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NIH Reauthorization Lost In The Shuffle As Congress Adjourns; NCI Budget $1.723 Bil.

Racing to complete the FY 1991 budget and leave Washington before the November election, Congress this week adjourned without approving legislation to reauthorize NIH, including renewal of the National Cancer Act. The House took up and passed a Senate bill that included only two provisions, one establishing a National Foundation for Biomedical Research and the second establishing a center for medical rehabilitation within the National Institute of Child Health & Human Development.

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In Brief

Tormey To Replace Carbone As ECOG Chairman; Bishop Delivers First B.J. Kennedy Lecture

DOUGLASS TORMEY, Univ. of Wisconsin Medical School professor of human oncology and medicine and associate director of the UW Clinical Cancer Center, has been elected chairman of the Eastern Cooperative Oncology Group. He will replace **Paul Carbone,** who is retiring after 20 years as ECOG chairman. Tormey has been ECOG's executive officer; he was elected by group members to a three year term which begins in November. Carbone continues as director of the UW Clinical Cancer Center. Tormey received his MD from UW Medical School in 1964 and a PhD from the school's McArdle Laboratory for Cancer Research in 1969. . . . **MICHAEL BISHOP,** 1989 Nobel Prize winner in medicine, delivered the first annual B.J. Kennedy Lecture last month at Univ. of Minnesota Medical School. The lectureship in honor of Kennedy, Regent's professor of medicine and Masonic professor of oncology, was established by a $100,000 gift to the Minnesota Medical Foundation. Bishop spoke on "Oncogene: Bench to Bedside." . . . **BERNARD WEINSTEIN,** director of the Columbia Univ. Comprehensive Cancer Center, was awarded the 1990 Silvio Conte Award of the Environmental Health Institute of Pittsfield, MA, named for the MA congressman. The prize carries a $5,000 cash award provided by General Electric Corp. . . . **LEE ROGERS,** chairman of the radiology department at Northwestern Univ. Medical School, is the new president of the American College of Radiology. Other new officers are: vice president, **Tearle Meyer;** chairman, **James Moorefield;** vice-chairman, **Karl Wallace;** secretary-treasurer, **Carl Bogardus;** and council speaker, **Milton Gallant.** At its recent annual meeting, ACR awarded gold medals for distinguished service to **Jack Edeiken,** M.D. Anderson Cancer Center, and **John Kirkpatrick,** Harvard Medical School.

NIH Reauthorization Lost In Rush Of Congress To Leave Washington

(Continued from page 1)

Those provisions had been included in a reauthorization bill, but the reauthorization portions were removed.

Congress adjourned in the early morning on Oct. 28, having finally passed a federal budget for FY 1991, the $492 billion, five-year deficit reduction measure. Congressional conferees also agreed on, and passed, an $8.3 billion budget for NIH (see next story). But the lack of authorization could threaten NIH's expenditure of some of the funds that Congress intended to appropriate.

NIH's current two-year authorization expired on Oct. 1. However, the institutes continue to exist on their general authority granted by the law that established the Public Health Service.

Most seriously threatened by the lack of authorizing legislation is the ability of NIH to fund construction projects and provide training grants, since those two activities are expressly permitted under the NIH authorization.

Construction and training are two of the "special" authorities that set NCI apart from most of the other institutes within NIH. Another of special authorities granted to NCI is the permission to transmit a professional needs budget directly to the President--the bypass budget. The bypass budget for FY 1992 has already been transmitted to the President.

The National Cancer Act also establishes the National Cancer Advisory Board and the President's Cancer Panel. The authorization law also provides a separate line item for prevention and control research.

Ironically, NIH authorization is threatened at a time when NCI's special authorities under the National Cancer Act are not being contested. Since the act's passage in 1971, most renewals have been marked by disputes ranging from complaints about certain authorities to outright opposition to the act.

The lack of authorization is not expected to adversely affect NCI's day to day operations, with the possible exception of funding construction grants. "We probably won't do anything differently," an NCI source told **The Cancer Letter.** It is not the first time Congress has failed to reauthorize NIH before its authority expired. Congress will reconvene in January.

In July, Sen. Edward Kennedy (D-CA) introduced an NIH reauthorization bill in the Senate, and in August, Rep. Henry Waxman (D-CA) introduced a reauthorization bill in the House. Neither bill altered the National Cancer Act, but the Waxman bill mandated that 10 percent of NCI's bypass budget for prevention and control be appropriated.

The Bush Administration opposed the Waxman bill primarily because it would have ended the federal ban on human fetal tissue research (**The Cancer Letter,** Oct. 5). A Sept. 23 letter from HHS Secretary Louis Sullivan to Rep. John Dingell (D-MI), chairman of the House Committee on Energy & Commerce, outlined the Administration's opposition to the fetal tissue provision, as well as a section requiring that NIH supported clinical trials assess gender and racial differences in treatments under evaluation "even in the absence of a scientific reason to suspect that such differences exist," the letter said.

Conferees Approve $1.723 Billion For NCI, 5% Increase Over 1990

Congressional conferees last week approved and Congress has passed an $8.3 billion FY 1991 budget for NIH, including $1.723 billion for NCI. The amount for NCI is $89 million more than FY 1990, or a 5.4 percent increase, and $29 million more than the President's request.

The budget figures include a 2.41 percent across the board cut to forestall a Gramm-Rudman-Hollings mandated reduction. However, the budget figures do not take into account a $50 million "salary savings reduction" that HHS was ordered to take. NIH does not yet know what will be its share of that reduction, the NIH budget office said early this week.

Following are the conference figures for the other institutes. The amounts include training and AIDS: National Heart, Lung & Blood Institute--$1.13 billion; National Institute of Dental Research--$149.6 million; National Institute of Diabetes & Digestive & Kidney

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Diseases--$617 million; National Institute of Neurological Disorders & Stroke--$543.4 million; National Institute of Allergy & Infectious Diseases--$910.7 million; National Institute of General Medical Sciences--$760.5 million; National Institute of Child Health & Human Development--$480.9 million; National Eye Institute--$253.9 million; National Institute of Environmental Health Sciences--$243.1 million; National Institute on Aging--$324.8 million; National Institute of Arthritis & Musculoskeletal & Skin Diseases--$193.7 million; National Institute on Deafness & Other Communication Disorders--$135.2 million.

Weinburger, Wynder Win Top Milken Awards; Six Others Honored

Robert Weinburger of Massachusetts Institute of Technology and Ernst Wynder of the American Health Foundation will be the recipients of the Milken Family Medical Foundation's major 1990 awards for distinguished basic and clinical research in cancer.

Each will receive $250,000, the largest single cash prizes available exclusively for cancer scientists and second only to the Nobel Prize in any biomedical research field.

Six additional awards of $50,000 each, in basic scientific and clinical investigations, will go to Michael Gottesman and Stuart Aaranson of NCI, Owen Witte of UCLA, Thaddeus Dryja of the Eye and Ear Infirmary of Boston, Robert Ozols of Fox Chase Cancer Center, and Ke Hong of M.D. Anderson Cancer Center.

The awards will be presented Dec. 2 at the annual Milken Awards Dinner in Los Angeles.

Weinburger, professor of biology at MIT, will receive the award in basic science for his studies which demonstrated human oncogene activity seen previously only in rodent tumors.

Wynder, president of the American Health Foundation, will receive the award in clinical research for proving the carcinogenicity of tobacco more than 40 years ago, with the subsequent impact that finding has had on clinical cancer.

Basic science awards: Gottesman, chief of Molecular Cell Genetics in NCI's Div. of Cancer Biology, Diagnosis, & Centers, has been a leader in the use of molecular genetics and recombinant DNA technology to approach the problem of multiple drug resistance. Aaranson, chief of the Laboratory of Cellular & Molecular Biology in NCI's Div. of Cancer Etiology, was the first to show the relationship of oncogenes to cell growth factors. Witte, UCLA, has made critical findings involving the Philadelphia chromosome.

Clinical science awards: Dryja, an ophthalmologist, collaborated with Weinburger in retinoblastoma studies. Ozols, whose systematic and scientific approach to clinical drug resistance has led to methods for reversing resistance, is now moving those concepts into clinical trials. Hong's studies with retinoic acid have demonstrated that recurrence can be prevented in patients with multiple primaries in head and neck cancer.

NCI Stops Screening Trial In Men To Add Women, Ovarian Cancer

The recent Congressional pressure on NIH concerning equal representation of women in clinical trials has prompted NCI to stop a trial that was set to begin late this year.

The trial, called the Prostate, Lung and Colorectal Cancer Screening Trial, was to have studied the mortality effects of screening in men at a cost of $42.2 million. The Div. of Cancer Prevention & Control Board of Scientific Counselors gave concept approval to the 16-year trial last October.

The trial was proceeding through all of the necessary approvals and an RFP for the trial's data management center was issued last May, when NIH reauthorization hearings this summer in Congress emphasized the issue of equal representation of women in clinical research.

In August, the NCI Executive Committee decided that the PLC trial should be redesigned to include women, since colorectal cancer affects women and men in roughly equal proportions.

"We got down to all of the signatures and it was discovered that no women were included, so we went back to the drawing board," Charles Smart, chief of the Early Detection Branch, told the DCPC Board at its meeting last week.

NCI is considering several options in its redesign of the trial: a large study of prostate, lung, colorectal and ovarian cancer for women and men that would cost an estimated $64 million, or separate smaller studies in women and men of combinations of the four cancers.

"On balance I think we have a very good record" with regard to participation of women in clinical trials, NCI Director Samuel Broder told the DCPC Board. "We have reviewed our clinical research and clinical trials programs and found that women participate in every phase of NCI sponsored clinical research. NCI has proportional representation of women in our clinical trials programs and we will continue this policy in the future.

"I do not think we necessarily need to have a

requirement in which we have appropriate statistical power for independent subset analysis of men versus women," Broder continued. "I do think we need to have proportional representation according to the prevalence of the disease. I think if we do that we will be in the position of making sure that women are adequately participating and that the results of our studies have meaning for the entire population."

Broder emphasized the seriousness of this policy. "This will be an extremely high priority and it will be NCI policy that where women are not included in a study or are included in a way which is vastly under-representative, that an extremely cogent scientific defense will have to be made for such a study. Without such a justification we will not fund the study. Investigators that in some way do not live up to this bargain will not be able to complete their studies. This an extremely important issue. The simple expedient that the incidence rate or the event rate would be more efficiently dealt with [using] only men, in large measure, will not fly."

At an NCI-sponsored workshop on ovarian cancer screening held in September, a panel of gynecologists recommended pilot studies of ovarian screening modalities in a high risk population before launching a trial, Smart said. However, investigations by the Early Detection Branch found that conducting such a study would require as large a study population as that needed for a screening trial.

In late September, the branch held a teleconference of the gynecologists, who unanimously recommended a full scale screening trial. Smart said the gynecologists preferred that a screening trial for ovarian cancer be conducted independently of the other cancer sites.

"We won't know what method [for detecting ovarian cancer] is most effective without a large trial," said John Gohagan, project officer for the trial.

The Early Detection Branch will come back to the DCPC Board with a concept for the redesigned trial--or a set of trials--at the board's next meeting in January. However, the branch presented a preliminary draft of its outline for the new trial to the board.

Under the plan for the original PLC trial, men between 60 and 74 years old were to be screened annually by chest x-ray for lung and by digital rectal exam and prostate specific antigen for prostate cancer for four years. The men were to be screened by flexible sigmoidoscopy and digital rectal exam for colorectal cancer in the first and third years of the trial. Follow-up of the 50,000 screened men and the 50,000 controls was to continue for at least 10 years. The trial included plans for a data management and coordinating center, up to 10 screening centers and a laboratory. A two-year pilot phase was planned before the full scale launch of the trial.

Under the preliminary design for a large trial of prostate, lung, colorectal and ovarian cancer, 37,000 men and 37,000 women aged 60-74 would be enrolled in each arm of a two-arm study. The control arm would receive usual medical care, while the intervention group would receive screening.

The objectives of the trial or trials would be to determine whether, in men and women, screening with flexible sigmoidoscopy can reduce mortality from colorectal cancer and screening with chest x-ray can reduce mortality from lung cancer. In men, whether screening with digital rectal examination plus serum prostate specific antigen can reduce mortality from prostate cancer. In women, whether screening with pelvic exam plus CA 125 and transvaginal ultrasound can reduce mortality from ovarian cancer. The intervention group also would be screened for skin, neck and oral cancer.

The secondary objective is to assess screening variables other than mortality for each of the interventions including sensitivity, specificity and positive predictive value, as well as incidence, stage and survival experience of cancer cases.

The subjects would be given initial screens and then would be screened annually for three years for all exams except sigmoidoscopy, which would be given initially and then at three years. For the chest x-ray, possible options are to x-ray everybody, just smokers or to let the subjects decide.

Exams for head, neck, oral and skin cancer will be included because of the low cost and because the opportunity to have the exams may increase initial compliance, according to the draft plan for the trial.

About 10,000 or more subjects would be recruited at each screening center. Proposals will be solicited from military and veterans' hospitals, HMOs, cancer centers and university or other groups capable of putting together the staff and facilities to recruit subjects, conduct screening and follow-up all patients for at least 10 years. A single contract will be awarded for a study coordinating and data management center, which will be responsible for receiving and processing data in all phases of the study and will provide logistical support for meeting and other activities.

Pilot studies would take place in the first two years of the trial to determine acceptability of randomization by randomizing 300 subjects, logistics, background level of usage of each screening modality by surveys in each center's catchment region, and testing data forms and procedures.

If recruitment in the pilot phase is satisfactory, full scale recruitment would begin in the second year of the study.

The following costs were estimated for the screening procedures: sigmoidoscopy--$40.50; single view chest x-ray and transvaginal ultrasound--$20 each; PSA and CA 125--$10 each; digital rectal exam--$2.50; pelvic exam--$10; screening of mouth, neck and skin--$2.50. The costs are assumed to include salaries for medical personnel and to reflect equipment and overhead costs. Costs for the screening center for the first and second years of the pilot phase were set at $1 million and $1.5 million. In addition, $1.5 million would be allocated per year, including indirect costs, to cover other screening center expenses in years 3-16 such as data coordination, quality control, training and follow-up. The budget for the data management center would be set at $600,000 a year for each year of the trial.

Smart brought in several outside experts to discuss the need for a screening trial. Jonathan Berek, Univ. of California (Los Angeles), told the board that 20,400 new cases of ovarian cancer are expected in 1990, with 4,000 deaths. The majority of patients have advanced disease, since the disease is asymptomatic and usually not discovered until it has spread to the abdomen. About one to one and a half percent of cases may be considered familial.

Berek said there is no data that confirm that the serum CA 125 test will result in decreased mortality. It is not an appropriate test for premenopausal women. According to a recent paper by Robert Bast, 80 to 90 percent of patients with documented ovarian cancer studied had elevated serum CA 125 levels. A phase 2 trial in Stockholm found that overall specificity of the test is "really excellent," Berek said.

Transvaginal ultrasound has the potential for higher sensitivity, Berek said. It is better at detecting smaller tumors than transabdominal ultrasound. The relatively low number of ovarian cancer cases requires a very sensitive and very specific test, Berek said.

The consensus of the workshop was that "we are ready for a trial, but this should be a separate trial," Berek said, mainly because of the logistics. The ovarian tests require personnel than the other screens and patients probably would have to make more than one visit.

Board member David Alberts asked what ultrasound would add to the CA 125 test. Berek said the two methods would be complementary, and the ultrasonography would add specificity.

Gerald Chodak, Univ. of Chicago, told the board that the public is receiving mixed messages on prostate cancer screening. "We're practicing two different things. Ont the one hand, we are saying it's good to get screened. On the other hand, we have no idea if it is useful." About 40 percent of patients have advanced disease at time of diagnosis, and due to the aging of the population, men will be at risk of developing prostate cancer for a longer amount of time.

Which tests or combination of tests is better for prostate cancer? "There's a lot of conflict and controversy. The only way to find out is to study it properly," Chodak said. Increasingly, PSA is creeping into practice. Screening can be harmful, resulting in unnecessary biopsies and the possibility of impotence after treatment. A trial is the "only way to determine optimum health care policy."

Myron Melamed, Memorial Sloan-Kettering Cancer Center, discussed lung cancer and Harmon Eyre, Univ. of Utah Medical Center and a DCPC Board member, discussed colorectal cancer screening.

A recent report from the Congressional Office of Technology Assessment on the cost of colorectal screening in the elderly cautiously supported screening, Eyre noted. "I think there is a probability of a 25 to 50 percent reduction in colorectal cancer mortality with screening," he said.

Board member Charles Hennekens said the "strongest rationale" existed for a prostate and colon screening trial in men and a separate ovary and colon trial in women. "Lung has the weakest scientific rationale" for a study at this point, he said. One problem is that fast-growing lung tumors may crop up in the subjects in between their annual screens.

Board member James Holland suggested that the patients be given a health questionnaire during the interval to try to discover any problems. If this resulted in finding a tumor, it would be counted as a positive detection for the screening modality.

DCPC Director Peter Greenwald asked the board for its views on whether to conduct several small studies or a large, complex study. He said he personally favored smaller studies. He suggested doing a prostate study alone and an ovary study alone, possibly in conjunction with ongoing breast cancer programs. "You would miss colon cancer, but there are several studies in progress on colon cancer," he noted.

Alberts said he agreed with Greenwald on a separate ovarian trial. "We need to couple anything we do on ovarian cancer with breast and cervical cancer." However, he also agreed with Eyre that a colon trial is needed to test sigmoidoscopy, but it could be a separate trial.

Holland disagreed with Alberts, saying he thought

the plan for a screening center all four cancers is "extraordinarily attractive." It is possible that the trial would drop out the most complex procedure, transvaginal ultrasound, if it were found ineffective.

"It seems to be that breast cancer screening doesn't need to be put in the same level of investigational circumstance here, this is proved. The centers could offer both the control and the screened population mammography, and its not something we should be spending this precious money for at this stage of the game," Holland said.

Board member Carol D'Onofrio raised the question of compliance, noting that the medical personnel trained to conduct the gynecologic procedures probably are not trained for the colorectal procedures. Unless the procedures are done at the same time, there will be a fall-off in compliance, she said.

"We already have in this country well-defined units for mammography and pap smear," Alberts continued. "I just cannot imagine not taking advantage of that structure, and I can't imagine not adding simply this serum test as a first step. That is already structured, the cost I think would be much, much less than what is being suggested here. I think we have to break these tests down somewhat. In terms of compliance, we already have a captured audience."

Board Chairman Edward Bresnick noted the costs estimated for each organ site. "If you set up a separate prostate study, as I read this, the cost would be $28 million. If you add an organ or two onto that, you don't proportionately increase the cost, you add small segments of cost onto that. The combined organ trial would give you more bang for the buck than if you did each one individually."

Greenwald said one of his main concerns about the larger trial is its logistics. "I'm not sure if the logistics are as easy as it seems."

Antoine To Leave As RRP Director, Will Join Radiation Oncology Branch

John Antoine, director of the Radiation Research Program in NCI's Div. of Cancer Treatment for the past five years, will leave that position before the end of the year to join the Radiation Oncology Branch in DCT's intramural Clinical Oncology Program.

"Five years is long enough," Antoine told **The Cancer Letter.** "It's time to let someone else do this job."

The Radiation Research Program is responsible for all of NCI's extramural research involving radiation therapy, imaging, hyperthermia, photodynamic therapy, and related activities.

Antoine will be a senior investigator in the branch headed by Eli Glatstein, one of the world's premier radiation oncologists. Antoine said he plans to focus his research on radioimmunotherapy, photodynamic therapy, and halogenated pyrimidines.

Antoine joined NCI from the Univ. of New Mexico after a long and agonizing search by DCT for an RRP director after David Pistenma left to return to private practice. DCT Director Bruce Chabner at that time blamed the difficulty of recruiting a qualified radiation oncologist on high salaries they can command in academia/private practice.

"I don't anticipate we will have an easy time finding John's replacement this time either," Chabner said. "This is an important program, and the person who runs it can make a major contribution." But the factors that hurt the recruiting effort in the past still exist, he added. "There is no easy solution."

Chabner said that Glatstein and Cancer Therapy Evaluation Program Director Michael Friedman will serve as acting codirectors of RRP while the search goes on. They will be assisted by a committee of the DCT Board of Scientific Counselors chaired by Robert Holden, head of the Dept. of Radiology at Wishard Memorial Hospital in Indianapolis.

Antoine's move to the Clinical Oncology Program will be the latest of an "inmigration" of extramural scientific managers and former administrators to DCT intramural research. It is a trend that appears to reverse the one which threatened to decimate the intramural program when Robert Young, Robert Ozols, Marc Lippman and several others all left over a span of a few months.

During the past year, Gregory Curt, former DCT deputy director, returned from academia to take over the positions of NCI clinical director and director of the Clinical Oncology Program; Robert Wittes, former director of CTEP, returned from Bristol-Myers-Squibb to become chief of COP's Medicine Branch; and Michael Boyd, director of DCT's Developmental Therapeutics Program, gave that job up to return to full time research in drug development.

DCT Board Ok's $10.6 Mil. Renewal Of 'Critical' CTEP Support Contract

NCI advisors gave concept approval this week to recompetition of the major support services contract for the Cancer Therapy Evaluation Program, worth approximately $10.64 million over five years.

The Div. of Cancer Treatment Board of Scientific Counselors unanimously approved the recompetition

of the contract that CTEP Director Michael Friedman called "absolutely critical" to the program's operation. The contract will be separated into three contracts in the recompetition.

Friedman sought and received approval for a nearly $150,000 increase in funding for the contract from FY 1991 to FY 1992, plus an additional $49,000 for expansion "during periods of increased Group C activities."

The board also gave concept approval to a new RFA for studies in new approaches to treatment of upper GI carcinoma and a program announcement for surgical oncology research.

The concept statements follow:

Contract A. Support Services for the Developmental Chemotherapy Section/Biologic Evaluation Section, Investigational Drug Branch, CTEP. Contract B. Support Services for the Drug Management and Authorization Section. Contract C. Support Services for the Regulatory Affairs Branch. This is a recompetition of a contract held by Social and Scientific Systems Inc. Estimated annual amount: contract A--$1,154,187, contract B--$339,557 (board approval requested for an additional $48,655 [$388,212 total] to provide for expansion during periods of increased Group C activities), contract C--$635,000. Total approximately $10.64 million over five years.

The Cancer Therapy Evaluation Program is responsible for administration and coordination of most of the extramural clinical trials supported by the Div. of Cancer Treatment. CTEP is also responsible for the development of over 150 agents on which the division has filed investigational new drug applications with FDA. As the sponsor of these agents DCT must monitor the safety, efficacy, and drug distribution of the agents in the trials it sponsors, report adverse reactions in a timely manner, and prepare IND annual reports to the FDA.

The contract has been modified and expanded several times since its inception. Each of the branch-related functions have been overseen by separate co-project officers from the Investigational Drug Branch and the Regulatory Affairs Branches. It is felt that it would be in the best interest of CTEP if the contract were separated into three smaller contracts, because the current contract now serves distinct functions assigned to separate branches. Additionally, such a separation will enhance the chances of receiving proposals from the widest range of candidates.

Contract A--Support Services for the Developmental Chemotherapy Section/Biologic Evaluation Section: The contractor shall provide technical assistance for clinical research as follows:

1. Gather and assemble clinical data for delivery to the IDB senior investigators for inclusion into investigational new drug annual reports for each investigational drug and biologic as required by FDA. Organize, index, duplicate, store, and distribute annual reports and drug data as necessary.

2. Provide in depth investigational drug development planning and toxicity monitoring by analyzing specific drugs and diseases and coordinating letters of intent.

3. Attend scientific meetings concerning drug development and summarize the results for delivery to the IDB senior investigators.

Contract B--Support services for the Drug Management and Authorization Section: The contractor shall provide technical and administrative assistance for investigational drug distribution as follows:

1. Provide administrative and word processing support for Group C and special exception investigator and patient registrations and assist with drug distribution procedures.

2. Perform analyses of protocols, drug and investigator records, drug supplies, and drug costs relating to present and future distribution, and communicate with investigators or designees as necessary.

3. Conduct investigator mailings, maintain and store files, and provide photocopy service as necessary.

Contract C--Support Services for the Regulatory Affairs Branch: The contractor shall provide assistance in meeting FDA regulatory requirements for investigational drugs and shall be responsible for maintaining the Protocol and Information Office of CTEP, as follows:

1. Staff an onsite Protocol and Information Office responsible for: receiving all proposed protocols; abstracting scientific and administrative information for the CTEP Information System; scheduling and following the protocols through CTEP review; tracking the progress of approved protocols including status information, receipt and review of amendments, annual data summary requests, and scanning the literature for protocol-related publications.

2. Provide offsite staff and capabilities to: coordinate record-keeping for reported adverse reactions, prepare IND filings; update clinical brochures for DCT sponsored agents; monitor pending INDs and FDA queries regarding INDs; and coordinator mailing of copies of adverse reaction reports, annual reports, and other IND related information to pharmaceutical companies.

The amount obligated to the original single contract increased $687,000 from FY 1987 to 1991. Friedman said there was a corresponding 250 percent increase in IND filings, which the program handles for new agents for cancer, AIDS and some infectious complications. The program made 1,400 shipments of Group C drugs in the first year, while in the fourth year, 10,400 shipments were made. "It's a very vigorous, very dynamic activity," Friedman said.

The board approved the concept unanimously.

New Therapeutic Approaches and Clinical Correlates in the Treatment of Upper Gastrointestinal Carcinoma. Concept for a new RFA. Proposed first year award $2 million; project period three years. Planned date of announcement December 1990, anticipated award date December 1991.

Carcinoma of the organs of the upper gastrointestinal tract (esophagus, stomach and pancreas) are lethal tumors. Development of resistance to treatment (as manifested by tumor progression) is rapid even when chemotherapy with or without radiation therapy is effective. Taken collectively, the incidence of these tumors represents a major health hazard to 62,000 patients per year. Relatively few complete responses are noted and no patient with metastatic disease has been cured. Recently, however, promising results utilizing combinations of radiation or surgery and chemotherapy have been reported for esophageal cancer. These promising results need confirmation and wider application.

NCI supports, through contracts, grants, and cooperative agreements, extensive research efforts in the clinic and laboratory to describe and understand the tumor biology and treatment resistance of malignancies. Such efforts form the basis for the development of new treatment modalities to circumvent drug and radiation resistance. These include biochemical modulators,

cytotoxics, biological response modifiers, oncogenes, and growth factors alone or in combination with other modalities. However, as promising scientific advances occur in the laboratory, there is currently insufficient financial support for mechanisms to rapidly assess their potential clinical relevance. While progress is being made in the treatment of some carcinomas, few researchers are funded to study the drug-resistance and tumor biology of upper GI carcinoma.

The purpose of this project is to provide funding for clinical trials which take advantage of new developments in the laboratory or for innovative laboratory studies which are related to therapeutic clinical trials. Investigators should have a tightly focused, integrated research program at the interface of laboratory experimentation and concurrent clinical trials in upper gastrointestinal carcinoma.

Examples of clinical trials based on new therapeutic approaches under 1) more effective combinations of chemotherapy and radiation therapy, 2) radiation modifiers to enhance cell kill or protect normal tissue, 3) treatment therapies for overcoming drug or radiation resistance, 4) treatment therapies based on novel mechanisms of action, or 5) immunotherapies including monoclonal antibody therapy, radioimmunotherapy, and the use of new immunotoxins.

Some examples of therapeutic correlates include 1) phenotypic or genotypic alterations that appear to correlate with the development of drug or radiation resistance, 2) oncogenes, growth factors, and specific antigen expression on tumor cells for antibody development, 3) pharmacokinetic and pharmacodynamic measurements, and 4) biochemical pharmacologic parameters.

Research is not limited to the above examples. In addition, attention could be given to identify potential differences between ethnic groups.

The objective of this RFA is to foster interactions between basic science laboratories and clinicians performing clinical trials in upper GI carcinoma to improve treatment results and clinical outcomes.

NCI has funded only 11 grants in the past few years on upper GI cancer, Friedman told the board. "That's a relatively trivial amount of support for an area I think is very exciting," he said. "There are some very interesting leads now and we haven't looked at them very carefully."

Board member Paul Carbone asked why pancreatic cancer was included in the concept. Friedman said he included it with esophageal and stomach "because it's close by" the other organs, and there are currently no studies of pancreatic cancer.

Carbone questioned whether the RFA would hit "a target group that can be predicted in advance," and wondered whether the RFA is necessary. "We had task forces a few years ago on this."

Friedman replied that esophageal and stomach cancer are areas that "really stand out where there's a lot of opportunity for clinical research. I'm not reconstructing the Organ Systems [Program] again," he said. He also noted that the incidence of lower esophageal cancer is increasing.

The board approved the concept unanimously.

Surgical Oncology Research. Proposal for a program announcement. Planned date of announcement December 1990.

The treatment of cancer has evolved as a multi-disciplinary effort involving (but not limited to) the disciplines of surgical oncology, medical oncology, pediatric oncology and radiation oncology. The disciplines of medical oncology, pediatric oncology, and radiation oncology have developed strong cadres of academic investigators while academic development in surgical oncology has not kept pace. It is felt that surgical oncology is not keeping pace because of an insufficient number of both surgical oncology research programs and surgeons undertaking research related to cancer. Continued development of superior multi-disciplinary treatment of cancer is the long range objective of DCT, and the attainment of the goal requires sufficient academic strength in investigative surgical oncology.

NCI's DCT is seeking applications for research grants (RO1, R29, PO1) concerned with research in surgical oncology. Examples of relevant studies include mechanisms of metastases, effect of surgery on tumor cell kinetics, and host responses to surgery. Preclinical and clinical research is encompassed in this program.

Categories of research include, but are not confined to, the following: 1) pathophysiologic studies in laboratory models or in humans related to surgery and cancer, 2) laboratory and clinical studies that examine the biochemical, cytokinetic, immunological, or nutritional effects of cancer surgery, 3) therapeutic studies in which surgery or a surgical question is the primary treatment modality, 4) novel immunotherapy procedures such as assessment of specific lymphokines, stimulated cells, and autologous vaccines that require surgical input, 5) new surgical techniques relevant to staging or care of patients, 6) studies to identify prognostic factors relevant to the treatment of cancer patients, 7) surgical supportive care, and 8) regional chemotherapy or hyperthermia or radiation in which a surgical approach to the treatment site is a major aspect of the procedure. This program announcement is not restricted to the areas of surgical oncology research listed above.

The objective of this program announcement is to continue to stimulate and encourage surgeons to undertake academic research careers in investigative surgical oncology.

"A disturbing trend" is how Friedman characterized the lack of grant awards on surgical oncology. But the board was concerned that the program announcement would be seen as a simplistic solution to what board member Ralph Weichselbaum called "a deep-seated problem."

"This is not the way to fix the problem," said Board Chairman John Niederhuber, who is a surgical oncologist. "We need better access to centers, and access to leadership and administration of centers."

"It's not meant to fix the problem," DCT Director Bruce Chabner said.

"What would be the reason for not doing this?" board member William Hryniuk asked.

"It looks like we're trying to put a Band-Aid on a problem, that's why I'd almost vote against it," Niederhuber said.

"It's a public recognition of a problem--that's all," Friedman replied.

The board approved the concept unanimously.