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NCI ADDS NEW WRINKLE TO DRUG DISTRIBUTION PLAN—INDIVIDUAL INVESTIGATORS TO WORK THROUGH CENTERS

Physicians in private practice who are qualified as anticancer drug investigators but who are not affiliated with any organized clinical research program now will be able to obtain from NCI a wide range of investigational drugs in phase II and phase III studies—but to do so, they will have to work through one of 44 clinical cancer centers.

NCI's Div. of Cancer Treatment last week revealed the latest wrinkles in its drug distribution program which makes it easier for private physicians to obtain phase II and phase III drugs but at the same time provides mechanisms for controlling their use and securing adequate reporting.

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In Brief

CONGRESS CORRECTS AN INEQUITY; CALIFANO GETS A HEALTH ASSISTANT—FORDHAM OF N.C.

NATIONAL CANCER Advisory Board, in presenting its arguments to Congress for extending the three-year limit on cancer center grants to five years, pointed out that this would only be fair, since the Heart, Lung & Blood Act authorizes five-year grants to centers in those fields. The House Health Subcommittee agreed that an inequity existed and proceeded to correct it by withdrawing the five-year grant authority from the National Heart, Lung & Blood Institute. All center grants now will be for three years. . . . **HEW SECRETARY** Joseph Califano finally found someone who would agree to be his assistant secretary for health—Christopher Fordham III, dean of the Univ. of North Carolina Medical School. Fordham is 50, a graduate of Harvard Medical School and former vice president of the Medical College of Georgia. He has been dean at North Carolina since 1971. Three others turned down the job, reportedly because Califano had already made a number of significant health decisions. They were David Hamburg, head of the Institute of Medicine at the National Academy of Sciences; Charles Sanders, director of Massachusetts General Hospital; and William Roy, former Democratic congressman from Kansas. . . . **TWO CHEMICALS** included in the infamous "backlog" in NCI's Carcinogenesis Bioassay Program were reported out of the backlog last week. Reports on trichloroethane and dimethoate were published in the *Federal Register* March 15 and 18, respectively. The trichloroethane report said that neoplasms observed are not believed attributable to that compound. For dimethoate, the report said, "Pathologic evaluation revealed no statistically significant increase in tumors associated with dimethoate treatment in either species of animal (mice and rats), and it is concluded that there was no carcinogenic effect under the conditions of the experiment." Copies of the reports are available from the Office of Cancer Communications, NCI, Bethesda, Md. 20014.

FIVE DRUGS STILL AVAILABLE TO PRIVATE PRACTITIONERS; OTHERS THROUGH CENTERS

(Continued from page 1)

NCI has traditionally provided anticancer drugs to physicians because there are relatively few available on the market (that is, approved for marketing by the Food & Drug Administration following submission of a new drug application). NCI felt it was proper to distribute investigational drugs for clinical use because of the desperate plight of most cancer patients and the fact that the drugs had been proven of some benefit to some patients.

In all cases, NCI asked physicians to follow approved protocols, to report adverse reactions immediately and to report regularly on results. Such reporting was not always done, however. When FDA clamped down and insisted on it, NCI feared it might be forced to stop the program.

A revised distribution program was put into effect late last year (***The Cancer Letter***, Jan. 7). Five drugs of proven efficacy but for which NDAs had not been obtained were made available to qualified registered investigators. Those drugs are BCNU, methyl-CCNU, daunomycin, 5-azacytidine, and streptozotocin. To qualify as a registered investigator, a physician must submit form 1573 (available from DCT). Drugs would be sent on written request, and physicians would be required to use them only as suggested by the guidelines and only for the conditions in which clinical efficacy has been shown.

Protocols using any drugs still in investigational stages, besides those five, would be available only to clinical investigators provided a proper protocol is submitted and approved. Much tighter reporting requirements were demanded for these drugs.

It was for this latter category of drugs that the program was further modified. Vincent Bono, chief of DCT's Investigational Drug Branch, explained the new system to the DCT Board of Scientific Counselors.

Investigational drugs have been grouped into three categories, Bono said—Group A, for drugs in phase I and limited early phase II studies; Group B, for those in broader phase II, phase III and phase IV studies; and Group C, those with proven efficacy for specific indications but for which NDAs have not been obtained (the five drugs named above).

Group A drugs will be available only to members of the Phase I Working Group which consists of seven contract supported investigators, nine non-funded investigators who are supported by their own institutions, and investigators on the DCT intramural staff.

Group C drugs will be available as described above.

Group B drugs will be available to the Phase I and II Working Group; phase III investigators on contracts with NCI; members of the Cooperative Groups; NCI supported study groups; NCI supported task forces; and cancer centers.

Individual investigators desiring to obtain Group B drugs will be required to work through cancer center directors. Bono said a formal mechanism for this has not yet been worked out with the center directors but expected that would be done soon. The centers at present are the 19 comprehensive cancer centers, and the 25 clinical centers supported by NCI core grants.

"It won't be limited just to those centers," Bono said. "After we develop criteria for identifying institutions capable of conducting phase III and IV trials, we will add them to the list."

Bono said individual investigators would be asked to go through the center in their respective geographic areas. But James Holland, member of the Board of Scientific Counselors, objected.

"Don't tie the individual to a cancer center in his geographic area," Holland said. "An investigator might be a former pupil of someone else and may wish to continue an alliance that would be beneficial to both."

DCT Director Vincent DeVita said, "We felt that if a center director could look out his window at the individual, or reach him after a short drive, he would be better able to monitor the drug's use. The key to the success of this is that the center director will be responsible for the individual physician's use of these drugs."

"Some windows can be pretty murky," Holland said.

BSC member Philip Rubin suggested that "this is a great scheme for single modality studies" but that it might not work for combined modality therapy. Bono agreed that combined modality, phase IV, studies might work better with the Cooperative Groups or the study groups and task forces. But he later told ***The Cancer Letter*** he saw no reason why individual investigators could not participate in such studies working through center directors.

BSC member Donald Morton said "it might be healthy" for an investigator if his former pupil "out in swampwater is forced to be associated with phase I or II evaluation groups. The data he gets will be organized in a useful way."

Holland said he agreed, "but I hope we won't force individuals to go to cancer centers that aren't interested in medical oncology."

BSC Chairman John Ultmann said that "it is the sense of the Board that we agree this is a good mechanism," but individuals should be permitted to work through centers other than those in their immediate geographic region when appropriate.

DeVita said he would go along with that, provided it was acceptable to FDA.

Bono said that two other drugs should be in Group C and probably will soon—hexamethylmelamine and cis-platinum.

Bono said he hopes the new program will be in operation by the end of June, but that is a tentative

goal at this time.

The 25 clinical centers on DCT's list are, with the directors:

Northern California Cancer Program, Stephen Carter; Stanford Univ., Henry Kaplan; Emory Univ., Atlanta, Charles Huguley; Univ. of Hawaii, Lawrence Piette; Mountain States Tumor Institute, Boise, Charles Smith; Mid-American Cancer Center, Kansas City, Kan., James Lowman; Cancer Research Center, Boston Univ., Sidney Cooperbank; Ellis Fischel State Hospital, Columbia, Mo., John Yarbro; Cancer Research Center, Albert Einstein, New York City, Harry Eagle; Hospital for Joint Diseases & Medical Center, New York City, Vincent Hollander; Institute for Cancer Research, Columbia Univ., Paul Marks; Cancer Center, New York Univ., H. Sherwood Lawrence; Univ. of Rochester, Robert Cooper; Cancer Research Center, Univ. of North Carolina, Joseph Pagano;

Next week's issue of *The Cancer Letter* will include reports on:

- **NCI's Div. of Cancer Treatment will recompete $10 million in resources contracts. The report will include details on the present contracts —who has them, how much is budgeted this year, and comments by DCT Board of Scientific Counselors on them.**
- **A famous and successful surgeon presents proposals from a group he headed to upgrade surgery and opportunities for surgeons in the National Cancer Program.**
- **The head of FDA's Bureau of Drugs subjects himself to a critical audience at NCI, gets an earful, and promises that the two agencies will work together productively, if not always harmoniously.**

Wake Forest Univ., Charles Spurr; Cancer Center Inc., Cleveland, Arthur Flynn; Oklahoma Cancer Center, Oklahoma City, G. Bennett Humphrey; Univ. of Puerto Rico Cancer Center, Enrique Perez-Santiago; Roger Williams General Hospital, Providence, R.I., Paul Calabresi; Memphis Regional Cancer Center, James Nickson; Univ. of Texas (Dallas), George Rose; Univ. of Texas Medical Branch Clinical Cancer Center, J. Palmer Saunders; Medical College of Virginia Cancer Center, Richmond, Walter Lawrence Jr. ; and Milwaukee Children's Hospital, Donald Pinkel.

That adds up to 24. NCI has on its list of clinical centers one at Roswell Park Memorial Institute, with David Pressman as director, in addition to listing Roswell Park as one of the comprehensive centers, with Gerald Murphy as director.

The other comprehensive centers are Sidney Farber, Boston; Yale Univ.; Memorial Sloan-Kettering, NYC; Univ. of Pa.-Fox Chase, Philadelphia; Johns Hopkins, Baltimore; Howard-Georgetown, Washington, D.C.; Duke Univ.; Univ. of Miami; Univ. of Alabama; Ohio State Univ.; Illinois Cancer Council; Mayo Clinic; Univ. of Wisconsin; Univ. of Texas System Cancer Center, Houston; Colorado Regional Cancer Center; Univ. of Southern California/Los Angeles County; and UCLA.

MAMMOGRAPHY REPORTS IN; BCDPs TO CONTINUE UNDER GUIDELINES

The three studies commissioned last year by NCI to take a look at use of mammography for breast cancer screening have been completed, and the reports so far have not moved NCI to make any changes in the Breast Cancer Detection Projects or in the mammography guidelines issued last summer.

The 27 BCDP centers supported jointly by NCI and the American Cancer Society will continue in operation under the guidelines, which limit mammography in the screening program to women over 50. NCI is tentatively planning to convene a meeting during the summer on mammography as a tool for screening.

The three studies were by Louis Thomas, who reviewed the histology of breast cancers discovered in the HIP (Health Insurance Plan of New York) study; Arthur Upton, who evaluated the relationship between benefit and risk in mammography screening; and Lester Breslow, who reviewed the benefits of adding mammography to physical examination and history.

A fourth study is still under way, by a group headed by Oliver Beahrs of the Mayo Clinic. This group is evaluating the results developed so far in the BCDP, and will have its reports ready in June. Information found so far suggests that mammography is beneficial.

BOARD CONVINCES DCT TO DIVIDE H & N PROJECT AMONG GROUPS, CONTRACTORS

A million dollar adjuvant chemotherapy trial in head and neck cancer, originally intended for funding entirely through contracts by NCI, will now be divided between grants to the Cooperative Groups and contracts for which the Groups and all others may compete.

The Div. of Cancer Treatment Board of Scientific Counselors last week challenged NCI's plan to compete the entire project through contracts. BSC member James Holland, who is a Cooperative Group chairman (Cancer & Acute Leukemia Group B), led the fight to reserve at least part of the project for the groups.

The Board split 5-5 on Holland's motion requesting DCT "to develop a mechanism in which prosecution of head and neck cancer research can be funded by both grants and contracts, and which permits a contrast of the two." But DCT Director Vincent DeVita said that "since it is obvious those who voted against the motion were concerned about preserving our flexibility, we can do both and still be flexible."

DeVita said that roughly half of the funds ear-

marked for the project ("which could but won't necessarily be $1 million"), will be set aside for supplemental grants to the Cooperative Groups. The groups will have to develop applications for the grants and submit them to the Cancer Clinical Investigation Committee for review.

The RFP, (NCI-CM-87154, announcement of which appeared in ***The Cancer Letter*** March 11) will remain in effect, with May 20 as the deadline for submission of proposals. The project will seek to compare the relative efficacy of preoperative chemotherapy and adjuvant radiotherapy in the surgical treatment of advanced head and neck squamous cell carcinomas.

DeVita said it had been his intention to encourage the Cooperative Groups to compete for the contracts, but Holland insisted that most groups do not have the administrative capability of forming contract proposals.

Franco Muggia, who heads DCT's Cancer Therapy Evaluation Program, said that "Cooperative Groups are in a good position to respond to the RFP. Some have radiotherapists . . . and can rally the necessary resources. This is an area that is largely neglected now. I would be skeptical that many head and neck surgeons would join the project. They haven't in the past."

"This is a new concept," said BSC Chairman John Ultmann. "The Board is being asked to determine if it is right for DCT to go into a multimodal head and neck program."

"I take exception to the way you are going about it," Holland said. "If you would say to four multimodal Cooperative Groups, 'Here's $200,000 or $300,000 to enrich your programs, you would get the response you need from surgeons. But if you put the money where head and neck surgeons can get it only by responding to the RFP, that will work against the groups."

"Not if the groups are involved," Muggia said.

"You will wind up with a half dozen institutions in a head and neck cancer group," Holland said. "You will miss input from surgeons, radiotherapists and others. The program will fragmentize, and you'll never get national coherence."

"The key point is to get the job done," commented BSC member Bernard Fisher, who is chairman of a Cooperative Group, the Primary Breast Cancer Therapy Group. "Flexibility is what it's all about. A combination of grants and contracts would be the ideal way. Our own experience (funded by both mechanisms in the National Surgical Adjuvant Breast Study) has worked out well."

"With the Cooperative Groups, the framework is there," said BSC member Carlos Perez. "It's ready to go. But we need the machinery to get surgeons involved."

BSC member Philip Rubin said, "The basic question before the Board is whether this kind of mechanism will increase or decrease conflict with the groups. All support the multimodal approach, but most groups aren't there yet. They haven't had the money. We have to splice contracts into the groups. Let's make it a clean, open competition."

"Ask yourself this question first," DeVita said. "Do we need something in head and neck cancer? Only seven protocols are being tried now, most emphasizing local control. If the need is there, it hasn't resulted in much. You're saying, if the money is available, we will go into it. You're suggesting that we make the money available exclusively to the groups."

"I didn't say that," Rubin answered. "I said that the groups should be given the opportunity to bid on the RFP."

"They can," DeVita said. "But if you are talking about supplemental grants, they have to go through CCIRC for review. It is not possible to award grants directly. Do you think we should proceed with the RFP, with a budget of about $1 million, on open competition, to including the groups and non groups?"

"I'm the only one around the table without a vested interest," BSC member Joseph Simone started.

"Anyone with a vested interest can't vote on this," Ultmann interrupted. "But I would say all of you have only vague vested interests, and therefore can vote."

"I'm concerned that this be carried out so that you get interpretable results," Simone continued. "That will be difficult, considering the diversity of the tumors and the remedies."

"In 1976, only three groups got twice as much as you are talking about here," Holland argued, "using head and neck surgeons, who would be probationary members in the groups. . . . Instead of advertising it only as an RFP, do it as a group supplement. Four or five groups would respond. Use this as a trial. If you have $1 million, set aside half for grant supplements."

"The last supplement didn't work very well," DeVita said. "We've cooled on that. But we could do it."

"Do I hear correctly, that DCT should go into a head and neck program?" asked Ultmann. "The answer is yes. The issues then are mechanisms. Grant supplements versus the faster contract mechanism. Some feel contracts would be divisive."

"We need firmer advice," DeVita said. "Should we proceed half and half?"

After Holland made his motion, DeVita said, "I interpret that to mean that we should go with both grants and contracts, but not necessarily 50-50."

"Yes," Holland said. "The groups feel they need more support for radiotherapists and surgeons."

"I can't understand why Cooperative Groups can't compete for contracts," commented BSC member Charles Heidelberger.

"It's an administrative problem," Holland said. "Groups are grant oriented, multi-institutional organizations. To compete for contracts, you would have

to go through all the many business offices. . . . I once heard Bernie Fisher say, 'That's the last time I'll mess around with a goddamn mickey mouse contract.' "

"When? I don't remember saying that," Fisher said.

"It was about a Cancer Control contract," Holland answered.

"Oh, well, control, that's something else," Fisher laughed.

Muggia said he felt it is "not as complicated as all that for groups to compete for contracts."

"I see a disturbing sense of territoriality," Heidelberger said. "There is a feeling that the large Cooperative Groups should dominate clinical cancer trials. On the other hand, it was felt this project was designed to bring in new blood."

BSC member Rose Papac said, "The overriding interest is that we get excellent data. The program should be flexible. I don't like to tie the hands of people who must make decisions based on excellence."

Fisher, Simone, Papac, Heidelberger and Ultmann voted against Holland's motion, but DeVita said he would follow its intent anyway.

Paul Chretien, a member of the DCT Surgery Branch staff, reported on NCI early studies with three drugs which will form the basis for the new trials. The drugs are cis-platinum, methotrexate and bleomycin. "Intensive chemotherapy should form the basis of new, randomized, controlled trials," Chretien said.

One wrinkle that differs from most other adjuvant trials is the application of chemotherapy before surgery or radiotherapy.

NCI's tests have involved use of all three drugs—cis-platinum, followed by bleomycin IV for seven days, and methotrexate administrered for 36 hours followed immediately by citrovorum rescue. "In our hands, every tumor responded dramatically," Chretien said.

"I believe that, with stage I and stage II tumors, within five years we will control those tumors with chemotherapy alone," Chretien said.

ADVISORY GROUP, OTHER CANCER MEETINGS FOR APRIL, MAY

Drug Development Committee—April 6, NIH Bldg 31 Room 8, open 9–9:45 a.m.

Committee on Cytology Automation—April 6-7, NIH Bldg 31 Room 7, open April 6, 8:30–9:30 a.m.

Clinical Cytopathology for Pathologists—April 11-22, Johns Hopkins postgraduate course. Contact John Frost, Hopkins Hospital, Baltimore.

Breast Cancer Experimental Biology Committee—April 11, NIH Bldg 31 Room 7, open 8:30–9:30 a.m.

Committee on Cancer Immunodiagnosis—April 11, NIH Bldg 10 Room 4B14, open 1–1:30 p.m.

Diagnostic Research Advisory Group—April 12, NIH Bldg 31 Room 7, open 8:30–10:30 a.m.

Joint Meeting of Diagnostic Research Advisory Group and Diagnostic Radiology Committee—April 13, NIH Bldg 31 Room 6, open 8:30 a.m.–3 p.m.

Carcinogenesis Program Scientific Review Committee B—April 13, Dulles Marriott Hotel, Washington D.C., open 9–9:30 a.m.

Virus Cancer Program Scientific Review Committee B—April 13-15, NIH Bldg 37 Room 1B04, open April 13, 8:30–9 a.m.

European Organization for Research on Treatment of Cancer—April 14-15, Brussels, symposium on experimental approaches to treatment of gastrointestinal tumors.

Committee on Cancer Immunotherapy—April 14, NIH Bldg 10 Room 4B14, open 1:15–1:45 p.m.

Diagnostic Radiology Committee—April 14, NIH Bldg 31 Room 7, open 8:30–9 a.m.

Carcinogenesis Program Scientific Review Committee A—April 14-15, Dulles Marriott Hotel, Washington, D.C., open both days 9–9:30 a.m.

President's Cancer Panel—April 15, NIH Bldg 31 Room 7, 9:30 a.m., open.

National Clearinghouse on Environmental Carcinogens Subgroup on Chemical Selection—April 18, NIH Bldg 31 Room 6, 9 a.m., open.

Cancer Control Intervention Program Review Committee—April 18-19, NIH Bldg 31 Room 7, 8:30 a.m. both days, open.

Clearinghouse Experimental Design Subgroup—April 19, NIH Bldg 31 Room 6, 9 a.m., open.

Clinical Cancer Program Project Review Committee—April 21-23, NIH Bldg 31 Room 8, open April 21, 9–10:30 a.m.

Management of Central Nervous System Malignancies—April 22, Roswell Park continuing education in oncology. Contact Claudia Lee, Cancer Control.

American Radium Society—April 24-28, Las Vegas, Nev., annual meeting.

Virus Cancer Program Scientific Review Committee A—April 25-26, NIH Bldg 37 Room 1B04, open April 25, 9-9:30 a.m.

National Pancreatic Cancer Project Working Cadre—April 26-27, NIH Bldg 31 Room 9, open April 26, 9–11 a.m.

Developmental Therapeutics Committee—April 28, Blair Bldg Room 110, open 9–11 a.m.

6th International Conference of Cytology—May 2-5, Cancer Institute Hospital, Tokyo.

Society of Surgical Oncology—May 4-8, Hilton Head, S.C.

Advances in Treatment of Childhood Cancer—May 12, Roswell Park continuing education in oncology. Contract Claudia Lee.

Oncology Nursing Society—May 14-15, Denver Hilton Hotel, second annual meeting.

American Society of Clinical Oncology—May 16-17, Denver Hilton Hotel, annual meeting.

American Assn. for Cancer Research—May 18-21, Denver Hilton Hotel, 68th annual meeting.

International Conference on Prospects for Treatment of Lung Cancer—May 22-24, Airlie House, Va., sponsored by NCI Div. of Cancer Treatment.

National Cancer Advisory Board—May 23-24, NIH Bldg 31 Room 6, open May 23, 9 a.m.–adjournment, May 24, 1:30 p.m.–adjournment.

Sixth Seminar on Dynamic Telethermography—May 23-26, Marseille.

Additional meetings for May will appear in *The Cancer Letter* April 29.

PROGRESS, OPPORTUNITIES IN CANCER RESEARCH, CONTROL RELATED BY NEWELL

Acting NCI Director Guy Newell has presented statements on behalf of the institute's budget request for fiscal 1978 to both the House and Senate HEW Appropriations Subcommittees. *The Cancer Letter* last week published excerpts from Newell's statement in which he called attention to a drop in cancer death rates for the under 35 age group in the United States.

The statement included comments on progress and opportunities in etiology, detection and treatment. Excerpts from the remainder of Newell's statement,

continuing with detection, follow:

Breast Cancer: (88,700 new cases, 33,100 deaths per year) In partnership with the American Cancer Society, the Cancer Control Program is supporting the Breast Cancer Detection Demonstration Program (BCDDP), a nationwide effort involving 27 BCDDP projects (29 screening centers) in 25 states. Some 270,000 women have received an initial, first annual screening and 130,000 have received a second annual screening. There will be smaller numbers for subsequent annual screenings. Some 1,544 women have been found to have cancer through project screenings as of the latest reports.

Of profound long-term importance is the fact that we have developed the technology to reduce radiation dosage to less than one rad delivered dose per exposure, while maintaining the quality of the x-ray. We have taken steps to transfer this technology to the general medical community by funding the Bureau of Radiologic Health of FDA to develop monitoring and technical assistance programs through state health departments. To date, such monitoring has been implemented in four states and is being initiated in five others.

Uterine Cancer: (47,000 new cases, 11,000 deaths per year) The Cancer Control Program for uterine cervical cancer screening is being conducted in collaboration with more than 30 state and territorial health departments. The objective was to mobilize statewide health care systems to motivate high risk, hard to reach women to seek cervical screening services and be provided with quality followup diagnosis when needed. In the areas that have developed a comprehensive plan and reached the implementation stage, more than 1,300 hospitals and clinics have screened approximately 544,000 women with at least one Pap smear. Altogether more than 750,000 screenings have been performed. At the time of the latest report, 290 women in a screening population of 231,723 were found to have cancer of the uterus, as confirmed by histology conducted by the medical community. This number will undoubtedly increase as reporting is received on current screenings.

Treatment

A major working hypothesis is that up to 60% of cancer patients have disseminated disease at the time of diagnosis; also that many patients experience recurrence because they probably had microscopic tumor cells that had spread from the original location but were not detectable at the first treatment. The rationale for cancer treatment, then, provides for the use of anticancer drugs earlier in the course of the disease to reach cancer cells wherever they are in the body, in combination with local treatment with surgery and/or radiation therapy. This approach offers the best opportunity to attack the cancer when the disease is initially diagnosed and the body's tumor burden is the smallest.

Much effort has been expended in the past year to integrate the activities of the Clinical Cooperative Groups into the total clinical treatment program of NCI. In various clinical trials, we have influenced the treatment of 280,000 cancer patients, and about 28,000 of these were entered in clinical trial protocols. This is important because these 280,000 patients were seen and evaluated by expert oncologists and were provided the best medical advice available, even though only one out of 10 actually entered a clinical trial.

The emphasis in the clinical program is on combinations of drugs, testing new combinations against standard therapy. The cancers being treated are cancers of the breast, colon and other parts of the gastrointestinal system including pancreas, as well as lung, and ovary. We are beginning combination treatment of prostate, bladder, and head and neck cancer.

The most recent results of the studies of breast cancer treatment have continued to show that early introduction of drug therapy for women found at surgery to have positive axillary nodes effectively delays and may prevent recurrence, particularly in premenopausal women. New studies have begun with additional drugs and the use of drugs with other methods of treatment, such as hormone therapy and immunotherapy, to increase survival while reducing the extent of surgery required.

In other studies, dramatic early results have been observed in combined chemotherapy and radiotherapy of small cell carcinoma of the lung, which accounts for about 20% of lung cancer cases. The addition of a new drug, cis-platinum(II)diamminedichloride, to a drug combination already in use has improved still further the significant response rate of a very malignant tumor of young adults, testicular cancer.

Although we now have nearly 40 drugs commercially available for treatment of cancer, we still do not have the best drugs. We are trying to establish a more rational system of selecting new compounds, and are establishing laboratory systems that will yield new types of agents for development into more effective anticancer drugs. The approach is to pass selected compounds through a pre-screen, which will indicate the ones that are sufficiently active to be studied more extensively in a second stage for anticancer activity.

One new drug of considerable interest is maytansine, a plant product related to known antiviral drugs. It has high activity against leukemia and other tumors in laboratory animals. Chlorozoticin, a new drug identified within the past two years, has considerably less toxicity for the bone marrow than other related anticancer drugs, such as CCNU. Both new drugs have been started into clinical trials.

Comments and questions by members of the committee will appear in the next issue of ***The Cancer Letter.***

CANCER RESEARCH EMPHASIS GRANTS (CREG)

Title: *Reasons for variation in cancer patient survival by race – DCCP-32*

Deadline: *Nov. 1*

NCI is accepting applications for support of research projects designed to increase knowledge concerning the basis for variation by race in cancer patient survival. For many forms of cancer, the survival experience for white patients is more favorable than that for black patients even when the disease is considered localized at diagnosis. Furthermore, a higher percentage of black patients than white have metastatic disease when cancer is first discovered.

Research in this area might include sociocultural parameters in an attempt to explain possible differences by race in delay from onset of disease to cancer diagnosis. Studies of recurrence and/or patient survival must take into account variables of known prognostic and etiologic significance, e.g. histologic type, extent of disease, and other demographic, morphologic, and physiological descriptions of neoplasm and host. Proposals should be oriented toward specific forms of cancer and should include detailed plans for data collection and statistical analysis.

Title: *Cancer epidemiology in collaboration with the NCI program of cancer Surveillance, Epidemiology, and End Results (SEER) – DCCP-33*

Deadline: *Nov. 1*

NCI is accepting applications for support of research projects in the field of cancer epidemiology and etiology which will be conducted in collaboration with cancer registries participating in the SEER program. The SEER program provides information on trends in the incidence of the various forms of cancer, variation in the occurrence of cancer among different population groups and in different geographic areas, changes, in general treatment practice, and the associated cancer patient survival patterns. Data are obtained from a selected number of population-based cancer registries that provide uniform information on a continuing basis and participate in ad hoc studies designed to identify and assess etiologic and prognostic factors.

Only limited pilot or feasibility studies can be supported under the present contract agreements with the participating registries. Therefore, NCI is now soliciting full-scale comprehensive CREG research proposals for analytic studies in etiology and/or prognosis for any form of cancer. Of special interest are research projects which may lead to identification of factors which can be modified to reduce the incidence and mortality of cancer. Purely descriptive studies are not desired. Although specific research protocols are requested, the actual approaches and methods will be left to the initiative of the applicants. Studies may be either retrospective or prospective in design.

Registries participating in the SEER program are: California State Dept. of Health, San Francisco Bay area; Charity Hospital of Louisiana at New Orleans, three parishes in the New Orleans area; Connecticut State Dept. of Health, entire state; Emory Univ., Atlanta, five county metropolitan area; Fred Hutchinson Cancer Research Center, Seattle-Tacoma area; Univ. of Hawaii, entire state; Univ. of Iowa, entire state; Michigan Cancer Foundation, Detroit metropolitan area; Univ. of New Mexico, entire state; Puerto Rico, entire island; and Univ. of Utah, entire state.

Application requirements:

All nonprofit organizations and institutions, state and local governments and their agencies, authorized federal institutions, and individuals are eligible, according to NIH grants policies, regardless of whether or not they are participating in the SEER program.

Applicants should propose individual projects. The application should very specifically describe the background for the proposed project, the rationale behind conducting the proposed study, measurable objectives, and significance in advancing knowledge of cancer etiology and prognosis. Applicants must complete portions of the application pertaining to procedural details including study design, assurance of high quality data and analytical procedures, the investigator's related experience, facilities available, budget, and biographical information for key professional personnel.

Use application form PHS 398. In both the covering letter and at the top of the space provided for an abstract on page 2 of the applications, identify this CREG announcement by its title and number. Mail the application and letter to Div. of Research Grants, NIH, Bethesda, Md. 20014.

For further information contact James Murray, Biometry Branch, Div. of Cancer Cause & Prevention, NCI, Room C-505, Landow Building, Bethesda, Md. 20014; telephone, 301-496-3116.

RFPs AVAILABLE

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

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

RFP NCI-CM-87145

Title: *Protocol toxicology prime contractor*
Deadline: *Approximately May 31*

The Laboratory of Toxicology, Div. of Cancer Treatment, is seeking a prime contractor to provide the government with coordinated, efficient and responsive ongoing technical management which will accomplish the following objectives:

1. Minimize time required for protocol and other studies without any loss of quality of data.
2. Implement the toxicology protocol at subcontractor facilities and begin/continue systematic accumulation of data.
3. Analyze existing methods of operation of the Laboratory of Toxicology and suggest improvements either through the prime contractor's organization or with subcontractor's staff.
4. Apply management techniques directed toward reducing lead times, enhancing exchange of scientific information, maximizing responsiveness to laboratory technical and administration requests and control of costs.
5. Organize staff facilities and other resources that offer the Laboratory of Toxicology an organization flexible and responsive to DCT.

It is anticipated that one award will be made for a three year period.

Contracting Officer: Stephen Gane
Cancer Treatment
301-427-7463

RFP NO1-CP-75897-56

Title: *Synthesis of new retinoids for in vitro studies of prevention of lung cancer and other epithelial cancers*
Deadline: *May 15*

NCI is interested in establishing a contract for this purpose. The basic objective of this project is the synthesis of new retinoids, which NCI will be able to test in several in vitro systems for desired activity in control of epithelial cell differentiation, both normal and premalignant.

Since these in vitro test systems are extremely sensitive, small amounts of new compounds, in the range of 25-100 milligrams, will suffice. The choice of new compounds to be synthesized will be left to the proposer, and may include variations in the ring, side chain, or terminal group of the retinoid molecule. Variations in structure may be proposed which might lead to new compounds with greater activity, lesser toxicity, or more desirable pharmacokinetic properties.

Contract Specialist: M. Hamilton
Carcinogenesis
301-427-7575

RFP NCI-CB-74159-31

Correction: *Antigenicity of precancerous lesions in animal models*
Deadline: *May 2*

Since the brief description of this project as contained in that announcement is incorrect, the RFP is corrected to read as follows: Proposals are sought for the discovery of new ways to identify and study the precancerous condition in animal models using immunological methods.

The incorrect announcement appeared in ***The Cancer Letter*** Feb. 11.

Contracting Officer: Robert Townsend
Biology & Diagnosis
301-496-5565

CONTRACT AWARDS

Title: Transfer factor and delayed hypersensitivity in the mouse
Contractor: Walter & Eliza Hall Institute of Medical Research, Melbourne, Australia.

Title: Production and detection of antibodies to chemical carcinogens and other small molecules
Contractor: Brandeis Univ., $88,638.

Title: Working group for the review of Breast Cancer Detection & Demonstration Projects
Contractor: Mayo Foundation, $220,340.

Title: Continue phase I studies of new anticancer agents
Contractors: Univ. of Texas System Cancer Center, $254,172; Mayo Foundation, $118,830; and Children's Hospital of Los Angeles, $156,071.

Title: Continuation of therapy of patients with pancreatic carcinoma
Contractors: Univ. of Miami, $163,119; Mayo Foundation, $607,393; and UCLA, $108,175.

Title: Cervical cancer screening program
Contractor: Virginia Dept. of Health, $216,518.

SOLE SOURCE NEGOTIATIONS

Proposals are listed here for information purposes only. RFPs are not available.

Title: Pharmacology and tumor bank
Contractor: Arthur D. Little Inc.

Title: Isolation and characterization of mammary epithelial cell membranes
Contractor: Worcester Foundation.

The Cancer Letter—*Editor* JERRY D. BOYD

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