THE CANCER LETTER

P.O. Box 2370 Reston, Virginia 22090 Telephone 703-620-4646

Vol. 7 No. 33

Aug. 14, 1981

Subscription $125.00 per year

TERRY TO LEAVE AS DRCCA ACTING DIRECTOR SEPT. 1, PETER GREENWALD IS DEVITA'S CHOICE FOR THE JOB

William Terry, for the last three years acting director of NCI's Div. of Resources, Centers & Community Activities and its predecessor, the Div. of Cancer Control & Rehabilitation, will leave that position Sept. 1.

Terry announced his decision to his staff members last week indicating that NCI Director Vincent DeVita had decided to appoint someone else to the permanent directorship of the division. ***The Cancer Letter*** has learned that DeVita's choice for the job is Peter Greenwald,

(Continued to page 2)

In Brief

AMOS SAYS CANCER PROGRAM SHOULD NOT HAVE CEILING OF $1 BILLION; OSHA DROPS EFFORT TO FIRE INFANTE

ONE BILLION dollars should not be the ceiling for the National Cancer Program, and we should not accept it as such," Harold Amos, member of the President's Cancer Panel and National Cancer Advisory Board, commented at the meeting of the American Assn. of Cancer Institutes earlier this summer. "The private sector should be more involved. It's a cop-out for universities to not want to dirty their hands with money from industry. It ought to be possible to forge some partnership with industry and still preserve academic freedom." . . . **OSHA DROPPED** its attempt to fire Peter Infante, head of the agency's Office of Carcinogen Identification and Classification, in the controversy over the alleged carcinogenicity of formaldehyde (***The Cancer Letter***, July 31). Thorne Auchter, OSHA administrator, dismissed charges of misrepresentation of the agency's position on formaldehyde. Auchter had been accused by Congressman Albert Gore (D.-Tenn.) of caving in to pressure from representatives of the formaldehyde industry and of interfering with freedom of scientific expression. . . . **EDWARD COPELAND III** has been appointed the new director of the National Large Bowel Cancer Project headquartered at M.D. Anderson Hospital & Tumor Institute. Copeland replaces his uncle, Murray Copeland, who headed the project for several years. Edward Copeland is professor of surgery at the Univ. of Texas Medical School and Univ. of Texas System Cancer Center/M.D. Anderson. Much of his research has focused on hyperalimentation and colorectal cancer. The National Large Bowel Cancer Project is one of four organ site programs supported through NCI grants, headquartered and administered at universities or cancer centers (the others: bladder, prostate, pancreas). . . . **JOHN PENTA** has left his job as chief of the Drug Regulatory Affairs section in NCI's Div. of Cancer Treatment Investigational Drug Branch to join a small drug company in Florida. Branch Chief Daniel Hoth is acting chief of the section until he can recruit a replacement.

TERRY OUT AT DRCCA, PETER GREENWALD REPORTEDLY IS CHOICE TO SUCCEED HIM

(Continued from page 1)

director of the New York State Health Dept. Div. of Epidemiology.

Terry, who headed both contract supported and intramural immunology research in the Div. of Cancer Biology & Diagnosis before NCI's reorganization which separated management of extramural and intramural programs, has remained director of the Immunology Intramural Research Program. He probably will return to that job full time.

During the early stages of the reorganization, in 1978, then Director Arthur Upton pulled the Cancer Centers Program out of the grants division (and then dismantled that division, replacing it with the Div. of Extramural Activities) and put Terry in charge. Morale among center executives was low, in the face of severe budget restrictions and proposed new core grant guidelines which would have drastically changed the way centers were operated.

Terry's determination to develop some new guidelines which would help resolve difficulties facing NCI in distributing cancer center funds at first offended some center directors. He eventually won most of them over, with his fairness in attempting to arrive at solutions they could accept, and with his good humor.

Upton removed Diane Fink as director of DCCR in mid-1978 and named Terry acting director. Later, the centers, organ site and manpower training programs were added to the division's cancer control activities, making it the most diverse of NCI's divisions, the one most directly under congressional guns and in the public eye, and probably the most difficult to manage.

Terry seemed to be working well with the division's new Board of Scientific Counselors (of which Greenwald is a member). Board members, center directors and others commenting on DeVita's decision regretted Terry's departure although accepting the NCI director's right to select his own staff.

Since division directorships are Senior Executive Service positions and appointments to them must be approved by HHS Secretary Richard Schweiker, DeVita has declined to comment on his selections until Schweiker has cleared them. Terry was not available for comment.

Greenwald had been a potential candidate for the position of NCI deputy director. As an epidemiologist, his forte is cancer prevention. Since DeVita's background is in treatment, he has felt he probably should have a deputy with credentials in prevention.

Greenwald is considered to be extremely bright, and has been an active, articulate member of the DRCCA Board.

With Terry leaving Sept. 1, DeVita will have to name an acting director of DRCCA, if Greenwald's appointment has not been approved by then. The division does not have a deputy director.

DeVita reportedly, although unofficially, has made his selections for his deputy and for director of the Div. of Cancer Cause & Prevention. Richard Adamson is DCCP acting director.

FCRC PREPROPOSAL CONFERENCE DRAWS 36 INSTITUTIONS, INCLUDING JOHNS HOPKINS

More than 50 representatives of 36 institutions, including Johns Hopkins Univ., last week attended the two day preproposal conference of prospective competitors for one or more of the five contracts being competed for operation of the Frederick Cancer Research Center.

NCI executives were delighted by the turnout, which encouraged them to think that this time, the incumbent, Litton Bionetics Inc., would have some competition for the major portions of the operation. When the contract was recompeted five years ago, no one except Litton submitted proposals. NCI in general has been pleased with Litton's conduct of the research and resource programs at the center but was embarrassed by the lack of competition for the largest ($25 million a year) contract in NIH's history.

The new arrangement almost assures there will be competition, and does assure that Litton will lose a segment of the operation. Contracts will be awarded for five separate tasks, including two—computer services and library services—which are small business set asides, automatically eliminating Litton from that part of the competition.

Litton may have spirited competition for the other three contracts—research, operations and technical support, and animal production—if the organizations which attended the preproposal conference follow through and submit bids.

Hopkins was the only academic institution represented at the meeting. When the decision was made to separate the research component from the rest of the FCRC tasks, NCI Director Vincent DeVita suggested that a university or consortium of universities might be interested in competing for it.

A Hopkins executive told ***The Cancer Letter*** that sending the representative to the conference "was a fact finding mission. . . our curiosity was piqued."

Other organizations represented at the conference were:

Automation Counselors Inc., Battelle Columbus Laboratories, Carrier Machinery Systems Div., Computer Technology, Charles River Breeding Labs, C.S.R. Inc., Corporation for Applied Systems, Data Management Systems, Digital Systems Corp., Dynamic Corp., E.G.G., Enviro Control Inc., E.R.A., Evaluation Technologies, Experimental Pathology Labs, Herner & Co., ITTRI, Information Management Systems Inc., K.C. Information Services,

L.A.M. Associates, Lockheed Corp., Lockheed Engineering Management Services Inc., Meloy Labs, Microbiological Associates Inc., Northrop Services Inc., Pathology Associates Inc., Program Resources Inc., Pharmaceutical Supplies, R.D.W. Systems, Republic Management Systems, Systems Sciences Inc., Tracor Jitco Inc., and Zimmerman & Associates.

NUTRITION RESEARCH TESTS HYPOTHESES, SEEKS EXPLANATION OF DIFFERENCES

Nutrition research carried out or supported by the Environmental Epidemiology Branch of NCI's Div. of Cancer Cause & Prevention was described by Regina Ziegler, nutrition epidemiologist, at a meeting earlier this year of the National Cancer Advisory Board's Subcommittee on Nutrition. Excerpts from the report:

Epidemiologists have begun to look at the relationships between dietary patterns, nutritional status, and cancer only recently. Analytic nutritional epidemiology is a promising, but young discipline. NCI's program in this area, though five months older than when I last spoke to you, is still developing. We who are responsible for the intramural epidemiology research at NCI feel it is important to build on a strong scientific foundation. We try to initiate studies in those areas where there are clear, testable hypotheses and where there are reliable, sufficiently sensitive methods to measure dietary exposures.

Several of our studies have been specifically designed to test in human populations hypotheses generated by animal experiments. One example is the dietary component of our case control studies of lung cancer in New Jersey and Texas. Vitamin A has been postulated to reduce the risk of cancer. In several animal studies, very high doses of analogs of vitamin A have been shown to protect against the development of cancer, while vitamin A deficiency often increases the risk. But the few relevant epidemiological studies of dietary patterns and cancer point to a broader association. In the epidemiological studies, those with an apparently higher intake of vitamin A did indeed have a reduced risk of several cancers; but their intake of fruits and vegatables in general seemed to be elevated. In the lung cancer studies we want to distinguish whether vitamin A intake itself is associated with reduced risk or whether the association is primarily with all fruits and vegetables; vitamin C; carotene; a subclass of vegetables, such as the Brassica genus; or something else, perhaps a nonnutritional correlate of dietary patterns. We tried to be open minded about all the possibilities in preparing the interview. We suspect there is sufficient variation in the intake of fruits and vegetables and vitamin pills within the U.S. for our study to distinguish between these various hypotheses. It is important that epidemiology studies be designed not simply to confirm laboratory findings but to independently assess them.

Also designed to test a hypothesis generated by animal experiments is the study of artificial sweeteners and bladder cancer. Laboratory experiments indicated that high doses of saccharin could initiate bladder cancer in rats and might also promote the carcinogenicity of other chemicals. However, it was not clear just how to extrapolate the dose response relationship measured in rats to humans. The Environmental Epidemiology Branch structured a large case control study that was able to place an upper bound on the risk of heavy saccharin ingestion. Saccharin, if a carcinogen at all, was only a relatively weak one in humans. The study identified a slight excess risk among very heavy users. This risk was more pronounced among nonsmoking women, the group in which one would have predicted that a small increase in risk might be detectable since it has a low background rate of bladder cancer. The study also suggested that saccharin might promote the bladder carcinogenicity of smoking, and further analyses are in progress. Information on coffee and drinking water quality, two other nutrition-related exposures, were also collected in this study and is now being analyzed.

Often epidemiological studies, rather than animal experiments, generate the hypotheses that we then assess in further epidemiological research. For example, several longitudinal studies on diet and coronary heart disease suggest that individuals with especially low serum cholesterol levels have an elevated risk of cancer. In conjunction with the Kaiser Permanente Health Plan, which has routinely measured the serum cholesterol of many members on admission to the plan, we will be able to assess this hypothesis in a reasonably representative and large American population (about 200,000 individuals). In particular, we want to determine whether preclinical cancer itself could be the cause of the low serum cholesterols, the spectrum of anatomic sites that are involved, and the relationship of serum cholesterol to both cancer incidence and cancer prognosis.

Another group of epidemiologica studies on diet and cancer currently underway at NCI are based on the U.S. cancer maps produced several years ago by the Epidemiology Branch. These cancer maps have generated multiple hypotheses about the relationship of cancer to environment and lifestyle. The Branch used county-wide mortality rates for various cancers to identify regions at unusually high risk. It was hoped that within these regions exposures would be high enough to be easily distinguished and identified.

One such area is Washington D.C., the U.S. metropolitan area with the highest rate of esophageal cancer for black males, the age-sex group in which esophageal cancer predominates. A case-control interview study revealed that poor nutrition and heavy alcohol consumption were the major risk factors. The

least nourished third of the study population had about twice the risk of the most nourished third, whether nutrition was measured by consumption of certain broad food groups, by relative weight, or by the number of meals eaten per day. When an overall index of dietary patterns was formed, and extremes were compared, the relative risk reached 13. There was no evidence for a specific vitamin deficiency; instead, generally poor nutrition seems to be able to increase the susceptibility of the esophagus in urban black men.

Another study suggested by the U.S. cancer maps focused on an unexpected "hot spot" of colon cancer in several counties in eastern Nebraska. Colon cancer is generally believed to be associated with an affluent diet and with urbanization. These counties were rural farming counties. However, many people of Czechoslovakian ancestry live in this area; and Czechoslovakians, when compared to other immigrants to the U.S., show elevated rates of colon cancer. We wondered whether their traditional ethnic diet could be placing them at risk and might provide a clue to colon cancer etiology. A case control study in this part of Nebraska indicated that the excess risk was primarily among the people of Czechoslovakian ancestry and seemed to be related to their high fat and cholesterol consumption and low vegatable and vitamin A consumption. Whether other Americans are similarly affected by a high fat-low vegetable diet or whether the Czechoslovakians were unusually susceptable because of genetics needs to be investigated further.

We are currently developing a third study suggested by the cancer maps. The maps showed clearly that colorectal cancer mortality rates for white men and women were lower in the South, by about 50 percent, than in the Northeast or North Central states. This regional gradient in risk could not be explained by differences in income or population density between the North and South. We then looked closely at the age specific cancer mortality rates in t hose counties in Florida where Northerners move at retirement, such as those around Miami Beach and St. Petersburg. Despite the large number of Northerners in these counties, mortality rates for colorectal cancer were as low as the rates in other Southern counties and did not seem to rise toward Northern rates at any age, not even at the older ages after retirement. We are now implementing a preliminary case control study to define precisely the characteristics of this reduction in risk and to quantify it, and to see whether it might be due to the migrants being a self selected subset of Northerners. Perhaps only healthy Northerners choose to migrate. If this last hypothesis is not the explanation, we will then proceed in a second study to identify the attributes of the Southern environment or lifestyle that are involved in reducing cancer risk—possibly increased consumption of fruits and vegetables or more vitamin A or C or the quality of the drinking water.

NCI has a special responsibility to collaborate with other federal agencies in developing national data resources that might contribute to cancer epidemiology. Several studies in our branch are utilizing HANES I, the first Health and Nutrition Examination Study of the American people, conducted in 1971-1974 by the National Center for Health Statistics. It collected dietary, biochemical, clinical, and anthropometric information on the nutritional status of a national sample of the U.S. population, about 23,000 people. With these data we are determining what foods are the major sources in the U.S. diet of various micronutrients; what foods are generally eaten by Americans of different ages, races and regions; what are the inherent patterns of the U.S. diet, if any, and what is the degree of variation. Such descriptive information is essential for the rational design and analysis of nutritional epidemiology studies.

We are also using HANES to assess specific cancer-related hypotheses. One such testable hypothesis is that the North-South difference in colorectal cancer mortality to which I alluded before can be attributed to regional differences in vitamin A or vitamin C intake. HANES data suggest this hypothesis is too simple. A second testable hypothesis concerns the recent finding of several prospective studies that low serum vitamin A is associated with risk of cancer. It has been argued that within a population as well fed as that in the U.S., serum vitamin A would only reflect individual genetic variation and would not be responsive to consumption of vitamin A containing foods. The data from HANES I suggest otherwise. Third, in international comparisons, age at menarche is inversely correlated with risk of breast cancer. It may well be an indicator of the dietary patterns that promote the disease. With HANES data we are investigating what food groups and macronutrients are most predictive of age of menarche in American women.

In cooperation with the National Institute on Aging, several other institutes, and the National Center for Health Statistics, NCI will be locating and reinterviewing in 1981-82 the adults examined in HANES 5 to 10 years earlier. Our major objective is to collect intervening cancer morbidity and mortality so that we can determine whether certain dietary exposures are associated wtih cancer at specific sites. The nutritional status of these people will have been measured prior to the clinical onset of disease and will thus not be a result of cancer. After these people are traced, we can keep informed of further mortality with the National Death Index.

Finally, I want to mention migrant studies. Migrants are a logical group in which to study lifestyle related cancers. Their genetic susceptibility to cancer is not altered by migration, but their lifestyle slowly

adapts. When Japanese migrate to Hawaii, their high rates of stomach cancer decline and their low rates of colon and breast cancer begin to rise. We are continuing to follow a cohort of 8,000 Japanese males, now living in Hawaii, whose dietary patterns were measured several times in the 1960s and 70s. Soon there should be sufficient cancer deaths to permit analysis of the associations between diet and cancer. We are also planning a large case control study of breast cancer among women of Japanese descent now living in Hawaii and the West Coast. Total fat, saturated fat, polyunsaturated fat, certain fatty acids, and cholesterol have all been postulated as causes of breast cancer, and most American women consume relatively high levels of all of these. However, it usually takes several generations of acculturation for the diet of Japanese-Americans to merge into that of white Americans, and several generations for their breast cancer rates to rise to white American rates. Thus we feel that among Japanese-American women, there may be sufficient variation in diet for us to separate and identify dietary risk factors for breast cancer.

In summary, we are trying to develop an intramural epidemiology research program on diet and cancer judiciously and carefully. Our present studies fall into several groups:

–Those studies designed to test in human populations hypotheses generated by animal experiments or by other epidemiological studies.

–Those studies that seek to explain the unusual geographic patterns in cancer risk revealed by the U.S. cancer maps.

–Those studies that develop and utilize national data resources.

–Those studies that focus on migrants and their gradual changes in lifestyle and cancer patterns.

FDA COMMISSIONER HOLDS UP IND WHILE REVIEWING NEW GUIDELINES

Arthur Hayes Jr., the new commissioner of the Food & Drug Administration, has ordered that no INDs involving use of the new toxicology guidelines worked out by NCI with FDA be approved until he has completed a review of those guidelines.

Hayes' action has resulted in delaying approval of one IND submitted by NCI, for tricyclic nucleotide. NCI submitted the IND on June 23 and was notified 30 days later that approval would be delayed "pending further review."

The new toxicology guidelines, which reduced the amount of preclinical toxicity testing required before a drug could be taken into phase 1 studies, were approved by FDA in 1979. Robert S.K. Young, who was group leader in the Oncologic Drugs Div. of FDA, bitterly objected and resigned his position (although remaining at FDA as a medical officer) in protest. Young subsequently filed a citizen's protest, demanding the commissioner reverse the decision.

The new guidelines were supported by Richard Crout, director of FDA's Bureau of Drugs. Crout told the President's Cancer Panel, meeting with the Board of Scientific Counselors of NCI's Div. of Cancer Treatment last June, "I personally don't see any hold up in INDs (as a result of the toxicology controversy), or any change in the agreement."

That was before the controversy reached Hayes' desk, however. Crout was on vacation this week, but his deputy, Jerome Halperin, told ***The Cancer Letter*** that the commissioner decided to personally review the guidelines. Crout still believes that they are rational and scientifically sound, Halperin said.

NCI plans to submit another IND within a few days, and will have two or three more ready to go during September. Halperin said he expects Hayes to complete his review by that time and that no further delays should ensue.

NCI has arranged with its phase 1 contractors for the tricyclic nucleotide trials and has four or five protocols prepared. The studies could begin within 48 hours after FDA approves the IND.

The new guidelines became a subject of congressional concern during hearings last spring, with some FDA personnel in addition to Young expressing their doubts. Young contends that they do not meet FDA legal requirements.

The President's Cancer Panel was invited to meet with the DCT Board to hear a presentation on the new guidelines and discuss the matter with Crout.

DCT Deputy Director Saul Schepartz presented a brief history of the development of the new guidelines, noting that it had become clear that toxicity tests in monkeys added little except a significant increase in costs. FDA's Oncologic Drugs Advisory Committee approved the guidelines in July 1979, agreeing to drop the monkey tests and that histopathology would not be required for initiation of phase 1 studies but would if the drug goes into phase 2. The DCT Board also approved the guidelines.

Schepartz said that INDs for 11 drugs, development of which followed the new guidelines, will be sought within the next 10 months.

Board member Enrico Mihich, who was a consultant to the FDA committee, commented that the question of whether the dog is necessary for predicting toxicity "is still open. Twenty years ago we tried to determine if one species is enough or if two is required. I don't think the answer in clear. The issue is one of what one wants to get out of it. If it is maximum tolerated dose, that's one. If it is a spectrum of toxicities, that's another."

The question of histopathology prior to phase 1 is the other major issue, Mihich said. "It is indeed so that a majority of the Board and the (FDA) committee agreed with the protocol (not requiring histopathology before phase 1), but it was not unanimous.

I was one of the minority."

"It is an issue of concern," NCI Director Vincent DeVita said. "We need long term studies to determine if histopathology before phase 1 is necessary."

Mihich noted that information needed for a new drug application is different than that required for phase 1.

Crout said he wanted to discuss "our understanding of certain aspects of the toxicology guidelines and why a controversy has arisen. It is easily evident why a controversy would arise. For many years cancer drugs have received less toxicity testing than most other drugs. In a superficial sense, this approach appears to be reducing that testing further, and thus is subject to more criticism."

That controversy "perhaps can be defused" by considering the philosophy behind the approach that anticancer agents can be safely tested in humans with less preclinical toxicology, Crout pointed out.

"We are dealing with a class of drugs in which the general toxicology is known," Crout said. "It is limited to cytotoxic drugs. . . . For any particular drug, animal tests can give false negatives. . . . Once the assumption is made that a drug in this class has passed the screen and has efficacy, basically there is no animal toxicity which could be discovered which would prevent testing it in humans. This shocks toxicologists. The usual function of toxicology in testing other drugs is to sort out the highly toxic drug and prevent it from being tested in man. The only rationale for cancer toxicology is to say, 'There is nothing I can discover that will prevent me from testing this drug in humans.' This philosophy has to be stressed. (The new guidelines) can be articulated too easily as cost cutting, at the expense of increasing human risk.

"A third factor," Crout continued, "is human monitoring. It must be excellent. Phase 1 studies (using the new guidelines) should be limited to major centers. This is an issue we're going to watch closely. We assume clinical pharmacologists are doing these studies."

Crout acknowledged, "We've had internal appeals to the commissioner to change the guidelines. I don't want to pre-empt the commissioner's right to change policy, but I personally don't see any hold up in INDs, or any change in that agreement. We're tough about applying these guidelines to other drugs, however."

"I've never heard those points articulated so well," DeVita said.

Panel member Harold Amos asked, "Is there a distortion of physiology in cancer patients which may be unique, and thus require a different approach by FDA, that we may have to accept some risks?"

"It's got a different approach from FDA and calls for different monitoring of patients," Crout said. "If cancer patients are unique, it imposes an extra burden on those doing the clinical testing."

"I personally feel the new protocol is reasonable," Board member Sydney Salmon said. "Yesterday we discussed new initiatives in colon cancer. There is a high incidence in the United States, with gross recurrences and no cure whatever. Should a new compound be identified and pass this preclinical toxicology, the public would desire greatly that it enter immediately into clinical trials. These guidelines should be reviewed later when we do have effective agents."

"We're exhibiting here today the scientific process," Panel member Bernard Fisher said. "When there is controversy, you need to point out what the controversy is, and that the scientific community is equally concerned about having drugs that are safe and effective. We've heard today that this protocol is provisional. I would be disappointed if this was your last protocol. I'm pleased with what I've heard. There is nothing here that is not reconcilable."

"It is a great source of pleasure to see the evolution of this relationship with FDA," Board Chairman Samuel Hellman commented. "This is a good operational guideline on how to work together."

CONSENSUS GROWING ON CAUSES OF CANCER PREVENTIVE STRATEGIES: HIGGINSON

There is a growing consensus on the part of scientists as to the causes of cancer and preventive strategies, John Higginson, director of the International Agency for Research on Cancer, said at a Brookings Institution conference last week on the major challenges confronting science and government in development of public policy to reduce environmental health risks.

Higginson said the popular belief that the U.S. is experiencing a cancer epidemic is not supported by the data. He noted that when adjusted for age, cigarette smoking, and alcohol consumption, most cancer rates are relatively stable and some cancers are actually declining.

Gilbert Ommen, a Brookings Fellow and formerly an official with the Office of Science and Technology Policy in the Carter White House, stressed the need to set priorities. "The assumption that all exposures to all chemicals are dangerous must be reconciled with results of increasingly informative tests," said Ommen, who has the OSTP representative to the National Cancer Advisory Board. "When people say, 'Oh, my God, now it's coffee; last year it was hamburgers; the previous year nitrites and saccharin; water, air and food are generally not safe; what's next?', we have failed to reach them with a balanced picture."

Ommen suggested that the major goals that must be achieved to integrate sound science into public policy are:

–To assure a process in which objective and timely review of available scientific information can be

assured, both in the early phases of proposal of a standard and in the later phases of decision making on the final standard.

–To enhance the quality of research in epidemiology, clinical investigation, and toxicology dealing with air pollutants.

–To identify especially sensitive populations and define the reasons for their sensitivity and levels at which they are adversely affected.

William Lowrance of Rockefeller Univ. said that the accurate assessment of hazards is a key factor in effective public health policy. He forcecast improvement in hazard assessment if risks are characterized explicitly so they can be faced if comparative approaches are taken and clear priorities are set if accommodation is sought between technical and lay perceptions; and if attempts are always made to weigh risks in appropriate context with benefits and costs.

Bruce Smith of Brookings called for a concerted approach to control environmental health risks which requires effective action by government, industry and the scientific community. "Laws have to be clearly drawn; regulators must act appropriately; the private sector must cooperate, including the need for industry and university scientists to assist in developing a more adequate knowledge base," Smith said.

AVAILABILITY OF RFA

Title: *Regional cooperative clinical trials groups*
Deadline: *Nov. 16*

NCI announces the availability of a request for applications inviting proposals for the establishment of regional cooperative clinical trials groups. At the present time, the NCI Div. of Cancer Treatment through the Cancer Therapy Evaluation Program supports clinical trials groups which cooperate together to perform statistically valid clinical research protocols. These groups presently are of four major types: (1) Groups that are specifically disease oriented; (2) Groups that are designed to deal primarily with high technology, single modality studies; (3) Groups in which the investigators have a particular expertise (such as pediatricians); and (4) multimodal national groups.

The purpose of the RFA is to encourage the establishment of groups that would have certain geographic advantages because they are compactly organized. These groups may have several advantages. For example, they may provide opportunities for practicing oncologists not currently involved in research clinical trials. Some of these groups may be organized around cancer centers. The groups can also take advantage of community outreach programs, provide state of the art therapies to patients, and strengthen accrual to research protocols.

It is intended that regional groups will be able to support clinical trials which take advantage of the scientific strengths of the communities in which they are organized. If, for example, a neutron generator is available, then a regional group could be established to accrue patients for neutron therapy trials in the geographic vicinity of that facility.

DCT intends to support these groups through the funding of institutions capable of serving as group operations and statistical offices. These offices would function as the centers of operation for consortia with reasonable geographic bases and unique patient resources and treatment capabilities. It is intended that these new cooperative groups will demonstrate the functional capability of regional consortia to perform innovative and meaningful cancer clinical research trials.

Awards under this announcement will be made as cooperative agreements. These are assistance relationships entailing substantial collaboration and involvement with NCI staff. The specific terms of this involvement by NCI staff are outlined in the RFA.

NCI anticipates making three to five awards as a result of this request. A total of $1.5 million has been set aside to fund the initial year's awards. Awards will be made for a project period of four years. Adjustments in the level of funding may be made annually. Renewal of the initial award beyond four years will be contingent upon satisfactory review of a competing renewal application by a peer review committee.

An RFA is available which outlines in greater detail the proposed study, the eligibility criteria for application, and the review procedures and criteria. An institution wishing to participate in this effort must submit an application in accordance with the guidelines specified in the RFA.

Additional information and copies of the RFA may be obtained from: John Y. Killen Jr., MD, Clinical Investigations Branch, DCT, National Cancer Institute, Landow Bldg. Rm. 4A16, Bethesda, Md. 20205, phone 301-496-2522.

Copies of the RFA were not available at press time. ***The Cancer Letter*** *will publish it in full when it is available.*

NCI CONTRACT AWARDS

Title: Computer support for resources management
Contractor: Information Management Services Inc., Bethesda, $708,389.

Title: Production and distribution of avian myeloblastosis virus and AMV reverse transcriptase
Contractor: Life Sciences Inc., St. Petersburg, Fla., $2,237,978.

Title: Prediction of hormone dependency in human breast cancer, continuation
Contractor: Univ. of Chicago, $33,000.

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. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs to the individual named, the Blair Building room number shown, National Cancer Institute, 8300 Colesville Rd., Silver Spring, Md. 20910. RFP announcements from other agencies reported here will include the complete mailing address at the end of each.

SOURCES SOUGHT

Synopsis No. 26

Title: *Operation of a cancer chemotherapy research collaborative office*

Deadline for qualification statements (10 copies): *Sept. 4*

Provide a liaison between the European Organization for Research on Treatment of Cancer (EORTC) and the Div. of Cancer Treatment, NCI. The principle functions of this liaison will include:

1) The maintenance of an office in Western Europe to foster close collaboration with EORTC concerning the exchange of information on new potential anticancer agents between European investigators and NCI.

2) Access and proximity to the EORTC data center which collects and processes data on clinical trials from Europe.

3) Acquisition of new compounds to be submitted to NCI's chemotherapy screening program located at the Institut Jules Bordet, Brussels.

4) Maintenance of direct contact with research institutes, pharmaceutical and chemical companies, medical schools and hospitals in Europe as potential sources of test agents.

NCI wishes to receive statements of interest in and qualifications for the maintenance and operation of a cancer chemotherapy research collaborative office which must be located in Western Europe. Invited to respond are organizations which have the capabilities and experience to perform the work described above. Interested organizations should be aware that contractual agreements with providers of compounds which protect the rights of these providers will preclude a contract award to chemical or pharmaceutical companies.

Organizations' capabilities will be evaluated on their qualifications to provide the above services as evidenced by the following types of information which must be provided:

Personnel—Suitability of training and experience of the principal investigator for the management of a liaison office between EORTC and DCT, NCI. This person shall have experience in clinical trials and chemotherapy research. Support staff should have sufficient experience in the field of antineoplastic drug development to establish and maintain sources of compounds for antitumor screening.

Facilities—The organization must have offices in Western Europe which include capabilities for compound shipping and collections as well as international communications such as telephone and telex.

Description of past experience and capabilities involving the exchange of information on new compounds having potential as anticancer agents, access to the EORTC data center which collects data on European clinical trials, access to the NCI supported drug screening program at the Institut Jules Bordet, Brussels, continuing direct contact with Western European research institutes, pharmaceutical and chemical companies, medical schools and hospitals.

NCI will evaluate qualification statements and will issue an RFP to those organizaions having acceptable qualifications.

Contracting Officer: Damian Crane
RCB Blair Bldg. Rm. 212A
301-427-8737

RFP N01-CP-15774-50

Title: *NTP computer support*

Deadline: *Sept. 17*

Total small business set aside.

The purpose of this RFP is to obtain a support contractor to continue the operations, statistical, systems analysis, and programming support for the Bioassay Program of the National Toxicology Program. Operations support includes forms handling and storage, input preparation, coding of histopathological diagnoses using a pathology coding system, error correction, keypunch and key-to-tape support, systems operation, user training, report production and validation of reports to insure accuracy.

Statistical support includes providing statistical expertise in the development of computer programs to perform statistical analyses. Systems analysis and programming support includes maintenance of six existing application systems, development of new applications including new reports when required, and assistance in the conversion to new systems.

Contract Specialist: Dave Monk
RCB Blair Bldg. Rm. 2A01
301-427-8774

The Cancer Letter _Editor Jerry D. Boyd

Published fifty times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston, Virginia 22090. Also publisher of The Clinical Cancer Letter.