care for these animals, and technical assistance for required surgical procedures and postmortem examinations. The contractor should be capable of preparing antisera to various virus and cellular antigens and be able to show that the sera contain antibodies against the injected antigens by using routine tests such as immunofluorescence, radioimmunoprecipitation or serum cytotoxicity tests."

• Preparation and supply of fresh and cultured mammalian cells, $280,000 first year of three years, multiple awards.

"The major objective of this contract is to provide large quantities of well characterized normal and neoplastic mammalian tissue culture and human fresh normal and neoplastic cells, particularly leukemic cells, to various laboratories in the Developmental Therapeutics Program. The contractor should be able to supply 250 gm of monolayer cells. This work includes production of cell lines developed from primary explants of fresh neoplastic material, both adherent and suspension cell in origin. The contractor should also be able to provide 250 gm of suspension (leukocyte) cells from human and nonhuman primates, and be able to assay the cell lines for the production of and stimulation by specific growth factors. The contractor should be able to obtain tissues from drug-treated animals for tests on the effect of certain drugs on DNA and RNA synthesis, and be able to infect some cell cultures with type C RNA tumor viruses. The contractor should also be able to process up to 100 samples of fresh human blood per

year, and supply large quantities of purified viable human blood lymphocytes, either in the fresh state or after short term culture with phytohemagglutinin or other mitogens."

• Screening of radioprotectors, $100,000 first year of three years, multiple awards possible.

"Previous work by Yuhas, Walter Reed and others has demonstrated the feasibility of screening for drugs with radioprotector properties. The aim is to find new agents which protect normal tissues (gut, bone marrow, etc.) from the damaging effects of radiation and cytotoxic agents. The radioprotector properties of selected agents will be examined in both normal and tumor-bearing mice in direct comparison with WR-2721, the current standard in clinical trial."

• Evaluation and development of prescreens for evaluation of crude natural products, $100,000 first year of three years, multiple awards possible.

"This is a project to develop sensitive prescreens which are able to detect minute quantities of an unknown antineoplastic agent in fermentation broths and plant and animal extracts. The prescreen should be simple and quick enough to evaluate 1,000-3,000 broths/year and can also be used as an assay tool for isolation of the compound from the natural product mix. The initial prescreens to be evaluated will use the aminopeptidase enzyme, beta-galactosidase lysogenic phage induction, and the 3 microorganisms Candida albicans, Xanthomonos sp., and Agrobacterium tumefaciens. The aminopeptidase inhibition screen has been used by Dr. Umezawa for three years to test fermentation broths and to isolate the inhibitors. Five pure compounds have been isolated and two of these were active against PS in vivo. All five compounds were new structures. Aminopeptidases are found in the cell surface and materials which inhibit these enzymes affect the cell's life cycle. The beta-galactosidase lysogenic induction test was evaluated against approximately 2,000 fermentation broths at FCRC and has shown about 3% of the materials active. Two compounds (novel by the Berdy system) have been isolated and are presently being tested in the tumor panel. This test detects agents that damage DNA. Eighty-eight known natural product compounds were tested in this screen. Ten were active at doses of <10 μg/mg and thus actives from that screen will have to be dereplicated against these compounds. Several microbial screen shave been used by various pharmaceutical companies to identify new antitumor agents. Candida albicans has been picked because it is resistant against most antibiotics and recently two antibiotics (rapamycin and ravidomycin) which had good C. albicans activity were found quite active in NCI screens. Xanthomonas compestris was chosen because of its unusual cell wall and compounds similar to tunicamycin are the ones active vs. this organism. Agrobacterium tumefaciens is the organism that causes crown gall (cancer of plants).

"Additional prescreens will be considered but a rationale should be given for their possible use. Since at this time one does not know which prescreen is best, the prescreens which can be most easily adapted to mass screening will be used preferentially. In order to obtain second generation antitumor compounds and to obtain new types of compound from natural products, it is essential to have sensitive prescreens which indicate that minute quantities of an unknown compound (1 microgram/ml) in a fermentation broth or plant and animal extract have an interesting activity. Such a prescreening capacity would also allow us to isolate more quickly the material for in vivo animal testing."

• Literature monitoring, $100,000 first year of three years, multiple awards possible.

"The objective of this project is to develop and maintain systematic literature surveillance effort for identifying compounds reported in the literature which warrant acquisition based on their biochemical and other biological properties and structural characteristics. The published chemical, biochemical, biological, and patent literature represents a potentially rich source of novel structures. This suggests a strong need to monitor the widest possible range of scientific literature on a continuing basis. DS&CB staff routinely scan primary and abstract journals and search selected literature to keep informed on developments of their subject areas of interest, and select a limited number of compounds for acquisition. The magnitude of publications in the cancer area, however, precludes relying on this method to assure any completeness in the coverage of the relevant literature. In the past, this need was partially fulfilled by the several synthesis contractors. It is the objective of this project to close up the gap consequent on the phasing out of the synthesis contracts."

• Characterization and analysis of proetinaceous materials, $150,000 first year of three years, multiple awards possible.

"A number of proteins and glycoproteins exhibit antitumor activity in experimental systems. For the further development and evaluation of these substances in larger animals and ultimately in man, studies must be undertaken to characterize the materials and develop suitable qualitative and quantitative methods to ascertain the purity and quality of the material from batch to batch in both bulk form and in pharmaceutical dosage units. This project will be vital for the evaluation and characterization of substances developed through the Biological Response Modifiers Program."

• Systematic evaluation of fungi, $100,000 first year of three years, multiple awards possible.

"The function of this new contract would be to systematically evaluate the various genera of the fungal world for their ability to produce antineoplastic agents. This is an area of fermentation in the obtaining of antineoplastic agents that is almost com-

pletely untouched. Even in the antibiotic field fungi have not been evaluated systematically and only a few genera of the fungal world have been explored. The effort in fermentation research has been primarily designed for the evaluation of streptomyces because of the larger numbers of these found in soil, because of their proficiency in producing antimicrobial agents, their superb metabolism for producing such antibiotics, ease of handling, lack of pathogenicity, short fermentation time and ease of scale-up. However, because streptomyces were the group of organisms most prolific in producing antimicrobial agents does not mean they would be best for antineoplastic agents. We know that streptomyces were poor at producing antifungal agents. Because of the past history of only a few genera of fungi being examined under limited routine fermentation conditions, a great deal of room is left for research into the exploration of fungi for the ability to produce new antineoplastic agents. For this reason it seems logical to place stress on another area of the microbial world such as fungi to identify their potential for other types of compounds differing from those produced by streptomyces. The reason fungi have not been heavily evaluated in the NCI program is that the fermentation program (industrial contracts) was an offshoot of the pharmaceutical companies' search for antibacterial products which mainly involved streptomycete research.

"Fungi are noted for their ability to produce unique substances during fermentation both in the fermentation broth and also in their spores. Fungi are exceptionally good at producing secondary metabolites and are used a great deal outside of the pharmaceutical world. They produce certain soy sauces, souples and food used in Asia. We hope to evaluate 1,000-2,000 different fungi for their potential production of antineoplastic agents."

Holland, commenting that there are very few antifungal compounds, asked that the program be expanded, adding $100,000 if necessary, to include tests for such agents. The Board agreed.

• CAPRI retrospective data abstraction, $50,000, one year only, multiple awards possible.

"The Cancer Patient Research Information (CAPRI) system is a computerized data base of clinical information for patients treated by the Clinical Oncology Program (COP). The system has been iniated with data from patients currently on study. However, it is essential for retrospective studies that past data are also entered. The purpose of this contract is to secure services which will allow the past data to be entered into the system. The contractor will provide the services of two RN-data abstractors for 12 months. The RN-data abstractors will review the medical records of COP patients with diagnoses of major interest treated since 1970, and will fill out computer coding forms of the CAPRI system. Work on this contract will be conducted on-site.

"Having a computerized data base of COP patients since 1970 will permit many retrospective clinical studies of prognostic factors, natural history, treatment selection criteria and therapeutic evaluations to be performed without redundant chart reviews."

The Board later this week considered proposals of its subcommittee, headed by Enrico Mihich, for the Biological Response Modifiers Program. Details of those proposals will appear next week in ***The Cancer Letter.***

"BRING CONTRACTS UNDER CONTROL, SAVE $100,000 A YEAR," SAMUELS TELLS NCI

Sheldon Samuels, appointed earlier this year to the National Cancer Advisory Board, has stirred the Board's interest in taking a closer look at NCI's extensive and varied contract programs. The Board has statutory responsibility for reviewing, after study section scientific review, all NCI grants $35,000 and over. But it has no review responsibility for contracts.

Samuels' interset has little to do with the ancient contracts vs. grants hassles, although he agrees with the effort by NCI to deemphasize research contracts in favor of grants. He believes that government agencies in general could perform much more efficiently with their own employees a significant amount of the work they contract out to industry.

Use of contracts has been abused, starting with the Eisenhower Administration, Samuels commented at last week's meeting of the NCAB Working Group on NCAB Activities. "It's use has been presented as containing government when in fact contracts are multiplying government. I'm talking about the basic efficiency of the process, bringing in contractors to do routine work.

"This really has multiplied the cost of government," Samuels continued. "I would guess that if we could bring the contract process under control, we could increase the effective spending of NCI by $100 million a year."

Samuels, who is director for health, safety and environment of the Industrial Union Dept. of the AFL-CIO, said he was not objecting to contracts for unique services but for more routine work "that could be done more efficiently and less costly with government workers." Acknowledging that many agencies, including NCI, are forced to contract for those services because of position ceilings imposed by the Administration, Samuels said, "Then we ought to go to OMB and the White House and lay it out for them, show them what we need, demand the slots."

Zeroing in on NCI's biggest contract, the $25 million a year support of the Frederick Cancer Research Center through a contract with Litton Bionetics, Samuels suggested the Board have a special meeting at FCRC to review the operation there.

Louis Sibal, special assistant director of the Div. of Cancer Cause & Prevention, said DCCP Board of Scientific Counselors members James Watson and Ber-

nard Weinstein have completed "an intensive review" of FCRC and will present their findings at the November meeting of that Board.

"That's okay for the science, but how about the management?" Samuels asked. "We need more than just what Nobel Prize winners can tell us about the science."

"Dr. Watson takes pride in his administration of Cold Springs Harbor Laboratory, which he runs very carefully," Sibal answered.

"I retreat in face of the Nobel Prize committee," Samuels said. "But I would still like to have people who know something about government administration look at that contract."

Jane Henney, special assistant to the director of the Div. of Cancer Treatment, pointed out that each of the divisions with programs at FCRC have had those components reviewed by their respective Boards of Scientific Counselors. Alan Rabson, director of the Div. of Cancer Biology & Diagnosis, commented that other NIH institutes also have various operations there.

Working Group Chairman William Baker suggested that the intensive reviews of FCRC be summarized for the NCAB at its January meeting. "We can decide then if we should have a special meeting of the Board at Frederick."

NCAB Chairman Henry Pitot said the Board might profit from setting aside half a day at each meeting to discuss contract programs with division staff and members of their Boards of Scientific Counselors. "Within a year we could be apprised of what's going on, with research and resource contracts—what was proposed, what was funded, the rationale for each contract."

Switching subjects, Samuels challenged the acceptance by NCI epidemiologists and other investigators doing research in occupational carcinogenesis that the institute has no authority to demand access to places of employment. He submitted the following statement to members of the working group:

"NCI personnel during Board meetings and informally reiterate the misconception that the National Cancer Institute does not have access to a place of employment without employer's permission. This has been the basis for negative ratings of some grants, specifically discussed by staff and summarized by misinformed review committees.

"With appropriate civil rights protection, Congress has delegated (and the courts have confirmed) right of entry by the Secretary [of HEW]. As the attached language and legislative history of the Occupational Safety & Health Act indicates, the director of NIOSH has been delegated the functions of the Secretary of HEW 'to the extent feasible.'

"However, it appears that when Congress, through the appropriations process and through its approval of the structure and function of HEW, has mandated occupationally oriented studies to be conducted by the National Cancer Institute, the Secretary can delegate his right of entry to the Director of the National Cancer Institute within the bounds of 'feasibility.'

"NCI ought to collaborate and cooperate closely with NIOSH in occupational programs. But the staff of the National Cancer Institute must be instructed clearly and definitively not to require the permission or cooperation of employers as a condition of the granting of funds or contracting of services in the investigation of occupational cancer and related problems, not to downgrade any proposal which has not the permission of an involved employer and to correctly instruct the review committees.

"Naturally, NCI investigators should seek voluntary cooperation from industry. But lack of cooperation is no longer a barrier."

Director Arthur Upton said that "the Secretary has delegated that authority to NIOSH. To my knowledge, that authority has not been delegated to NCI."

Pitot said that a copy of Samuels' statement should be sent to each study section. But Upton suggested that first, "it might be appropriate for me to pursue this with legal counsel and the Secretary and ask that the authority be delegated to NCI for use when appropriate."

Samuels said he did not know of any grant proposal that had been turned down specifically because of a study section's view that accesss to employee or other work records was not possible. "It was a factor in one I know of, but I want to make it clear that it should have been turned down for other reasons anyway."

The Working Group asked NCI staff to prepare a proposal for discussion by the Board at its meeting later this month on whether to ask Congress to raise the $35,000 limit on grants which can be awarded by the NCI director without concurrence of the Board.

Inflation has cut drastically into the number of grants that could be awarded with that authority. The Working Group suggested that the limit should be increased to $50,000. The Senate was scheduled to mark up Cancer Act renewal legislation this week. Group members agreed the approach would have to be made to the House Health Subcommittee, which has not yet held hearings on a renewal bill, with the hope the Senate would agree to a higher limit in conference if there was no increase in the original Senate bill.

Thomas King, director of the Div. of Extramural Activities, prepared a background statement on the issue for the Group:

"The National Cancer Act of 1971 authorized the director, NCI, to award research grants under $35,000 after initial scientific review without secondary review by the National Cancer Advisory Board. The amount was interpreted to mean total costs (direct

plus indirect) for each of the budget periods of the project.

"In 1974, when the National Cancer Act was renewed, the authority was extended to grant applications with less than $35,000 in direct costs. This had the effect of increasing the dollar level by approximately 32%, the amount of indirect costs contained in an average new award.

"The purpose of the authority is to permit more timely awards by eliminating the time interval between initial review and NCAB action. The authority does not affect competing renewals which cycle on an established anniversary date.

"The time interval between initial review and secondary review by the NCAB is relatively short for the January and May meetings and more lengthy for the September/October round. For the latter, an application reviewed by study section in the summer and presented to the NCAB in September/October would have an award date of Dec. 1 or later. The time period is approximately five months.

"Under the authority granted to him the director has the option of funding the grant immediately in the current fiscal year or considering the application for funding in the subsequent fiscal year. NCI has used the authority to award traditional grants (R01), young investigator grants (R23), conference grants (R13) and research career development awards (K04). In some cases the awards were part of the institute's original funding plan and in other instances were made as an effective use of funds placed in the director's reserve near the end of the fiscal year. In all cases the applications selected were of high scientific merit and within the institute's funding guidelines."

"Even with $50,000, the way inflation is going, we're going to get fewer grants that would qualify," Pitot said. "There isn't much you can do with $50,000."

SOURCES SOUGHT

PROJECT NO1-CP-05603(291)

Title: *Independent and critical assessment of the existing information on the possible relationships of dietary components (nutrients and toxic contaminents) and nutritional factors related to the incidence of cancer*

Deadline for statement of qualification: *Nov. 16*

NCI proposes to contract with the National Academy of Sciences. However, other organizations which feel they are qualified may request copies of the RFP.

The assessment is to include review of pertinent available literature, transcripts and summaries of conferences, workshops and literature as well as information on current research studies. The state of the art assessment is to make recommendations on the information which should be communicated to the public and biomedical community on the dietary factors and nutritional components related to cancer incidence.

The contractor will also be expected to identify areas of research which are required to increase knowledge on the role of diet in the incidence of cancer. It is expected that the assessment will require meetings of experts in appropriate biomedical disciplines. The potential contractor must supply evidence that experts in disciplines including biochemistry, biostatistics, carcinogenesis, epidemiology, food science, medicine (including oncology), microbiology, nutrition, pathology, pharmacology, public education/information, etc. will participate in the study.

To provide the opinions to the public views of nutrition and the incidence of cancer, the contractor must provide for one or meetings with members of the interested public. In order to provide easy access to NIH staff dealing with research in nutrition, it is desireable, but not mandatory that the contractor be located in the Washington Metropolitan Area.

Organizations who feel they possess the necessary capabilities and who can meet the criteria listed below must supply the following required information:

1. Evidence of staff qualification in areas of diet and nutrition and management of similar studies as requested in this sources sought announcement. Curriculum vitae and other appropriate supporting documentation as required.

2. Access to and demonstrated evidence of collaboration with experts in biomedical disciplines required in the study. A list of consultants and/or collaborators and their project involvement for the preceding 12 months will be required.

3. Evidence of experience in and acceptance of other studies which have resulted in determinations of national federal policy. Contract numbers, titles, sponsoring agency and agency contact point for such studies must be supplied.

Ten copies of the resume of experience and capabilities must be submitted.

Contracting Officer: S.W. Ranta
Chemical & Physical Carcinogenesis
301-427-8764

NCI CONTRACT AWARDS

Title: Sera collection from high cancer risk populations, continuation

Contractor: Philadelphia Geriatric Center, $33,153.

The Cancer Letter _Editor Jerry D. Boyd

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