THE CANCER LETTER

Vol. 8 No. 32
Aug. 20, 1982

Subscription $125 year North America/$150 yr elsewhere

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

CCOP RFA RESPONSE SO FAR POINTS TO MORE CONSORTIA APPLICATIONS, REASONABLE GEOGRAPHIC DISTRIBUTION

Response to the Community Clinical Oncology Program RFA has been keeping NCI phone lines busy and is starting to provide some clues on the number and makeup of applications due by the Nov. 9 deadline.

(Continued to page 2)

In Brief

MAUER RESIGNS AS ST. JUDE DIRECTOR; BRESLOW NAMED DRCCA BOARD CHAIRMAN; SENATE CONSIDERS LINE ITEMS

ALVIN MAUER has resigned after 10 years as director of St. Jude Children's Research Hospital, effective when a successfor has been hired. "There is a periodicity in institutions and in people," Mauer said. "Don Pinkel was here 10 years and achieved the goals and objectives of the first phase of our development. We are approaching the end of the second phase of that growth, and the next decade will see a different kind of growth with different demands." Mauer said he has not made any plans for himself. . . . **LESTER BRESLOW**, dean emeritus of the UCLA School of Public Health and codirector of the Jonsson Comprehensive Cancer Center Div. of Cancer Control, will be the new chairman of the Board of Scientific Counselors of NCI's Div. of Resources, Centers & Community Activities. He replaces Stephen Carter, who gave up membership on the Board in anticipation of the heavy demands of his new job with Bristol-Myers. . . . **LINE ITEM** authorizations for organ site programs and cancer center core grants, opposed by NCI and the National Cancer Advisory Board, appear at this time to have a better than even chance of being written into National Cancer Act renewal legislation. Sen. Daniel Moynihan (D.-N.Y.) has been planning to offer an amendment on the Senate floor which would maintain the four (prostate, bladder, bowel, pancreas) projects intact, with nongovernment headquarters for each and each conducting its own peer review of grants. Sen. Edward Kennedy (D.-Mass.) has suggested a compromise which would continue four nongovernment headquarters but would return peer review to NIH. The NCAB has approved a plan which would consolidate the headquarters into one and bring peer review into NIH. The Kennedy plan would require recompetition of headquarters grants and review of the entire program by the NCAB every three years; Moynihan's would not. Meanwhile, Sen. Howell Heflin (D.-Alabama) has indicated he will get into the record during floor discussion support for the line item authorization for cancer center core grants which is in the House bill. That would encourage Senate conferees to accept the House position, Heflin reasons. That could lead to a deal: House conferees going along with the Senate on the organ site line item (if it is included), the Senate accepting the core grant line item.

RESPONSE PROVES COMMUNITY PHYSICIANS WANT TO PARTICIPATE, FRELICK SAYS

(Continued from page 1)

Letters of intent are due Aug. 23, but CCOP Program Director Robert Frelick said that since the RFA did not make it clear whether letters had to be at NCI by that date or merely postmarked by then, those with Aug. 23 or earlier postmarks would be accepted.

The deadline for applications will be firm, however: they must be at the NIH Div. of Research Grants and to NCI's Grants Review Branch no later than 5 p.m., Nov. 9.

Frelick said that the phone calls he has received indicate "there may be fewer letters of intent than we had anticipated. We are seeing much more interest in consortia. Even those hospitals which could do it on their own are pulling others together into consortia."

That could mean fewer, although more complicated, applications for NCI to process and review. It also could mean that the average CCOP will be larger, covering a larger percentage of its community, and entering more patients into clinical trials.

The geographic distribution seems to be reasonable, Frelick said. More responses are coming in from the East Coast but there have been significant numbers from the Midwest, South and West Coast. "There is tremendous interest all across the country. We've been getting an awful lot of phone calls."

Frelick said the responses are proving that "our basic concept—that there are experienced clinical investigators out there who are not participating in clinical research but would like to—was sound. It seems we have started people talking to each other. People are waking up. A group in San Diego had not realized that there is a university clinical center there that they can work with. They could do that without CCOP. We're making people think about the opportunities."

Frelick said there has been "surprisingly little criticism" over omission from the RFA of requirements for cancer control activities (although they are permitted and will be considered in the review). In fact, "some were pleased that cancer control was not in. They said they would not be interested if it were."

The first two letters of intent received were not from hospitals but from physician groups. "I guess that shows that if you don't have to put up with hospital red tape, you can do something fast," Frelick said.

NCI will assess each letter of intent, try to determine which are on the right track, encourage those to submit applications, advise others on shortcomings. A preproposal conference may be called if it appears one is needed.

OBEY INSISTS IARC SOFTENED REPORT ON BENZENE BECAUSE OF NCI PRESSURE

Congressman David Obey (D.-Wisc.) has renewed his charge that the International Agency for Research on Cancer altered the report of a scientific panel, largely because of pressure by NCI staff members, The change eliminated reference to increased risk of leukemia from exposure to benzene at a level of 10 ppm.

The report instead cited estimates of 140 to 170 excess leukemia deaths per 1,000 exposed workers at an exposure level of 100 ppm. The reference dropped from the report said that 10 ppm could increase leukemia deaths by 17 per 1,000 workers exposed over working lifetime.

IARC sponsored a working group of 16 scientists in October, 1981, to review scientific data on a number of chemicals and their carcinogenic potential. Two, including benzene, were reviewed to determine what data were available on cancer risk at different levels of exposure.

There was heated debate over inclusion of data on benzene that showed 17 additional cases of leukemia would occur in 1,000 exposed at levels of 10 parts of benzene to one million parts of air. The panel voted to include the data and it became part of a written draft that was adopted at the close of the meeting on Oct. 20. But the final document included only the statement that "minimum estimates of 140 to 170 excess leukemia deaths per 1,000 exposed workers over a working lifetime were calculated for an exposure level of 100 ppm."

Obey obtained a copy of a memo written by a representative of the Chemicl Manufacturers Assn. which the congressman interpreted as implicating NCI staff members in an effort to pressure IARC to soften the report. The memo states:

"In an effort to correct problems with this developing publication, Dr. (Richard) Adamson (director of NCI's Div. of Cancer Cause & Prevention) has instructed their representatives, Dr. (Herman) Kraybill and Dr. (Morris) Kelsey to raise the issue at the Feb. 8-12 meeting and recommend that IARC not engage in risk assessments."

The memo notes that the new IARC director, Lorenzo Tomatis, had reversed a policy advocated by his predecessor, John Higginson, and planned to develop risk assessments on various chemicals. The memo said the benzene findings were based on an unpublished paper by a National Institute of Occupational Safety & Health scientist "which has serious procedural flaws. . . . It appears that the IARC assessment was engineered primarily by Dr. Tomatis and Dr. (P.J.) Landrigan of NIOSH (a member of the working group).

"At the suggestion of Dr. Higginson, discussions were held with Dr. Adamson to solicit his support.

NCI contributes approximately $500,000 to the IARC budget. Dr. Adamson understands the regulatory impact of risk assessment by IARC and does not believe that IARC should engage in this activity. He has asked the NCI representatives, Drs. Kraybill and Kelsey, to the Feb. 8-12 meeting of IARC to question this activity and express the position of NCI in opposition to the preparation of estimates."

Adamson has maintained all along that he did not attempt to change the monograph and in fact specifically instructed Kraybill and Kelsey not to discuss quantitative risk assessment of benzene. They were told to discuss risk assessment in general, however.

"NCI raised only the general issue of risk assessment," an NCI spokesman said. "We said only that we should be careful, that quantitative risk assessment should be based on scientific methodology."

Obey said his investigation found that none of the participants in the IARC panel which prepared the benzene report had been consulted about the change and "none felt that a change was possible under IARC procedures. . . . Alteration of scientific findings without the consent of the scientific panel which had agreed to those findings appears to be without precedent in the 11 year history of the IARC monograph program."

Interviews by his staff with Tomatis and other IARC staff and with NCI officials "failed to provide a satisfactory explanation for the change," Obey said.

Landrigan of NIOSH and David Hoel, of the National Institute of Environmental Health Sciences, both members of the IARC panel, subsequently have been quoted as saying that the 10 ppm risk was supportable and that they were astonished when it was not included in the report.

However, Tomatis, in a telex message to NCI Director Vincent DeVita, insisted that both Landrigan and Hoel had been informed of the changes and the reasons for them.

Tomatis denied that the changes were made because of NCI pressure. He said the complete monograph would in fact present the report as drafted and that the change which dropped reference to 10 ppm was made in the "annex" to the report. The annex was revised in an attempt to make it a "solid, scientific document," Tomatis said.

Both Adamson and Kraybill, who is scientific coordinator for environmental cancer in DCCP, were away from Bethesda and not reachable by phone last week.

Obey said the investigation would continue. "I find it difficult to believe that the extraordinary steps taken by IARC staff in altering the findings of a scientific panel without approval from that panel were not at least partially a result of pressure from the National Cancer Institute officials who control IARC funding."

REQUESTS FOR APPLICATIONS

RFA NIH-NCI-DCT-CTRP-82-13

Title: *Studies of acquired immuno-deficiency syndrome (Kaposi's sarcoma and opportunistic infections*

Deadline: *Oct. 22, 1982*

NCI invites applications for cooperative agreements to support working group research projects into the etiology and treatment of patients with Kaposi's sarcoma, unexplained opportunistic infections or other manifestations of acquired immunodeficiency. Since June, 1981, the Centers for Disease Control in Atlanta have learned of an increased occurrence of KS, pneumocystic carinii pneumonia, and other serious OIs concentrated among homosexual men in the United States. Investigation to date has identified an apparently new syndrome which has reached epidemic proportions.

In addition to the association with homosexuality there is an underlying state of profound immunosuppression characterized by marked suppression of peripheral blood inducer/helper T-lymphocytes. Affected patients have very often presented with a symptom complex of chronic fever, weight loss and lymphadenopathy as a prodrome to the development of KS or serious OI. To date epidemiologic studies have failed to reveal an etiology, although abuse of certain drugs (especially nitrites) and previous or concomitant infection with certain viruses and other agents has been common.

This serious public health problem deserves intensive investigation. In addition, research into this epidemic could yield important new information on the etiology of cancer in man. The purpose of this RFA is to encourage such research by providing support to institutions possessing an interest in the problem, as well as a population of affected patients and/or laboratory facilities and personnel appropriate to the conduct of such research.

It is intended that this research will be conducted in the context of a working group, i.e., a group of institutions carrying out various research projects funded as a result of this RFA or other mechanisms. NCI staff will serve as a resource of information and will work to facilitate exchange of information and material between involved investigators. It is NCI's assessment that such collaboration between investigators will permit achievement of the goals of this RFA—i.e., definition of etiology, treatment and prevention—in the most rapid and efficient manner possible.

Studies to be proposed should stress innovative approaches to this problem and should include any or all of the following three components:

1. Epidemiologic studies designed to identify risk factors in patients with KS, the acquired immunodeficiency syndrome or prodromal conditions, along with appropriate control populations.

2. Laboratory research projects in etiology and pathophysiology. These would include both in vitro and in vivo studies in such areas as immunology, microbiology, virology, and toxicology, and would comprise studies of the immunodeficiency syndrome, prodromes, Kaposi's sarcoma and opportunistic infections.

3. Innovative treatment and prevention research projects involving patients with Kaposi's sarcoma, unexplained opportunistic infections, other manifestations of acquired immunodeficiency, or prodromes to this syndrome. Most appropriate would be therapy studies linked to etiologic hypotheses or observations.

Encouraged, but not required, are applications from institutions or consortia possessing resources and expertise in all areas. All applicants should clearly document access to an adequate patient population base (either directly or through explicit collaboration) since a major criterion for review will be an ability to complete meaningful studies in a reasonable period of time.

NCI plans semiannual meetings of the working group. It is hoped that these meetings will provide an opportunity for the development of collaborative arrangements between investigators performing complementary research.

Cooperative agreements are assistance relationships involving substantial involvement with NCI staff. NCI anticipates making multiple awards as a result of this request. It is anticipated that a total of $1 million will be set aside to fund the initial year's awards. Awards will be made for project periods of three to five years. Future renewal applications will not compete for earmarked funds.

NCI approval will be required for all treatment protocols developed following award. NCI staff will hold regular protocol review meetings chaired by the associate director, CTEP, or his designee. The primary purposes of this review are 1) to assure that the proposed research is in compliance with all FDA requirements for NCI funded clinical treatment research and 2) to identify and prevent undesirable duplication of efforts. Protocols may be disapproved by NCI on the basis of patient safety and toxicity, obvious duplication, or failure to meet FDA regulations, particularly those concerning NCI sponsored investigational drugs.

If a proposed protocol is found to be unacceptable for any of the above reasons, the specific reasons for lack of approval will be communicated to the investigator within 30 days of protocol receipt by NCI. NCI staff will work with the investigators to develop a mutually acceptable protocol compatible with the research interests and needs of the working group and NCI.

NCI will establish an appeals process for determining the suitability of treatment protocols it has found unacceptable on initial review, and for which a mutually acceptable protocol cannot be arrived at through discussions between the group and NCI staff. An arbitration panel composed of one working group participant, one NCI nominee, and a third member with clinical trials expertise chosen by the other two members will be formed to review NCI decisions. This NCI arbitration process in no way affects the right of a recipient to subsequently appeal an adverse determination using the NIH informal appeals system and the formal Dept. of Health & Human Services procedures. If the investigator proceeds with performance of a protocol disapproved by the arbitration panel, the results of that study will be subject to careful monitoring and targeted for peer review when the competitive renewal application is under consideration. In addition, NCI may withdraw the portion of funding designated for a disapproved protocol, if the grounds for disapproval are patient safety and toxicity, or unnecessary duplication.

Applicants are encouraged to include in their budgets travel funds for one investigator to two meetings per year in Bethesda. The words "Proposal in Response to RFA NIH-NCI-DCT-CTEP-82-13" should be typed across the top of the face page of the application, using PHS Form 398. Additionally, a brief covering letter should accompany the application indicating that it is being submitted in response to this request. The original and six copies of the application should be submitted to the Div. of Research Grants, NIH, and an additional two copies should be sent to the following: Dr. Harold Waters, Chief, Special Review Branch, Div. of Research Grants, Westwood Bldg., Room 2A16, Bethesda, Md. 20205.

All curricula vitae should be limited to three pages each. This is a one-time request for applications. NCI has no plans to reissue this announcement at any future date. Investigators interested in submitting applications in response to this announcement are encouraged to contact: John Y. Killen Jr., MD, Head, Medicine Section, Clinical Investigations Branch, CTEP, Landow Bldg. Room 4A14, Bethesda, Md. 20205, telephone 301-496-2522.

RFA NIH-NCI-DCCP-SPB-82-1

Title: *Epidemiologic studies of rare tumors*
Deadline: *Nov. 1, 1982*

The Div. of Cancer Cause & Prevention of NCI invites grant applications from interested investigators for epidemiologic studies of rare tumors. Epidemiologic investigations have tended to emphasize the more prevalent forms of cancer. A number of tumors which occur with less frequency have lacked the research interest of investigators.

Among the less frequently studied tumors from

which important information may be gained are, for example, malignancies of the thyroid (1.3 percent of all malignant tumors); anus, anal canal and anorectum (0.2 percent); soft tissues, including heart (0.6 percent); bone and joints (0.2 percent), male breast (0.1 percent) and salivary gland tumors (0.3 percent).

The study of rare tumors may provide insight and establish causal assocations with environmental risk factors—DES and clear cell adenocarcinoma in offspring; and vinyl chlorid and angiosarcoma of the liver. Investigations of rare tumors may also lead to better understanding of more common tumors, for example, male breast cancer and female breast cancer. In addition, studies which compare risk factors in low and high incidence areas may provide clues for further environmental and/or familial studies of possible etiology.

The primary objective of this RFA is to encourage studies aimed at the elucidation of causal factors in the development of rare cancers. The tumors to be investigated will not be specified by this RFA. Potential etiologic factors to be addressed could include occupational/environmental exposures, genetic/familial factors, diet, drug use (therapeutic and other), cigarette smoking, behavioral factors, or any other variables which the investigator chooses to examine.

This RFA proposes to fund research to generate causative/etiologic hypotheses, to provide clues of association; and/or to develop improved research design/methodology for the study of rare cancers. Such studies can provide the basis for more extended research designed to provide information on etiology and the natural history of specific rare malignant tumors or to develop studies which may provide insight into the more common tumors. These applications may include studies to determine the feasibility of studying specific rare cancers.

It is anticipated that subsequent case-control or cohort studies of less common tumors developed from these initial studies could compete in the traditional investigator-initiated research grant program (R01).

The intent is to fund a maximum of eight projects with total costs amounting to approximately $400,000 for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. This award may not be used to supplement support for an ongoing project.

Applications must be submitted on form PHS 398. The words "Response to RFA NIH-NCI-DCCP-SPB-82-1, Epidemiologic Studies of Rare Tumors" must be typed in bold letters across the face page of the application. The completed original application and six copies should be sent or delivered to: Div. of Research Grants, NIH, Westwood Bldg. Room 240, Bethesda, Md. 20205.

Inquiries should be directed to: Elaine S. Millner, Dr. PH, Special Programs Branch, Div. of Cancer Cause & Prevention, NCI, Landow Bldg. Room 8C16, Bethesda, Md. 20205.

RFA NIH-NCI-DCCP-SPB-82-11

Title: *Biochemical epidemiology*
Deadline: *Nov. 15, 1982*

Although a significant proportion of human cancers is thought to be attributable to life style and other environmental factors and therefore potentially preventable, the task of identifying the effects of specific factors and evaluating their relative importance is an enormous one. The process of induction and progression of human cancer is exceedingly complex, multiple exposure to a variety of agents over time is the rule rather than the exception, past exposure is difficult to assess, host factors which may influence susceptibility are poorly understood, and the importance of promiting and/or anticarcinogenic exposures in humans have not been adequately defined.

Epidemiologic studies have resulted in the identification of factors which appear to increase or decrease cancer risk and have suggested the importance of host-susceptibility factors. The usual epidemiologic techniques, however, have been limited in their ability to reach firm conclusions by the difficulties in defining past carcinogen exposure levels and susceptibility states, in measuring low levels of risk, in evaluating directly host environmental interactions, and in identifying dietary determinants of cancer. Fortunately, a variety of sensitive and specific laboratory methods are now becoming available which are likely to facilitate epidemiologic investigations by providing better measures of exposure to initiators, promoters, anticarcinogens and inhibitors of carcinogenesis. Increased collaboration between laboratory scientists and epidemiologists in the application of these emerging techniques would be highly desirable.

Modifying factors related to diet and nutrition have been implicated in several epithelial cancers including those of the gastrointestinal tract and reproductive organs. Hence these types of cancer (among others) might be especially suitable for collaborative studies involving epidemiologists and experimentalists, including biochemists, analytical chemists, immunologists, and nutritionists.

The purpose of this RFA is to stimulate epidemiologic/laboratory collaboration in developing and/or applying objective measures useful in studying the etiology of human cancer. Respondents must demonstrate expertise in sound epidemiologic design and laboratory methods. Appropriate interaction between epidemiologic and laboratory expertise should be evident in all phases of the proposed research from planning through implementation,

analysis, and reporting.

Examples of types of laboratory measurements which might be appropriate would include: 1) assessment of specific host factors which might influence susceptibility to carcinogenesis (e.g., DNA repair assay,s examination of chromosomal defects or susceptibility to cell tranformation, assays for immunocompetence or analysis of serum levels of vitamins or micronutrients), 2) detection and quantitation of chemical carcinogens or their metabolits in tissues or body fluids (e.g., analytical chemical measurements, mutagenesis assays or immunologic detection techniques) 3) measurement of interaction of specific agents with cellular target molecules (e.g., adduct formation with proteins and nucleic acids, excretion levels of excised adducts or markers of altered gene expression). Applications with be consistent with the state of the art; feasibility stuides or pilot studies are acceptable when developmental research is needed as preparation for a population study.

Applications must be submitted on form PHS 398. The words "Proposal in Response to RFA NIH-NCI-DCCP-SPB-82-11, Biochemical Epidemiology" should be typed in bold letters across the face page of the application.

The completed original application and six copies should be sent or delivered to: Div. of Research Grants, NIH, Westwood Bldg. Room 240, Bethesda, Md. 20205.

Two copies of the application should also be sent to: Dr. Genrose Copley, Special Programs Branch, Div. of Cancer Cause & Prevention, NCI, Landow Bldg. Room 8C-16, Bethesda, Md. 20205. Telephone 301-496-9600. Inquiries may also be directed to Dr. Copley.

RFA NIH-NCI-DCCP-SPB-82-12

Title: *Accuracy of questionnaire derived historic dietary information*

Deadline: *Nov. 15, 1982*

The Div. of Cancer Cause & Prevention of NCI invites grant applications from interested investigators for studies designed to investigate the accuracy and reproducibility of historical dietary information by comparing current information obtained by questioning individuals or their surrogates with actual records (date reflecting past dietary intake) of the same individuals recorded at some earlier point in time.

In chronic disease epidemiology in general, and cancer epidemiology in particular, the long intervals between exposures of interest and clinical onset of disease make studies of etiologic association extremely difficult. This problem is particularly acute in studies designed to investigate the initiating or modulating effects of past nutritional exposures. Such investigations require that individuals attempt to mentally reconstruct their pattern of food consumption at some time in the past. In the rare event that the investigation is focused on some single dietary component (e.g., coffee consumption), it might be expected that recall would be reasonably accurate. In the usual situation, however, where the investigation requires that information be obtained on a much broader spectrum of dietary components, or even on the diet as a whole, it can be anticipated that recall will be much less accurate and will be affected by a variety of factors.

With the current emphasis on nutrition as a potential etiologic or modulating factor in human carcinogenesis, it has become increasingly important to attempt an assessment of the degree to which dietary histories can be relied upon as substitutes for hard data on past food consumption or changes in dietary patterns. The recall period of interest to investigators in the cancer research area is likely to be years rather than months or weeks.

Useful information about the reliability of recall can be gained by comparing information obtained currently about previous diet with actual records of the dietary intake of the same individuals recorded at some discrete time in the past. In this context it must be stressed that no totally accurate methods for assessing dietary intake for noninstitutionalized individuals currently exist. Even the maintenance of intake diaries or 24 hour recall methods do not provide totally accurate information on usual intake since bias may be introduced by a number of factors such as, for example, deliberate changes to simplify record keeping or selective recall. This fact complicates our usage of the terms "validity" and "accuracy" for the purpose of this RFA and it must be remembered that the primary focus is on the value of historical dietary information as a predictor of cancer risk. The cancer epidemiologist needs information on how well historical dietary data separates individuals into low, middle and high consumers of a specific dietary component or food group. It would also be of interest to determine the "accuracy" of recall information from surrogate respondents since this procedure is often necessary in the conduct of studies in cancer epidemiology where the individual of concern is deceased or unable to respond adequately.

The elapsed time between the questioning and the dietary events of interest, for the purpose of this RFA, should be on the order of years rather than months or weeks. Variables, other than elapsed time, investigated in such studies might include: the age and sex of subjects, educational level, health status, complexity of questioning, dietary variability, and the effects of "out of home" food consumption. It might be desirable to assess the usefulness of special techniques to improve recall, validity of the original dietary data, its generalizeability and/or the avail-

ability of laboratory markers of past exposure.

Investigators responding to this RFA are encouraged to propose innovative approaches to data collection and analysis on methodology. The active involvement of persons experienced in the use of historical dietary information in the conduct and analysis of epidemiologic studies and access to appropriate historical dietary data are essential in responses to this application.

The intent is to fund multiple projects with total costs amounting to approximately $300,000 for the first year. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of NCI, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose. This award may not be used to supplement support for an ongoing project.

Applications should be submitted on form PHS 398. The words "Proposal in Response to RFA NIH-NCI-DCCP-SPB-82-12, Accuracy of Questionnaire Derived Historic Dietary Information" must be typed in bold letters across the face page of the application.

The completed original application and six copies should be sent or delivered to: Div. of Research Grants, NIH, Westwood Bldg. Room 240, Bethesda, Md. 20205.

A copy of the application should be sent, and inquiries may be directed to: Dr. Marthana C. Hjortland, Special Programs Branch, Div. of Cancer Cause & Prevention, NCI, Landow Bldg. Room 8C-18, Bethesda, Md. 20205, phone 301-496-9600.

RFA NIH-NCI-DCCP-SPB-82-14

Title: *The pharmacological role of nicotine in diseases related to tobacco products*

Deadline: *Nov. 1, 1982*

The Div. of Cancer Cause & Prevention of NCI invites grant applications from interested investigators to investigate the pharmacological role and biological effects of nicotine related to tobacco product carcinogenesis.

Past studies have shown nicotine to be the only controlled variable in tobacco smoke condensate which is consistently related to the rate of tumor incidence in test animals. However, in separate studies, nicotine itself has not been shown to be a carcinogen. It has been noted that the relationship between carcinogenic activity of smoke condensates and their nicotine contents may be caused in part by the conversion of nicotine to tobacco-specific nitrosamines or to the co-occurrence of nicotine and some other carcinogen or cocarcinogen. Tobacco products made from the lamina of plants grown on high levels of nitrate fertilizer contain higher levels of nicotine and following combustion show higher levels of volatile nitrosamines.

The exact role of nicotine, its metabolic and pyrolytic products, needs to be clarified in relation to carcinogenesis associated with tobacco smoke inhalation. Such information would be applicable in evaluating health effects produced by smoking tobacco products having various tar/nicotine ratios.

The primary objective of this RFA is to define the pharmacological role of nicotine in selected animal models, or humans, exposed to cigarette smoke under chronic conditions. The proposed work should address precursor states which have indications of being ralted to cigarette smoke carcinogenesis in animals and/or humans. These may include markers in body fluids or organ specific markers which may be demonstrated by immunological, histochemical, biochemical or other functional indices with the objective being to characterize and quantify different degrees of response and/or injury associated with exposure to nicotine, its metabolites or selected cofactors. The proposed studies should not be planned as merely screening tests, but should have a rationale based on previous findings described in peer reviewed publications.

To maximize the findings of the investigations in regard to the role of nicotine and other selected components, the inhalation experiments must be planned so that valid comparisons may be made both in regard to dosimetry and end point observations.

Applications which propose studies with the use of human subjects must be in compliance with 45 Code of Federal Regulations 46 (Revised 01/26/81).

The duration for applications submitted in response to this RFA should not exceed five years. The intent is to fund multiple projects with total costs amounting to approximately $350,000 for the first year.

Applications should be submitted on form PHS 398, and the words, "Proposal in Response to RFA: Pharmacological Role of Nicotine in Diseases Related to Tobacco Products" must be typed in bold letters across the top of the front page of the application.

The completed original application and six copies should be sent or delivered to: Div. of Research Grants, NIH, Westwood Bldg. Room 240, Bethesda, Md. 20205.

A copy of the application should also be sent to Dr. Thomas B. Owen at the address shown below, and a copy to the following: Dr. Harold Waters, Chief, Special Review Section, Div. of Research Grants, Westwood Bldg. Room 2A16, Bethesda, Md. 20205.

Inquiries may be directed to: Dr. Thomas B. Owen, Special Programs Branch, Div. of Cancer Cause & Prevention, NCI, Landow Bldg. Room 8C18, Bethesda, Md. 20205, phone 301-496-9600.

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.

RFP NCI-CO-33854-41

Title: *Management information system support service (programming)*

Deadline: *Sept. 23*

Note: This announcement supercedes and corrects the announcement published July 30 in ***The Cancer Letter.***

NCI is soliciting proposals for a small business firm to provide technical support services for the office of the director, NCI, in the expansion, maintenance and operation of NCI's Management Information System and in support of other computer related activities of the MIS Project Office.

This proposed procurement is a total set aside for small business concerns. A small business, for purposes of this procurement, is a firm, including its affiliates, that is independently owned and operated, is not dominant in the field of operations in which it is bidding on government contracts, and its average annual receipts for its preceding three fiscal years do not exceed $4 million.

This project is for a three year period. Offerors will be limited to those firms having operating facilities within a 40 mile radius of Bethesda, Md., as daily person to person contact is required.

Contracting Officer: Patricia Rainey
RCB, Blair Bldg. Rm. 332
301-427-8877

RFP NCI-CM-37555

Title: *Analysis of chemicals and pharmaceutical formulations*

Deadline: *Approximately Sept. 20*

The Pharmaceutical Resources Branch, Developmental Therapeutics Program, Div. of Cancer Treatment, NCI, is seeking laboratories to supply analytical services for the analysis of bulk pharmaceutical substances and formulated drug products.

Reports of these analyses will be used as a basis for assessing the suitability of these materials for use in advanced antitumor screening toxicological studies, formulation studies or for clinical trials. Data provided in these analytical reports will be supplied to the Food & Drug Administration as part of NCI's IND filings for new antitumor agents and related compounds.

Historical summaries of the data are used in preparing specifications for the various bulk pharmaceutical substances. These specifications are used in procurement actions as well as for the routine quality control of these materials.

The contractors selected should be experienced in the analytical assessment of bulk pharmaceutical substances and parenteral drug products and should have in-house operational equipment and capabilities at the time of contract award. The contractor selected will be expected to develop multiple analytical methods to establish the identity and purity of the materials analyzed. The contractors shall also provide data validating the assay methods developed.

It is anticipated that the contracts will be awarded for a period of four years. The total level of effort required for this project is 18 staff-years of effort per year. A minimum of two contracts will be awarded. All offerors must propose at a level of six technical staff-years per year. Additionally, offerors are encouraged to propose at a level of 12 technical staff years per year.

The principal investigator must be thoroughly familiar with the analysis of bulk pharmaceutical substances and parenteral dosage forms. It is expected that the principal investigator should spend 70 percent of his/her time on this project at the 12 staff year level of effort. At the six staff year level of effort the PI should spend 50 percent of his/her time on this project. The principal investigator should be trained in chemistry (analytical, pharmaceutical, organic, etc.), preferably at the PhD level from an accredited school. He/she should have at least three years of recent experience in the analysis of chemical compounds. He/she should also have one year of recent experience in the analysis of clinical dosage forms.

Offerors proposing at the six staff year level of effort should include one professional staff member (preferably at the masters level or above) to supervise and coordinate the actual laboratory work on a daily basis. Offerors proposing at the 12 staff year level of effort should include two such staff members.

Contracting Officer: John Palmieri
RCB, Blair Bldg. Rm. 228
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Published forty-eight times a year by The Cancer Letter, Inc., P.O. Box 2370, Reston Virginia 22090. Also publisher of The Clinical Cancer Letter.