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NCI EXPECTED TO FUND CANCER EDUCATION GRANTS IN FISCAL 1986; FINAL FATE TO BE DECIDED THIS WEEK

Although the final decision on the fate of NCI's Clinical Education Program is to be decided by NCI's Executive Committee late this week, the institute is expected to continue funding all awards for this fiscal year, including those with start dates in July. Because the Executive Committee

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In Brief

SUSUMU TONEGAWA TO RECEIVE BRISTOL-MYERS AWARD; MARK GREEN NAMED DIRECTOR OF UCSD CANCER CENTER

SUSUMU TONEGAWA, professor at MIT's Center for Cancer Research, has won the ninth annual Bristol-Myers Award for Distinguished Achievement in Cancer Research. Tonegawa's work with T cells and B cells "has broadened our scientific understanding of the body's immune system and has provided researchers with a basis for designing treatments for cancer, as well as AIDS and other diseases," Bristol said in announcing the award. Tonegawa will receive his $50,000 prize at a luncheon in New York April 17. . . . **MARK GREEN,** who has been acting director of the Univ. of California (San Diego) Cancer Center since last May, has been appointed permanent director by UCSD Chancellor Richard Atkinson. Green replaces John Mendelsohn, who moved to Memorial Sloan-Kettering. Green has directed clinical and inpatient oncology at UCSD since 1982, and is a PI with Cancer & Leukemia Group B. . . . **NCI'S CANCER** Therapy Evaluation Program is wrapping up a lengthy, in depth review of clinical trials and how they are being done by NCI grantees and contractors, primarily the cooperative groups. Outside advisors will be brought in within the next one to two months to look over the various reports, and a summary report may be released a month or two later. CTEP Director Robert Wittes said, "I don't foresee any major consolidations or cutbacks. There will some changes as the result of the natural process of peer review." He denied a rumor that NCI intends to phase out all cooperative groups and conduct all extramural clinical trials through CTEP contracts. . . . **THE PBS** airing of a documentary on the instability of cancer research funding, scheduled for March 19, has been delayed to April. Producer-writer Harry Mantel was forced to hold up the production because of the delay in presentation of the FY 1987 budget. Pernell (Trapper John) Roberts will narrate the program. . . . **PETER HOWLEY,** chief of NCI's Laboratory of Tumor Virus Biology, has received the Wallace P. Rowe Award for Excellence in Virologic Research for his "outstanding contributions in defining the molecular structure and function of papillomavirus genomes."

EDUCATION PROGRAM "ALIVE AT LEAST ONE MORE ROUND," NCI OFFICIALS SAY

(Continued from page 1)
is expected to abide by the National Cancer Advisory Board's recommendation that the program not be phased out, some new awards will probably be made in order to keep the program alive, but at this point no one is even guessing how many or what level of funding to expect in the coming year.

Members of NCI's Cancer Education Review Committee, however, were told at their Feb. 28 meeting to go ahead and review the applications "as you always would" by Barney Lepovetsky, chief of the Div. of Cancer Prevention & Control's Cancer Training Branch. "The program is not being phased out," he told the committee, adding, "there may be some budget reductions, but that's not unique to this program. I suggest you carry on as usual."

Responding to a question by committee Chairman James Lowman if the group "is alive for at least one more round," Div. of Extramural Activities Director Barbara Bynum replied, "as far as I know. There is no reason to imagine" otherwise. Bynum told the meeting that NCI staff is "having to look at everything in the institute's program with an extremely cautiouse eye" due to the budget cuts mandated by the Gramm-Rudman-Hollings balanced budget legislation. "There are adjustments that will be made across NCI's programs and probably also NIH's," she said, adding that institute staff does not yet know the consequences of the GRH budget restraints. "There is a fair degree of inflexibility in the NIH budget structure itself," she said. "There are line categories between which we can't switch funds." Bynum added that "the part of the NIH budget that is flexible, amenable to cuts is very small," and that NIH will usually make necessary budget cuts on its commitment base, new starts and initiatives.

Because NIH operates on an annual budget and cannot legally obligate money for more than a year, it funds a five year project on a year by year basis, and is not legally bound to fund another year if funds are not available.

NCI has about 40 type 5 (noncompeting renewal) awards slated for funding under the program in fiscal 1986, for a full funding total of $4.7 million. If no new (type 1) or competing renewal (type 2) awards were made, the number of competing renewals would drop to approximately 29 in FY 1987; to about 19 in FY 1988, and roughly 14 in FY 1989. If those grants were funded at full levels, the amount would total an estimated $3.3 million in FY 1987, $2.1 million in FY 1988, and $1.5 million in FY 1989.

Although various options for continuing the program are under consideration by NCI, one possibility is that the awards could be funded at less than the full level.

NCI's Executive Committee had planned to phase out the program, but the NCAB Committee on Budget & Planning asked the institute to maintain at least a minimal level of funding for the program. NCI Director Vincent DeVita had said that the program was "the kind of thing one might expect medical schools to do themselves in this time" of budgetary constraints (**The Cancer Letter**, Feb. 14).

Supporters of the program disagree, however, and maintain that if it were phased out, curriculum development in cancer education supported by the grants would be suffer severely or even disappear.

"If the program were phased out, "cancer education in medical schools will suffer," Lowman said. Although he said he understood the difficulties faced by NCI because of the GRH budget cuts, he emphasized that "it is important to recognize that doing away with this program will alter" cancer education in medical schools and that the programs currently in existence "simply will erode rapidly. Unless someone's out there giving money, those kind of things just aren't done."

Review committee member Ross McIntyre also emphasized the importance of the program for curriculum development in medical institutions, noting that the program's impact extends beyond the number of institutions that are funded. "There are a number who apply" for grants whose programs have changed by engaging in competition even if they don't get funded, he said.

"This type of activity is especially vulnerable because it is not supporting directly new individual projects, it is not an RO1 type program and it is perceived differently at various [levels] within NIH and perhaps outside," he said. For example, McIntyre cited the Jan. 31 Cancer Letter article in which DCPC Director Peter Greenwald is quoted as saying the NCI Executive Committee decided to phase out the program because of budget constraints and its success in training medical oncologists. To terminate the program, "especially on the basis of the misperception that it's training medical oncologists" is a mistake, he said. "People who pushed this concept were concerned that cancer was not being taught as a multidisciplinary function." When the program was initiated, interdisciplinary teaching was not common, he added. He noted that the emphasis of grant applications in the program has switched to areas such as screening and prevention, nutrition and epidemiology.

NCI STUDY: "LITTLE EVIDENCE" AGAINST FORMALDEHYDE; SOME CRITICS DISAGREE

As predicted when the study of workers exposed to formaldehyde was approved in 1980, industry involvement has given ammunition to critics of the results and NCI's interpretation of those results.

NCI announced this week that the study conducted by the Div. of Cancer Etiology's Epidemiology & Biostatistics Program had found "little evidence" that formaldehyde is carcinogenic. The study, which cost about $1 million, was given concept approval in 1980 by the DCE Board of Scientific Counselors despite concern expressed by then National Cancer Advisory Board members Irving Selikoff and Sheldon Samuels that participation by industry could "skew the results" or at best cast doubt on its findings (**The Cancer Letter**, Oct. 17, 1980).

The Formaldehyde Institute, an industry supported organization, and two of the largest producers of the widely used substance, Dupont and Monsanto, helped NCI investigators and outside consultants write the report on the study. The Formaldehyde Institute had paid for a preliminary feasibility study and had offered to pay for the full study. However, the DCE board decided it should be paid for entirely by the government and that the study should be designed by NCI.

Westat Inc. performed the data collection under a $260,000 contract with NCI, and Dynamac Corp. monitored the study under a $230,000 contract. NCI intramural staff time cost about $500,000.

The study of 26,000 workers exposed 20 years or more had an excess of 32% of lung cancer deaths. NCI's interpretation that this was not convincing evidence of formaldehyde's carcinogenicity drew criticism from union officials and also from Philip Landrigan, former director of epidemiology at the National Institute of Occupational Safety & Health and now director of occupational medicine at Mt. Sinai Medical Center.

Aaron Blair, chief of occupational studies in the Environmental Epidemiology Branch, who was NCI's project officer for the study, defended the conclusion on the basis of the finding that there was no difference in lung cancer mortality among those exposed at low, medium and high levels. "Dose response is the single most powerfull tool in an epidemiological or lab study," Blair told **The Cancer Letter.** "We have to assume that getting an increased dose increases the risk." He said the chief suspect in the increased lung cancer mortality is cigarettes. There was no effort to gather cigarette smoking data. "To do that at the front end is enormously expensive." It will be much less expensive to determine smoking incidence now among the identified cases and appropriate controls, and Blair said NCI staff may recommend such a study be done.

Another concern of the critics is that only those companies who agreed voluntarily to allow investigators access to their files were included in the study. The critics contend industry could stack the study with the "clean" companies. Blair acknowledged that some firms refused to cooperate but insisted that those who did were representative of the industry. "We looked carefully at the range of exposures we found, and they mimicked published figures for the entire industry."

DES–BREAST CANCER RISK STUDIES TO BE ENCOURAGED BY DCE ANNOUNCEMENT

NCI's Div. of Cancer Etiology's Board of Scientific Counselors has approved a concept to encourage studies of breast cancer in diethylstilbestrol treated mothers and in DES-exposed offspring. The concept was approved unanimously by the board. NCI hopes to make five awards following the issuance of a program announcement.

Sample questions to be addressed by investigators are (1) Is there an increased incidence of breast cnacer in DES exposed individuals relative to appropriate comparison groups; (2) If so, can increased incidence be clearly associated with DES exposure (as distinguished, for example, from association with difficulties in maintaining pregnancy that precipitated the use of DES; (3) In relation to breast cancer development, is DES exposure interactive with, or potentiated by, any other known risk factors for breast cancer, e.g., other exposure to exogenous estrogens, or family history of breast cancer; (4) What are the pathologic types, receptor status, and other characteristics of breast cancers developing in DES-exposed persons; and (5) Is there an increased incidence of benign or premalignant breast lesions in DES-exposed individuals, and what are the histopathologic and other characteristics of any such benign or premalignant lesions, especially in women who subsequently develop breast cancer.

Aspects that have been identified as being of particular interest include:

a) Possible documentation of dosage, timing and duration of DES treatment, and any comparison of doses.

b) Reason(s) for DES treatment, and any information on hormonal characteristics of exposed and comparison women, and of DES-exposed women who developed breast cancer compared with those who did not.

c) Any data on alternative or other hormone exposures.

d) Incidence of, and information on, breast cancers

developing in DES-treated mothers and DES-exposed daughters: age of onset, pathologic type, receptor status, prior benign or premalignant breast lesions and details of such lesions, etc.
e) Similar information on benign breast lesions: incidence in DES-treated mothers and DES-exposed daughters, age of onset, histologic type, treatment, etc.
f) For breast cancer cases and comparison women, epidemiologic information on other risk factors related to breast cancer.
g) Information on other cancers developing in DES-exposed mothers or offspring and time relationship of these to breast cancer and/or premalignant breast lesions.

Collaborative investigations "should be feasible and are to be encouraged, to use comparable methodology, to increase sample sizes, and/or to achieve standardized pathology review," the concept says. "Observational followup studies on women known to have been exposed to DES have already been shown to be appropriate, feasible and fruitful."

It adds that a case control study design might also be feasible, possibly among women in the age group of daughters exposed in utero, especially if such studies focused on areas or groups known to have had a particularly high frequency of DES exposure during the years of peak usage of the compound for pregnant women.

"The time is appropriate for gathering this information since most DES mothers are post-menopausal and most DES daughters are pre-menopausal," Elinor Spring-Mills told the board. Spring-Mills heads the Organ Systems Program's Breast Cancer Working Group. DES administration to pregnant women peaked in the 1950s, so the majority of DES mothers are now in their 60s, she said. An estimated total of about 2 million to 3 million mothers were treated with the substance in the U.S., and an estimated 1 million to 1.5 million daughters exposed to DES in utero.

Studies have suggested a long latency for the compound, which was frequently prescribed to reduce fetal loss and prevent some of the complications of pregnancy in the 1940s and 1950s.

Two recent observational followup studies have reported an excess risk of breast cancer of 40% or more associated with DES treatment during pregnancy. In the largest cohort, the relative risk increased with interval after exposure, from 1.6 in years 20 to 29 after exposure to 2.5 for those followed 30 years or more. The results also suggested that spontaneous abortion, the major indicator for DES use, did not confound the association between DES treatment and subsequent breast cancer.

"There certainly is more than a hint that after a long interval, breast cancer incidence may really rise" in women exposed to DES, BSC Member Noel Weiss said in support of the concept. He told the board that he believed the concept will be valuable in a practical sense by providing additional information with which to counsel DES exposed women, and by providing theoretical knowledge on the role of exogenous hormones in breast cancer.

Noting that DES "is a very complicated compound," BSC Member Lee Wattenburg asked if the study could be piggybacked to assess the role of DES on tumors other than breast cancer. For example, DES causes kidney tumors in hamsters and has been associated with breast, ovarian and pituitary cancer in animals, he said.

NCI currently funds only one grant involving the role of DES in human breast cancer, and no grants on animals and DES. One grant application is pending, Elizabeth Anderson, program director for the Breast Cancer Working Group of NCI's Organ Systems Program, told the board

The project's objectives are to evaluate whether there is an increased incidence of breast cancer among women with prior exposure to DES, to characterize the types of breast cancer and of "benign" or premalignant breast lesions that develop in these women, and to compare women exposed to DES who develop breast cancer with women so exposed that do not in order to explore possible interacting factors.

NCI anticipates that information on breast cancer associated with DES exposure should lead to a better understanding of breast cancer pathogenesis in relation to estrogens.

"For this reason, it is important to explore in considerable detail the question of DES and breast cancer, as the 1985 Task Force recommended," the concept advises. "It is also important to understand possible interaction of DES exposure with other, perhaps avoidable, risk factors for breast cancer. The cohort of DES-exposed individuals is large. For their possible benefit, it is of concern to assemble as accurate a picture and as much potentially useful information as we can acquire."

The administration of DES to pregnant women continued through the 1960s. In 1970, unusual occurrence of a rare clear cell adenocarcinoma in young women was linked to exposure in utero to DES, with various subsequent studies associating certain cancers and other health risks with DES exposure. A 1978 government task force recommended careful followup of all exposed individuals, with attention to possible breast

cancer risk for DES treated mothers.

HHS reconvened the DES task force in 1985 following the more recent reports of excess risk of breast cancer. Released in July, the report concluded that "compared to the situation in 1978, the weight of the evidence ...now indicates that women who used DES during their pregnancies may subsequently experience an increased risk of breast cancer. However, a causal relationship is still unproven." The task force recommended continued followup of exposed individuals, specifically citing breast cancer in DES mothers and epithelial abnormalities of the reproductive tract in DES daughters as examples of potential risks already reported that could receive further attention.

An NIH implementation plan prepared at the request of HHS recommended the preparation of a research initiative dealing with the "risk of breast cancer in those with prior exposure to DES." The concept notes that "the biological rationale for increased risk of breast cancer from DES exposure exists for daugthers exposed in utero, as well as for mothers. These offspring are only now reaching likely ages for breast cancer appearance, and an examination of their risk is likewise important."

Other concepts approved by the board are:

Resource for human esophageal tissue and cells from donors with epidemiological profiles. NCI plans to recompete a four year, $346,530 resource award. The contract is currently held by the Univ. of Maryland.

Proposed first year funding for the award is $80,399 for fiscal year 1987, versus the project's current FY '86 funding level of $90,105. The decrease in funding reflects NCI's cutback in contracts, Project Officer Glenwood Trivers told the board.

The contractor will provide DCE's Laboratory of Human Carcinogenesis with matched normal esophageal tissue and cell cultures from each human donor. These tissues and cells will be used in LHC to study malignant transformation caused by chemical, microbial and physical carcinogens and cocarcinogens. The tumorigenic potential of treated cells will be further tested in athymic nude mice.

The contractor will also provide tumor and nontumorous tissue from patients with esophageal carcinoma. These tissues will be used for studies of (a) DNA polymorphisms, i.e., restriction enzyme fragment length polymorphisms using DNA probes on localized to various chromosomes including chromosome 11; (b) karotypic abnormalities; and (c) isolation of transforming genes.

The contract is intended to be a resource for (1) the collection of normal appearing and neoplastic human esophageal tissue and cells at the time of surgery (cancer and non cancer donors) and at immediate autopsy (non cancer donors), and (2) the culture and storage of esophageal epithelial and fibroblastic cell stocks. Essential components of the resource will include (a) approval of the institutional committee for the protection of human subjects, (b) an epidemiological profile of the donors obtained by trained interviewers, (c) proven methods for collecting, culturing, and transporting the specimens in a viable condition to the NIH, and (d) an evaluation (characterization) of the functional and pathological status of the tissue by histochemical and immunological methods and by light and electron microscopy.

Tumor marker analysis includes: (a) AB/PAS for mucus and adenomatous differentiation; (b) immunostaining for keratin and epithelial origin of tumors and differentiation; and (c) cytoskeletal proteins (i.e., actin, tubulin, calmodulin); growth factors and receptors (EFG, EGF-receptors, and alpha TGF); hormones (alpha-HCG, beta-HCG); and oncogene products (e.g., immunostaining of ras Hp21, raf protein).

CONCEPT REVIEW FIGURES ARE ESTIMATES ONLY; RFPs, RFAs NOT YET AVAILABLE

The dollar estimates with each concept review brought before the various boards of scientific counselors are not intended to represent maximum or exact amounts which will be spent on those projects. They are intended only as guides for board members to help in determining the value of the projects in relation to resources available to the entire program or division. Responses should be based on the workscope and description of goals and methods included in the RFPs (contracts) and RFAs (grants and cooperative agreements). Availability of RFPs and RFAs will be announced when the Institute is ready to release them.

The resource contract supports research projects underway by LHC in patterns of expression of epithelial differentiation markers (keratins, involucrin, and cross linked envelopes) during the course of normal differentiation and development in neoplasia. In addition, it supports research involving in vitro human epithelial carcinogenesis studies utilizing human epithelial cell culture systems.

Highlights of the LHC projects include the identification of a common abnormality in chromosome 11p in all 15 esophageal carcinoma cell lines newly established from tumors provided by this resource contract, and the development of serum free medium to culture normal human esophageal cells. Other highlights are: when compared to normal epithelial cells, keratin patterns were altered in esophageal carcinomas and were dependent on the tumor type and the degree of tumor differentiation; in contrast to reports of an increased number of epidermal growth factor receptors on skin carcinomas, esophageal carcinomas have fewer receptors than do normal human esophageal and epidermal epithelial cells; and transforming growth factor type beta inhibits the growth and induces terminal differentiation of esophageal epithelial cells.

The concept states that model systems for the

study of carcinogenesis using cultured human cells are providing new opportunities to assess: (a) mechanisms of carcinogenesis in human cells; (b) host factors that influence an individual's susceptibility to carcinogenic agents; (c) logical approaches for the qualitative extrapolation of carcinogenesis data from experimental animals to the human situation; and (d) methods to inhibit the multistage processes of neoplastic transformation and progression. The conduct of parallel studies in epithelial tissues and cells from experimental animals so that interspecies comparisons can be made is an important aspect of this approach, it adds.

The role of Omega-3 polyunsaturated fatty acids in cancer prevention.

The board approved a concept to encourage basic mechanistic studies on the role of omega-3 polyunstaurated fatty acids in cancer prevention. Areas of particular interest are: (1) anti-carcinogenesis studies in various organ systems, particularly those organ systems in which the type and level of fat have been shown to play a role; (2) determination of whether efficacy obtains during the initiation period by modifying the susceptibility of the host to early events, or whether these fatty acids modulate the carcinogenic response in the post initiation period, or both, and including determination of efficacy over the lifetime of the animal; (3) pharmacokinetic studies on the absorption, distribution, metabolism and excretion of these fatty acids, including such studies performed under the experimental conditions demonstrating cancer prevention; (4) studies on toxicology of the agents, including life time administration studies under defined dietary conditions in several species of animals; (5) comparative metabolic studies in human versus animal systems; (6) indepth studies of mechanisms of action, especially as related to conditions known or demonstrating anticarcinogenic efficacy.

NCI particularly wants mechanism studies on anticarcinogenesis to be reflective of the current state of the art in molecular and cellular carcinogenesis, experimental pathology, immunology, endocrinology, cocarcinogenesis and tumor promotion. Program projects and/or consortial arrangements under traditional RO1 grants are encouraged where collaborating agencies, special facilities and equipment are deemed necessary to approach and carry out these investigations.

The concept notes that "it has been generally observed that cancer risk is higher among people who consume diets high in fat and low in fiber, vegetables and micronutrients. Recent studies have also demonstrated that not only the amount of fat, but the composition and type of fat consumed have a significant influence on the development of cancer."

Fats containing polyunsaturated fatty acids (PUFA) of the omega-6 family are apparently more favorable to the growth of tumor cells. The PUFA generally consumed are derived from vegetable oils that contain high levels of linoleic acid. Experiments with laboratory animals have demonstrated that dietary linoleic acid favors the growth of tumor cells. The mechanism(s) of fatty acid enhanced tumorigenesis and tumor growth are not well defined, the concept says. Possible mechanisms include the fact that polyunstaurated fatty acids can easily undergo oxidation to yield a variety of mutagens, promoters, and carcinogens, such as fatty acid hydroperoxides, endoperoxides, enals, aldehydes, alkoxy, and hydroperoxy radicals that promote the growth of tumor cells. In addition, polunsaturated fatty acids such as linoleic acid give rise to arachidonic acid when elongated and desaturated. Arachidonic acid is the precursor for biologically active prostaglandins, such as prostaglandin E2 (PGE 2). PGE 2 exerts suppressive action on immunological cells, which is postulated to enable tumor cells to escape the immunosurveillance of the body and metastasize and proliferate. There is stong evidence that omega-6 PUFA are conducive to promotion of cancer by virtue of their ability to elicit production of immunosuppressive prostaglandins.

The concept acknowledges that "it is not feasible to eliminate PUFA completely from the human diet to reduce the risk of cancer because these PUFA are needed for normal biochemical functions and the maintenance of normal human health. There is also widespread advocacy for increased consumption of omega-6 PUFA (vegetable oils) to improve serum lipid levels and reduce coronary heart disease.

"Ideally, we need a source of dietary PUFA that would exert beneficial effects on coronary heart disease while suppressing PGE 2 production, thereby decreasing cancer," the concept says. The omega-3 PUFA that occur in fish oils, particularly from fish that live in deep, cold waters, may serve that function. Fish oils extracted from mackeral, bluefish, herring, and menhaden, for instance, have low levels of omega-6 fatty acids, but contain high levels of omega-3 PUFA, such as eicosapentaenoic acid (20:5) and docosahexaenic acid (22:6). Epidemiological studies with Greenland Eskimos, Japanese and Icelanders indicate that populations consuming seafood regularly are less prone to coronary heart diseases, atherosclerosis, hypertension, and cancer. Changes in their food habits to western style diets is correlated with increased mortality rates from cancer. Recent studies have demonstrated that diets containing these omega-3 fatty acids effectively retard the growth of tumor cells in animal models. Despite these observations, the mechanism underlying the relationship between dietary fat and cancer is not well understood.

The program annoucement that will result from the concept is similar to one issued by nine other institutes in December. Neither NCI nor the National Heart, Lung & Blood Institute joined in issuing the program announcement on biological mechanisms of omega 3 fatty acids, resulting in the criticism of NCI by some members of the nutrition community

for its "refusal to participate." Program Director David Longfellow, however, told the board that NCI was very interested in the concept, but that the announcement had been developed at the NIH level, and was not targeted to individual institutions.

There are currently two grants funded by NCI that are investigating omega 3 fatty acids, Longfellow told the board. One grant is in the Div. of Cancer prevention & Control, the other in NCI's Diet Nutrition Program. DCE Director Adamson told the board that two grants in collaborative cooperative groups regarding cancer prevention with the use of omega 3 fatty acids are pending review.

The concept was approved with only one member opposed, Lee Wattenburg, who asserted that the data on fish oil's role in carcinogenesis inhibition is "very skimpy" and questioned whether now is an appropriate time to conduct the studies.

NCI CONTRACT AWARD

TITLE: Supportive services in virology, tissue culture and immunology
CONTRACTOR: Biotech Research Laboratories, Rockville, Md., $1,227,364.

RFPs AVAILABLE

Requests for proposal 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-CM-67886-68

Title: Provision of tissues and cells and conduct of routine tests in support of tumor cell biology studies

Deadline: Approximately May 3

The Developmental Therapeutics Program of NCI's Div. of Cancer Treatment is seeking an organization qualified to supply tissues, cells and small quantities of fresh type C RNA tumor viruses, and conduct routine tests for viral antigens and antibodies in support of ongoing studies in tumor cell biology and virology.

It is anticipated the contractor will examine (A) human tissues and cultured cells for type C RNA tumor virus antigens; (B) serum samples for antibodies to human and subhuman primate type C viruses; (C) human peripheral blood or serum samples for the presence of biologically active virus by infectivity assays; (D) fresh human tissue explants and established cell lines for the presence of growth factors; (E) human normal and neoplastic tissues for growth in culture in the presence and absence of growth factors; and (F) supply small quantities of 1,000x concentrated type C RNA tumor viruses.

All aspects require strict quality control and maintenance of complete records. The contractor must have a minimum of P2 biohazard containment facility, and must be able to deliver freshly prepared specimens to the government project officers's laboratory within one hour after harvest, on wet ice.

It is anticipated that a cost reimbursement incrementally funded type contract will be awarded as a result of the RFP for a period of 60 months, beginning Dec. 1, 1986. This RFP represents a recompetition of the contract which had been awarded to Litton Bionetics Inc. but which was assumed by a Netherlands company, Organon Technica when the latter purchased most of LBI from its parent firm, Litton Industries, last year. At that time, NCI executives said there was some doubt that a non-U.S. firm would be allowed in the recompetition for this and the following contract, both of which support Robert Gallo's Laboratory of Tumor Cell Biology. Since then, NCI and HHS has determined that Organon Technica could compete for NCI contracts, including the big contracts at Frederick Cancer Research Facility which will be recompeted later this year. LBI, now Organon Technica, holds the contract for FCRF's Basic Research Program.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and reported in The Cancer Letter, Oct., 25, page 4.

Contract Specialist: Karlene Ruddy
RCB Blair Bldg Rm 212
301-427-8737

RFP NCI-CM-67884-68

Title: Provision of hematopoietic cell cultures, growth factors and type C virus protein

Deadline: Approximately May 3

The Developmental Therapeutics Program is seeking an organization qualified to provide raw materials for the experimental procedures of the intramural research program. The major objective of this contract is to provide primate hematopoietic growth factors, cell cultures of diverse hematopoietic and primate lymphotropic retrovirus origin, purified viral proteins, and antisera against the purified factors and proteins. The contractor should be able to provide PhD level principal investigators with three to four years of experience in the task objectives of this contract and technical personnel capable of working at the biocontainment level for human lymphotropic retroviruses (P2/P3).

As a minimum, the contractor must have biocontainment facilities for the culture of cells and human viruses, have NRC licensed radioisotope facilities and abe able to deliver to NIH freshly prepared specimens within one hour after harvest.

It is anticipated that a cost reimbursement incrementally funded type contract will be awarded as a result of this RFP for a period of 60 months, beginning March 23, 1987. This RFP represents a recompetition of the contract now held by Organa Technica (see above).

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and reported in The Cancer Letter Oct. 25, page 7.

Contract Specialist: Karlene Ruddy
RCB Blair Bldg Rm 212
301-427-8737

RFP NCI-CM-67885-68
Title: Preparation and supply of fresh and cultured mammalian cells
Deadline: Approximately May 3

The Developmental Therapeutics Program is seeking an organization qualified to provide large quantities of well characterized normal and neoplastic mammalian tissue culture cells and receive, process, distribute, store and maintain fresh human leukemic cells and tissues. It is anticipated that 100 grams of fibroblastic cells grown as monolayer and 100 grams of suspension cultured cells will be required each year. The contractor should also be able to process up to 125 samples of human leukemic blood and supply the leukocytes to the government. The contractor should be able to freeze fresh cells in a viable state.

All aspects require strict quality control and maintenance of complete records. As a minimum, the contractor must be able to deliver freshly prepared specimens to the government project officer's laboratory within one hour after harvest, on wet ice, to enable the government to carry out biochemical and immunological studies.

It is anticipated that a cost reimbursement incrementally funded type contract will be awarded as a result of this RFP for a period of 60 months, beginning March 30, 1987. This RFP represents a recompetition of a contract now being performed by Biotech Research Laboratories.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and reported in The Cancer Letter Oct. 11, page 4.

Contract Specialist: Karlene Ruddy
RCB Blair Bldg Rm 212
301-427-8737

RFP NCI-CM-67887-68
Title: Preparation and purification of viral components
Deadline: Approximately May 3

The Developmental Therapeutics Program is seeking an organization qualified to supply substantial quantities of human T cell leukemia virus (HTLV). The contractor shall (1) provide 30-40 liters of 5,000x concentrated virus per week; (2) furnish quality control data including number of virus particles/ml. (E.M.), reverse transcriptase activity and the level of p24 in each lot of virus; and (3) monitor the cells biweekly for contamination with mycoplasma and other cell lines.

As a minimum, the contractor must have a P3 biohazard containment facility and be able to deliver freshly prepared specimens to the government project officer's laboratory within one hour after harvest, on wet ice.

It is anticipated that a cost reimbursement incrementally funded type contract will be awarded as a result of the RFP for a period of 60 months, beginning April 1, 1987. This RFP represents a recompetition of a contract now held by Organon Technica.

The concept from which this RFP was derived was approved by the DCT Board of Scientific Counselors last fall and reported in The Cancer Letter Oct. 11, page 4.

Contract Specialist: Karlene Ruddy
RCB Blair Bldg Rm 212
301-427-8737

RFP NCI-CN-65022-50
Title: Formulation dosage form preparation of chemopreventive agents
Deadline: May 20

NCI is seeking organizations interested in the following: Task 1—Preparation of solid oral dosage forms (6,080 hours); Task 2--Preparation of soft gelatin capsule dosage forms. An offeror may propose on one or both task areas. One or more task order, term type contracts with a five year duration will result from this RFP.

The Cancer Chemoprevention Program is aimed at testing the concept that certain natural or synthetic agents may lower cancer incidence. Potential chemopreventive agents include, but are not limited to, substances such as retinoids, ascorbic acid, alpha tocopherol, selenium and others such as antioxidants, phenolics, protease and prostaglandin inhibitors, secondary plant constituents, miscellaneous chemicals, etc.

The Chemoprevention Program needs to establish qualified contractors who possess the facilities, personnel and equipment to handle quick response production of finished dosage forms and/or are capable of providing these forms appropriately packaged and labeled according to randomized allocation schemes in accordance with the Good Manufacturing Practice regulations of FDA.

Contract Specialist: David Monk
RCB Blair Bldg Rm 2A07
301-427-8745

RFP NCI-CM-67888-72—Amendment
Title: Operation of an animal virological diagnostic laboratory

The deadline for receipt of proposals has been changed from approximately May 9 to approximately June 24 (This announcement appeared in last week's Cancer Letter).

The Cancer Letter _Editor Jerry D. Boyd Associate Editor Patricia Williams
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