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FDA IND Approval Of New Cancer Drug Is First Based On Phase 1 Clinical Trials In Europe

For the first time in its history, the Food & Drug Administration has approved an IND for a new anticancer drug based on European clinical data. The drug, a DuPont compound known as DUP-785, will be tested in two abbreviated phase 1 trials in the U.S. in patients with solid tumors.

To date, three patients have been enrolled in the trials,

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In Brief

EORTC-NCI Exchange Program Invites U.S. Applicants; USC Seeks Eye Melanoma Patients

EORTC AND NCI are inviting candidates to apply for participation in the exchange program which they jointly sponsor. Scholars with at least three years of post-doctoral research may apply for fellowships to do fundamental research in laboratories in the U.S. or Europe. Fifteen fellows from Europe and Israel were selected from 38 applicants last year for studies in U.S. labs. Competition is now open for U.S. investigators for studies in European labs. The competition will take place April 15 and Nov. 15; applications should be sent well ahead of those dates. Contact EORTC-NCI Exchange Program, Boulevard De Waterloo 125, 1000 Bruxelles, Belgium. . . . **PATIENTS** with melanoma of the eye are being sought by the Univ. of Southern California's Norris Cancer Hospital and affiliated Estelle Doheny Eye Foundation for a collaborative pilot study using hyperthermia and radiation therapy. USC physicist Melvin Astrahan developed the prototypical instrument to combine hyperthermia and radiation. Contact Zbigniew Petrovich, MD, director of radiation oncology, or Dierdre Cohen, MD, at 213-224-6646. . . . **FIFTH INTERNATIONAL** Conference on the Adjuvant Therapy of Cancer, March 11-14 in Tucson, will include reports on IL-2-LAK cells; hyperthermia, biological therapy and radiation therapy as adjuvants; effect of dose intensity; concept of neoadjuvant therapy; and sessions on breast, GI, gynecologic and genitourinary cancers and hematologic malignancies. Contact Mary Humphrey, Conference Coordinator, Arizona Cancer Center, Univ. of Arizona College of Medicine, Tucson 85724, phone 602-626-6044. . . . **MOST AMERICANS** favor tougher restrictions on public smoking and on tobacco industry promotional activities, according to a public opinion poll sponsored by the American Cancer Society, American Lung Assn. and American Heart Assn.

Approval Allows U.S. Investigators To Conduct Abbreviated Phase 1 Trials

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two at the Univ. of Texas (San Antonio) by PI Daniel Von Hoff. The third patient was enrolled this week at John Hopkins by PI Martin Abeloff. So far, the trial includes patients with colorectal cancer and non small cell lung cancer.

Close to 100 patients have been tested with the drug in three phase 1 studies that are ongoing in Europe. The drug is a substituted carboxylic acid derivative that has shown antitumor activity in colon, mammary, lung and stomach tumor xenografts in preclinical studies.

When the European investigators reported on their trials at the Fifth NCI/European Organization for the Research and Treatment of Cancer Symposium on New Drugs in Cancer Therapy in Amsterdam in late October, none had reached the maximum tolerated dose for the drug. No major side effects have been observed.

The European studies used three different i.v. dosing schedules: Heine Hansen of Copenhagen's Finsen Institute is studying a weekly schedule; Herbert Pinedo of Amsterdam's Free University Hospital is studying a single dosing schedule every three weeks, and Jean-Pierre Armand of France's Institut Gustave Rossy is studying five daily administrations repeated every four weeks.

The two U.S. trials will use the five daily adminstrations to be repeated every four weeks that is used by Armand. Francis Lee, associate medical director for DuPont, told **The Cancer Letter** that the firm plans to conduct a third trial using the same weekly adminstration schedule that Hansen has used.

In Hansen's Copenhagen trial, one patient with bladder cancer with metastasis to the lung has already achieved a partial (50 percent) response to the drug, "very exciting" for a phase 1 trial, he said.

Lee commented on the drug and the planned trials at a recent NCI Phase 1 meeting.

Because the European data was accepted by FDA, American investigators will be able to start their trials with a higher level of the drug than they would have been able to otherwise. They will also be able to conduct an abbreviated phase 1 trial before going on to a phase 2 trial. That also translates into money savings.

"In the U.S., we can do abbreviated phase 1 trials" because the European data was accepted, he said. "I think it is a major development for the clinical cancer research area in which clinical data from Europe can be used to start an abbreviated phase 1 trial in the United States."

Lee described the approval as "a historical case." FDA has accepted clinical data from Europe for new drug approvals, but had not given an approval for an investigational new drug based solely on European clinical data.

Lee attributed the development to several factors. "In Europe, we're utilizing very reputable investigators with a long track record of doing good research."

He also cited the help of NCI's liaison office in Brussels. Headed by Omar Yoder, the office assisted DuPont personnel in Europe to closely monitor the clinical data from the phase 1 trials. "The data in Europe is so good, and the monitoring was done so well with our joint staffs," he said. NCI's Clinical Monitoring Program in Brussels audited the data.

Although the drug underwent clinical testing in Europe, it was synthesized, screened and underwent preclinical toxicology testing in the U.S. The novel structure was picked out of 200 candidates, and initial preclinical testing was a joint effort between DuPont and NCI.

One of the primary goals of NCI's Clinical Monitoring Program in Brussels has been to gain the acceptance of data from European clinical trials in the U.S.

"Until recently, any drug that passed through the U.S. [regulatory] system had to be reevaluated clinically in the U.S.," Yoder said. When interviewed in October, he said, "that is now changing" and successfully predicted that "probably by the end of the year, we will have an example of a drug that has undergone clinical trials in Europe that will presented to FDA for IND approval" without clinical trials in the U.S.

The Clinical Monitoring Program began in 1984 and is responsible only for the monitoring of phase 1 trials. Celestina Arrigo, one of two full time employees in NCI's small Liaison Office in Brussels, serves as the clinical monitor. Sylvia Marsoni, former head of NCI's Clinical Monitoring Section who is currently in Milan, serves as a consultant to the program.

The clinical monitoring program is part of NCI's small European liaison office. NCI

directly supports two operations at the Institut Jules Bordet in Brussels.

An NCI grant supports a drug screening program for new compounds, which currently screens more than 25 percent of all new compounds coming into NCI from throughout the world. The other program supported by NCI in Brussels is the EORTC Data Center, also located at the Institut Jules Bordet. NCI initially provided about 90 percent of the data center's budget, but NCI funding, also in the form of a grant, currently represents only 10 to 15 percent of the center's budget. The main funding sources for the center are the European Economic Community and the EORTC Foundation.

Under the clinical monitoring program, data is collected on computerized NCI forms by participating institutions that have computers and software. Investigators currently submit their data to the office on diskettes, but future plans call for a computer network.

When a trial ends, the data is sent to the U.S. The program is currently monitoring five drugs in five institutions. Arrigo conducts site visits at all the centers to ensure that they meet specific standards such as staffing, drug storage.

Both Yoder and Arrigo emphasized the quality of European data collection.

Arrigo said the data collected from European centers, particularly in phase 1 trials, is of "very, very good quality," adding that she never encountered major problems even when the institutions had been working independently.

Although European investigators didn't have as much data to collect before the NCI forms were introduced, she said the detailed forms have been helpful to investigators. Since the forms were introduced, "people have really started to work in a standardized way now," she said. "When people work on the same form, they start to work in the same way," she said. And by using the same form, "standards start to develop."

She noted that coordinating standardized data collection is more difficult in Europe than in the U.S. because of the need to work with different languages and countries. In Europe, physicians are usually directly linked with trained data managers.

"The only way to have data collected in a good way is to have data managers, someone responsible for it," she said. A group of data managers was organized in EORTC two years ago in order to connect managers from different centers and countries so they could see how working and how organized.

In addition to its Clinical Monitoring Program and the drug screening contract, the NCI liaison office also conducts followup of compounds on test and reporting results. It provides assistance in the development of compounds for clinical trial in such areas as bulk synthesis, formulation, toxicology, pharmacokinetics, and phase 1 and 2 trials.

Yoder estimates that the number of new drugs entering phase 1 trials in Europe is comparable to the number entering NCI supported phase 1 trials in the U.S.

More than 25 percent of all compounds that come into NCI from all sources worldwide for screening receive initial screening for anticancer activity by the European drug screening laboratory located at the Institut Jules Bordet in Brussels.

The lab may soon be responsible for the screening of 40 to 50 percent of all new compounds entering the NCI screen. The NCI contractor will be one of two remaining contractors when NCI phases out its two other screening contracts.

25,000 Compounds Screened

Since the screening program was established in 1972, the Jules Bordet lab has screened a total of 25,000 compounds. The number of compounds screened by the lab has risen from 365 compounds in 1973 to a peak of 3,500 in 1977, after which time NCI decreased the number of compounds to be screened. In 1985, the program screened about 2,300 compounds.

Jules Bordet was awarded its first competitive screening contract in 1975. By 1980, the screening program had advanced to the point where Europe was responsible for 25% of the total new drug input into NCI.

The first contract of $15,000 to the European screening lab was made in 1972, the same year NCI established its liaison office in Brussels.

The acquisition of compounds from European universities and industry for the screening lab was one of the primary goals of the new office, which has been headed by Yoder since its inception in 1972.

The NCI liaison office selects novel compounds as potential antitumor agents for the screening program on the basis of the novelty of the structure, the type of biological activity and other biochemical rationale.

Following submission of a compound to the NCI Liaison Office, NCI in Bethesda assigns an NSC number based on the novelty of the structure. The primary screen is performed on the P388 leukemia mouse leukemia model and/or tested in in vitro systems.

The Brussels lab is currently developing a disease oriented in vitro system and expects to be able to begin screening a limited number of compounds in 1987. The in vitro system will run in parallel with the in vivo screen until a comparative evaluation can be made.

Lung, colon, melanoma, and CNS lines have already been established and other tumor types are in development. The lab plans to have a total of 50 different tumor types originated from human tumors available in the in vitro strategy.

Under the new strategy, it is expected that drugs active in selected cell lines could be evaluated in a phase 1 study in patients with the particular tumor type. The NCI liaison office can also carry out testing in additional tumor types through the EORTC.

The screening lab is able to conduct tests for about half the cost per test of U.S. contractors, Yoder said.

Following initial screening, the test results are evaluated by NCI staff, who then send results to the compound's supplier. If the compound's activity is confirmed in tumor panel testing, it is reviewed by NCI's Decision Network Committee, and then may be developed for clinical trial in the U.S. or Europe.

The liaison office obtains approval from the supplier, EORTC's New Drug Development Committee or the United Kingdom's Cancer Research Campaign before the compound is selected for a clinical trial.

Although preclinical toxicology performed in Europe must meet the regulatory requirements of the respective countries, guidelines adopted by EORTC and CRC are normally acceptable.

Phase 1 trials of drugs of interest to NCI are performed in recognized centers within CRC and EORTC. The liaison office coordinates the data collection and monitoring of the phase 1 trials in close collaboration with the Cancer Therapy Evaluation Program in Bethesda.

Trilateral Agreement Reached

This summer, NCI, the European Organization for Research on Treatment of Cancer and Britain's Cancer Research Campaign signed a trilateral agreement for collaboration in drug development.

While the agreement serves primarily to formalize an informal association already existing between the three entities, its existence is due in large part to more than a decade of work by Yoder in the small liaison office.

The agreement formalizes who is responsible for what activities, and stipulates that any collaboration with NCI will be coordinated through a joint EORTC/CRC steering committee.

The steering committee is composed of representatives of both European groups, and is cochaired by Thomas Connors of CRC and Heine Hansen of EORTC. The role of NCI's liaison office as secretariat of the group is an indication of its standing in the European cancer research community.

Prior to the agreement, all drugs coming through NCI's liaison office were handled on an informal basis. "We wanted a little more formal mechanism to work through," Yoder said, adding that he hopes the new committee and structure will result in less confusion.

Both groups have access to any drug going into clinic.

The only direct support provided by NCI for clinical trials in Europe is in the form of $50,000 per year for a clinical monitoring program that provides small amounts of money to centers for administrative costs.

"The major incentive is that they want to be associated with the NCI program, they want to participate in clinical trials, and they want access to drugs that NCI is developing," Yoder told **The Cancer Letter.**

"We haven't had to give financial incentives to participating institutions" as is necessary in the U.S., he said. The situation may change, however, "as Europe becomes more independent."

Because national health insurance in European countries pays for patient care costs, including experimental treatments, it is much cheaper and easier to conduct phase 1 trials in Europe than in the U.S.

In addition, cancer drugs are often able to move faster through European drug regulatory agencies than in the U.S.

NCI "doesn't run clinical trials in Europe. They are run by Europeans," Yoder emphasized. Many investigators who are now in key positions in Europe, however, were trained by NCI or worked at the institute as fellows.

NCI cannot directly support or run clinical trials in Europe because it is not allowed to support any drug that FDA has not approved. It does receive data on the trials and cooperates with European investigators.

NCI's affiliation with the investigators is conducted in "a friendly way," he said. The institute has "lots of input, but doesn't dictate" what should be done.

NCI's indirect costs for its European operations total slightly more than $100,000, which pays for all liaison office staff. Yoder is the only NCI staff person in Brussels. The office employs one full time administrative assistant, a full time clinical monitor, and two part time secretaries, all local.

When the office was started, it was charged to act as a liaison between NCI and EORTC, and to collect EORTC clinical protocols for NCI.

The office conducts a variety of liaison activities. It is intended to promote scientific exchanges between the U.S. and Europe, as well as within Europe, and acts as a liaison between European and international organizations on cancer research and the U.S.

It also assists with the organization of meetings and symposia in collaboration with EORTC, and acts as a liaison with EORTC cooperative groups through the EORTC Data Center, as well as with the CRC Phase 1/Phase 2 Working Group. The office also collects clinical protocols throughout the world, excluding Japan and America for NCI.

When the office was started, NCI was also interested in seeing whether it could establish contact with the European pharmaceutical industry. "It took a few years to publicize what we were doing," Yoder said, adding that the European pharmaceutical industry was "initially very suspicious" of NCI's activities in Europe.

While it required several years to gain the trust of industry, "things took off much faster than anyone anticipated," he said.

"It was almost an accident that" the office was started at all, Yoder said.

Credit for the idea that led to the establishment of the office is given to Henri Tagnon, former president of the EORTC and chief of medicine and clinical investigation at the Institut Jules Bordet. Tagnon, who has held various posts at American institutions, including Memorial Sloan-Kettering Cancer Center, Harvard, New York Hospital and Cornell, mentioned to Abraham Goldin and former DCT Deputy Director Stephen Carter that he thought it would be nice if NCI set up an office in Europe. He pointed out that the institute would be able to access a large number of new compounds.

Goldin went to Europe and talked about how much space would be needed to start a small lab. Gordon Zubrod, who was then DCT director, initiated a small contract of about $15,000, began shipping mice, and researchers at Bordet began screening.

Yoder accepted a one year temporary assignment to Brussels in the fall of 1972. He has been at the office and an integral part of the European cancer research community for 14 years now.

The first part of NCI's European program focused on the acquisition of new compounds for screening. As those compounds have entered clinical trials, the program has changed, he noted. As new drugs became available, toxicology and pharmacokinetic studies have become necessary, as has followup for trials.

"By 1980, the program had evolved to the point where we had an almost comprehensive program here, from screening to clinical trials. Now we even have a clinical monitoring program.

"In doing this, it was very important to become associated with various [oncology and research] organizations in Europe."

At one point, NCI had thought of starting a similar operation in Japan, but Yoder thinks that such a program is unlikely now because Japan is so technologically advanced.

He noted that in the time since NCI established its office in Brussels, that European cancer research and treatment has come up to a level equal to that of the U.S.

Yoder speculated that if NCI decides at some point that new drugs are not a high priority, that the institute may have to rethink its orientation in Europe. He believes, however, that collaboration with Europe will always be important.

"We've established a good base. NCI has a close association with all the major cancer centers in Western Europe." In fact, a number of European investigators serve on NCI advisory committees.

This article is the first in a series on the European cancer scene. Next week, **The Cancer Letter** *will report on activities of two leading European cancer organizations, the EORTC and the CRC.*

First Compound From New In Vitro Screening System To Enter Trials

The first clinical trial of a drug that has been screened in NCI's new in vitro screening system will begin in the coming year at the National Naval Medical Center.

The compound, 4-ipomeanol, "is the first example of a drug which was screened in the human tumor cell line being used in patients in phase 1 studies, in patients with that specific disease," Gregory Curt, deputy director of the Div. of Cancer Treatment, reported at a recent NIH meeting on "Progress in Cancer Therapy: Impact on Nursing."

Toxicology studies on the drug have already been completed.

The drug "is not active in mouse lymphoma, and is not active in mouse leukemia, but when it was screened in the in vitro cell line, it was specifically active against adenocarcinomas of the lung."

When the drug was placed in rats, "the response or the activation of the drug was very high in lung tissue, with very little activity in the liver, kidney, heart or other parts of the rat."

Curt cited the compound as an example of "some very interesting leads" from NCI's new screening system.

The new screening system was approved by the Div. of Cancer Treatment's Board of Scientific Counselors in February, 1985.

The new system utilizes primary tumor human solid tumor cells instead of mouse leukemia cells. The change in the screening system was accompanied by a shift in attention away from purely cytotoxic drugs to other classes of agents, such as agents that induce differentiation or counteract the process of metastasis.

Another example of the shift in focus is research on the process of cancer cell attachment in metastasis being carried out by NCI investigator Lance Liotta.

"The process of attachment when the tumor is either getting into the vessel or out of the vessel occurs by the tumor cell membrane attaching to a constituent protein of the basement membrane called laminen," Curt explained. Tumor cells have a receptor that recognizes laminen, and laminen acts as an anchor. Liotta has made small units of laminen, called laminen fragments, in order to block the receptors, which could provide a way to block the entire process of metastasis, Curt said.

Minorities Increasingly Involved In NCI Research, Training Programs

"Minority involvement in cancer research and training activities sponsored by NCI has increased significantly over the past few years," Lemuel Evans, director of the Comprehensive Minority Biomedical Program in NCI's Div. of Extramural Activities, told the National Cancer Advisory Board at its last meeting.

"Minority individuals and institutions are increasingly being considered as potential resources for long and short term solutions," Evans said. NCI programs directed at increasing minority involvement in cancer research and cancer control include, Evans said:

*Minority investigator supplements. "These grants provide immediate access to participation in state of the art research activities by minority scientists by providing support for the inclusion of minority investigators on already funded NCI supported grants."

*Minority satellite supplements. "This interesting variation of the supplement mechanism seeks to promote participation of minority patients in clinical trials and other treatment programs at hospitals and institutions which serve large or predominately minority populations. The thrust is to enter minority patients in an expanded and organized fashion into cancer treatment protocols."

*Travel fellowships. These encourage participation in annual meetings of the American Assn. for Cancer Research and American Society of Clinical Oncology by providing travel support for minority students engaged in cancer research or who have training that could lead to contributions in this field.

*Minority focused cancer control intervention research activities. These studies included health services access and utilization, primary prevention, coordinated intervention trials, research on differences between blacks and whites in cancer survival.

*Cancer centers. The first minority consortium cancer center has now been funded. This involves Charles R. Drew Postgraduate Medical School in Los Angeles; Morehouse School of Medicine in Atlanta; and Meharry Medical College in Nashville.

*Cancer information programs. NCI's Office of Cancer Communications has embarked on a major program aimed at encouraging black Americans to minimize their cancer risks.

DCBD Board Approves Concept For Recompeting Animal Facility Contract

The Board of Scientific Counselors of NCI's Div. of Cancer Biology & Diagnosis gave concept approval at its recent meeting for recompetition of a contract for an animal holding facility.

The contract is presently held by Bioqual Inc., of Rockville, MD. The new contract will be for six years. NCI estimated the contract will cost a total of $600,000 a year.

The contract calls for maintenance of inbred small research animals and supplemental research services. The colony consists of approximately 250 different strains of mice, six strains of rats and New Zealand white rabbits. Included in the 250 different strains are both inbred and congenic recombinant strains. A total of 10-12,000 mice, about 350 rats and 20-25 rabbits are housed at the Bioqual facility.

The facility was designed chiefly for the holding of mice and maintenance of mouse strains procured from outside sources. Breeding of certain strains of mice and rats for experimental needs of the Immunology Branch are performed when such animals are not available commercially. Frozen samples of sera and cells are stored in freezers of appropriate temperatures and are transferred to NIH as required.

In addition, production of hybridoma ascites and antisera and skin grafting experiments have been pursued on this contract by several investigators. These protocols involve the use of inbred mouse strains, immunization of each strain with appropriate cells and the production of antisera that can be used by senior investigators in the Immunology Branch.

The new contract will require continuing maintenance of the colony of approximately 250 strains of inbred mice, at approximately the same number of 10-12,000, consisting of about 50 strains as breeders, mice in treatment studies, production of breeders and rats and rabbits as needed. The contractor also will be required to prepare and ship biological products from mice such as immune sera, ascites and mice to investigators upon request. The contractor must possess technical skill to carry out skin graft experiments, immunizations and bleeding. Reagents and mice will be shipped to outside investigators as directed by the NCI project officer.

New Publications

"Management of Advanced Melanoma," edited by Larry Nathanson, with 22 contributors. Comprehensive monograph addresses the entire range of clinical and basic research studies directly related to the therapy of advanced or recurrent malignant melanoma. Churchill Livingstone Inc., 1560 Broadway, New York 10036, $39.50.

"Advances in Cancer Control: Health Care Financing and Research," edited by Lee Mortenson, Paul Engstrom and Paul Anderson. Prevention and screening efforts, marketing issues in cancer program development and the new field of health care financing research, oncology nursing management, clinical research in community settings, research in geographically based cancer control. Alan R. Liss Inc., 41 E. 11th St., New York 10003, phone 212-475-7700, $74.

"Alternatives: New Developments in the War on Breast Cancer," by Rose Kushner. Updates such topics as prevention, diet, how to find the best doctor, what to expect in examinations and diagnostic tests, how to get the most effective and least damaging treatment, breast reconstruction. Warner Books, 666 Fifth Ave., New York 10103, $5.95 plus $1 postage, discounts for quantities 25 and over.

"All About Fat and Cancer Risk," booklet published by the American Institute for Cancer Research. Explains how to cut down on dietary fat. Free from AICR, Dept. FC, Washington DC 20069.

"Cancer Drug Resistance," edited by Thomas Hall. New data from in vitro animal systems and human clinical studies. Alan R. Liss Inc., 41 E. 11th St., New York 10003, phone 212-475-7700, $48.

"Chemical Carcinogenesis Research Information System Database," produced by NCI. Information on carcinogenicity, tumor promotion and mutagenicity test results, derived from primary journals, current awareness tools and a special core set of sources. Nine track computer tape available either 1600 or 6250 bpi from National Technical Information Service, Springfield, VA 22161, phone 703-487-4650, $160.

The following are available from Raven Press, 1140 Avenue of the Americas, New York 10036, phone 212-575-0335:

"Adenomas and Adenomas Containing Carcinoma of the Large Bowel: Advances in Diagnosis and Therapy," edited by C.M. Fenoglio-Preiser, and F.P. Rossini, $48.

RFAs Available

RFA 87-CA-15

Title: Cooperative agreements for national collaborative chemoprevention projects
Application receipt date: Feb. 23

NCI's Div. of Cancer Etiology invites applications for national collaborative chemoprevention projects conceived as new approaches to cancer prevention. The projects should develop new approaches to cancer prevention, to acquire basic knowledge in significant biological systems for carcinogenesis/anticarcinogenesis; derive new insights into practical means for chemoprevention of the carcinogenic process; and rapidly translate these understandings into new chemopreventive entities with known ranges of efficacy and defined pharmacologic/toxicologic properties.

The new projects are envisioned as a means to enhance and expand chemopreventive entities and strategies for cancer prevention. Each NCCP would consist of a number of laboratory research programs representing diverse scientific disciplines and expertise. Scientists in a given project could derive from any combination of the academic, nonprofit and for profit communities. Scientists in an NCCP could also be drawn from a single organizaation possessing necessary diversity and in depth expertise to accomplish project objectives.

Each project is expected to consist of a project director, program leaders in several broad scientific disciplines and an NCI coordinator. The project director has the responsibility for organizing the project, assembling the multidisciplinary group of program leaders, preparing the cooperative agreement application and serving as principal investigator. This individual provides scientific and administrative leadership and, in addition, is expected to provide a laboratory program. A high degree of interaction and focus are expected in project efforts.

Many classes of chemopreventive agents have been investigated in numerous biological systems, and of these, a significant number appear promising for substantial developmental efforts. These classes include, but are not limited to, protease inhibitors, antioxidants, micronutrients, calcium compounds, vitamin D, its metabolites and analogs, free radical scavengers and inhibitors of free radical producing sequences, factors modulating growth and/or maturation, including lymphokines, modulators of arachidonic acid metabolism, nucleophiles and potential new classes of inhibitors/suppressors existing in natural products such as foods consumed by man, as exemplified by green and yellow vegetables. In depth, coordinated studies are also needed on the influence of macroconstituents of the diet on carcinogenesis. Since there is already extensive activity in retinoids research and development, applications in this area will be considered nonresponsive.

NCI anticipates the funding of multiple awards for project periods of five years and has set aside $1.5 million for the initial year's funding. The expected starting date for these awards is Sept. 1, 1987.

Awards will be made as cooperative agreements. These involve substantial participation by NCI staff during performance of the project.

Further information and copies of the complete RFA are available from Carl Smith, PhD, Program Director, Biological & Chemical Prevention, Chemical & Physical Carcinogenesis Program, DCE, NCI, Landow Bldg Rm 9B-06, Bethesda, MD 20892, phone 301-496-4141.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Blair building room number shown, National Cancer Institute, NIH, Bethesda MD 20892. Proposals may be hand delivered to the Blair building, 8300 Colesville Rd., Silver Spring MD, but the U.S. Postal Service will not deliver there. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CP-71013-58

Title: Resource procurement of human tissues from donors with an epidemiological profile
Deadline: Jan. 15

NCI has a requirement for (1) collection of non-tumorous and tumorous lung, bronchus, colon and pleural mesothelium human tissue at the time of surgery; (2) delivery by contractor specified means, viable human tissue and cells promptly (within two hours of excision) to the Laboratory of Human Carcinogenesis at NIH; (3) provide an epidemiological profile of the donors obtained by trained interviewers using a form provided by NCI.

This procurement is restricted to contractors located within 90 minutes by land of NIH. The incumbent contractor is Georgetown Univ.
Contract Specialist: Diane Smith
RCB Blair Bldg Rm 119
301-427-8888

AMENDMENT

The preproposal conference, listed in the announcement of the availability of RFP NCI-CN-75405-43, support contract for public health agency initiative (**The Cancer Letter**, Nov. 7), has been canceled. The new deadline for proposals is Dec. 23.

NCI CONTRACT AWARDS

Title: Operation and coordination of a nationwide multiple study, high volume death certificate acquisition and management system
Contractor: Westat Inc., $623,413

Title: Epidemiology of human T-cell leukemia/lymphoma virus in Trinidad and the Caribbean region
Contractor: Caribbean Epidemiology Centre, Pan American Health Organization, $764,835

Title: Plant collections
Contractors: Missouri Botanical Garden, $653,883; New York Botanical Garden, $626,826; Univ. of Illinois, $1,402,978

Title: Shallow water marine organism collection
Contractor: SeaPharm Inc., $2,077,980

Title: Primary rodent production center
Contractor: Charles River Laboratories, $6,525,366

Title: Deep sea marine organism collection
Contractor: SeaPharm Inc., $5,354,529

Title: Dosage form and delivery system, new agents
Contractor: Univ. of Kansas, $306,134

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