NIH GUIDE for GRANTS and CONTRACTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Vol. II, No. 9, August 13, 1982

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HAVE YOU MOVED?

If your present address differs from that shown on the address label, please send your new address to: Grants and Contract Guide Distribution Center, National Institutes of Health, Room B3BN10, Building 31, Bethesda, Maryland 20205, and attach your address label to your letter. Prompt notice of your change of address will prevent your name from being removed from our mailing list.

The GUIDE is published at irregular intervals to announce scientific initiatives and to provide policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in grants and contracts activities administered by the National Institutes of Health.

Two types of supplements are published by the respective awarding units. Those printed on yellow paper concern contracts: solicitations of sources and announcement of availability of requests for proposals. Those printed on blue paper concern invitations for grant applications in well-defined scientific areas to accomplish specific program purposes.

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NOTICE

DEADLINE FOR SUBMISSION OF ASSURANCES OF COMPLIANCE WITH REVISED HUMAN SUBJECTS PROTECTION REGULATIONS

On January 26, 1981, the Department of Health and Human Services (DHHS) published final regulations amending basic DHHS policy for the protection of human research subjects. Institutions holding an Assurance of Compliance were encouraged to implement new provisions of the regulations prior to the negotiation of a revised Assurance of Compliance. Since August, 1981, the Office for Protection from Research Risks (OPRR) has been negotiating Assurances of Compliance with the new regulations.

This notification establishes a deadline of December 31, 1982, for submission of a general (Multiple Project) assurance prepared in accord with DHHS regulations published in the Federal Register on January 16, 1981 (46 FR 8366).

Institutions are encouraged to submit an Assurance of Compliance at the earliest possible date. A sample assurance is available from OPRR (301 - 496-7041). Although it is possible that approval of a multiple project assurance might not be transmitted until sometime after December 31, 1982, institutions may continue to function under their former assurance until such time as approval for the revised assurance is given. Special (Single Project) assurances will continue to be approved on a single project basis. GENERAL ASSURANCES WHICH HAVE NOT BEEN REVISED TO MEET THE 1981 REQUIREMENTS AND SUBMITTED TO OPRR WILL BE TERMINATED EFFECTIVE JANUARY 1, 1983.

NOTICE

SPECIAL CONSIDERATION FOR HEALTH PROFESSIONAL STUDENTS SEEKING RESEARCH CAREERS

NIH training Program Directors are reminded that NIH training grants may support individuals who wish to interrupt their medical, veterinary, dental, or other professional school studies for a year or more to engage in full-time research training before completing their professional degrees. The stipend should be paid at the predoctoral level of $5,040 per year. Program Directors are advised to consult with NIH staff in the awarding Institute before appointing such trainees unless such training was part of the approved training grant. National Research Service Award (NRSA) stipends may not support studies leading to the M.D., D.O., D.D.S., D.V.M., or other similar medical degrees, nor may they be used to support residencies.)

REQUEST FOR COOPERATIVE AGREEMENTS APPLICATIONS: RFA

NIH-NCI-DCT-CTRP-82-13

STUDIES OF ACQUIRED IMMUNO-DEFICIENCY SYNDROME (KAPOSI'S SARCOMA AND OPPORTUNISTIC INFECTIONS)

NATIONAL CANCER INSTITUTE

Application Receipt Date: October 22, 1982

I. BACKGROUND INFORMATION

The National Cancer Institute (NCI) invites applications for Cooperative Agreements to support "Working Group" research projects into the etiology and treatment of patients with Kaposi's sarcoma (KS), unexplained opportunistic infections (OI) or other manifestations of acquired immunodeficiency. Since June, 1981, the Centers for Disease Control in Atlanta have learned of an increased occurrence of KS, Pneumocystis carinii pneumonia, and other serious OI's 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 have 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

This program is described in the Catalog of Federal Domestic Assistance No. 13.395, Cancer Treatment Research. Awards will be made under the authority of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

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.

II. RESEARCH GOALS AND SCOPE

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 inclue 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.

The NCI plans semi-annual 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. At this time it is impossible to explicitly outline the nature of such arrangements since the scope of projects to be funded is unknown. An example, however, would be the provision of biological specimens from patients enrolled in epidemiologic studies to investigators performing in vitro studies of immune function. It is NCI's assessment that this cooperation will hasten the resolution of the important questions relevant to this epidemic and will result in a more efficient allocation of funds. It is anticipated that NCI staff will play a key role in coordinating and facilitating such collaboration as various research activities evolve. Further details of this involvement are outlined below under "Terms of Award."

III. MECHANISM OF SUPPORT

Awards will be made as Coopperative Agreements. These are assistance relationships involving substantial involvement with NCI staff, as outlined under Part IV, "Terms of Award." NCI anticipates making multiple awards as a result of this request. It is anticipated that a total of $1,000,000 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. All policies and requirements which govern the grant programs of the PHS apply, including the requirement for cost sharing.

IV. NATURE OF COLLABORATION WITH NCI STAFF: TERMS OF AWARD

This section outlines the collaboration between recipients of these cooperative agreements and NCI program staff.

A. Scientific Resources

1. The Awardees shall develop research protocols and plans in accord with their individual interests and strengths as well as the minimum requirements included in these terms of award.

2. The NCI staff will serve as a resource of information on the activities of various members of the working group and will act to facilitate collaboration among involved researchers. It is in the context of the Working Group semi-annual meetings that the awardees, with the assistance of NCI staff, will identify and develop these collaborative areas.

B. Treatment Studies

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, Cancer Therapy Evaluation Program, NCI, 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 the 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 the 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 Department of Health and 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, the 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.

V. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications submitted in response to this RFA will be reviewed in competition with each other by:

1. an NIH peer review group and
2. the National Cancer Advisory Board

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals (see II. GOALS AND SCOPE). If the application is judged by the National Institutes of Health to be unresponsive, the applicant will have the opportunity of having the application considered along with other unsolicited applications received by the National Institutes of Health.

The factors considered in evaluating each response to this RFA will be:

1. Scientific merit of research approach, design, and methodology.
2. Research experience and competence of the Principal Investigator and staff to conduct the proposed studies.
3. Adequacy of time (effort) which the Principal Investigator and staff would devote to the proposed studies.
4. Adequacy of existing/proposed facilities and resources. This includes adequacy of patient resources to ensure completion of meaningful studies in a reasonable period of time.
5. Scientific, technical or medical significance and originality of proposed research.
6. Reasonableness of proposed costs.

VI. METHOD OF APPLYING

A. Format of Applications

Applications must be submitted on form PHS 398 (Rev. 5/80), the application form for research grants. Application kits are available at most institutional business offices, or may be obtained from the Division of Research Grants, NIH. The format and detail applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (V.B.) must be fulfilled. The NCI plans semi-annual meetings of the Working Group. Applicants are encouraged to include in their budgets travel funds for one investigator to two meetings per year in Bethesda, Maryland. 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. 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 Division of Research Grants, NIH, as directed in the Grant Application Instructions. An additional two copies should be sent to the following:

Dr. Harold Waters
Chief, Special Review Branch
Division of Research Grants
Westwood Building - Room 2A16
Bethesda, Maryland 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. The single deadline for receipt of applications is October 22, 1982. Applications received after this date will be considered unresponsive and will be returned without additional review.

Investigators interested in submitting applications in response to this announcement are encouraged to contact:

John Y. Killen, Jr., M.D.
Head, Medicine Section
Clinical Investigations Branch
Cancer Therapy Evaluation Program
Landow Building - Room 4A14
7910 Woodmont Avenue
Bethesda, Maryland 20205

Telephone: (301) 496-2522

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NCI-DCCP-SPB-82-1

EPIDEMIOLOGIC STUDIES OF RARE TUMORS

NATIONAL CANCER INSTITUTE

Application Receipt Date: November 1, 1982

The Division of Cancer Cause and Prevention (DCCP) of the National Cancer Institute (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.

Grants are awarded to nonprofit and profit organizations and institutions, governments and their agencies, and occasionally to individuals. This type of grant solicitation (the RFA) is utilized when it is desired to encourage investigator-initiated research projects in areas of special importance to the National Cancer Program. Applicants funded under the RFA are supported through the customary NIH grant-in-aid, in accordance with PHS policies applicable to Research Project Grants, including cost-sharing. The RFA solicitation, however, represents a single competition, with a specified deadline for receipt of applications. All applications received in response to the RFA are usually reviewed by the same National Institutes of Health (NIH) Initial Review Group (IRG). The specific deadline for the receipt of response to this RFA is November 1, 1982. Applications should be prepared and submitted in accordance with the aims and requirements of the following sections:

I. BACKGROUND INFORMATION

Forty-two percent of all malignant cancers are accounted for by cancer of the three primary sites of colon/rectum, breast and lung. Although males generally experience higher cancer incidence rate than females, striking differences occur among race, sex groups, and geographic areas with respect to the incidence of cancer of various sites.

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention Research. Awards are under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended, 42 USC 241, 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

Among the less frequently studied tumors from which important informtion may be gained are, for example, malignancies of the thyroid (1.3% of all malignant tumors); anus, anal canal and anorectum (0.2%); soft tissues, including heart (0.6%); bone and joints (0.2%) male breast (0.1%); penis (0.1%) and salivary gland tumors (0.3%).*

The study of rare tumors may provide insight and establish causal associations with environmental risk factors, as for example, DES and clear cell adenocarcinoma in offspring; and vinyl chloride 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.

II. OBJECTIVES AND SCOPE

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, for example, 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).

III. MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health grant-in-aid. The RFA identifies the scope of the Institute's interest. It is expected that responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. The intent is to fund a maximum of eight (8) 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.

* Percent distribution of all malignant cases in Surveillance, Epidemiology and End Results: Incidence and Mortality Data 1973-77, NCI Monograph No. 57, June 1981. NIH Publication No. 81-2330.

IV. REVIEW PROCEDURES AND CRITERIA

Applications must be responsive to this RFA, in the sense of being directed towards the attainment of the stated programmatic goals and fall within one or more of the specified research categories (see II. OBJECTIVES AND SCOPE). If the application is judged by the National Cancer Institute not to be responsive, the applicant may have it considered as a traditional R01, along with other applications in the next regular review cycle. Arrangements will be made by the Division of Research Grants for the review of responsive proposals.

The factors considered in evaluating each response to this RFA will be:

1. Scientific merit of research approach, design, and methodology.

2. Research experience and compétence of the Principal Investigator and staff to conduct the proposed studies.

3. Adequacy of time (effort) which the Principal Investigator and staff would devote to the proposed studies.

4. Adequacy of existing/proposed facilities and resources. Applications which specify a proposed use of human specimens need to provide assurance and details concerning the nature, source, and availability of those specimens.

V. METHOD OF APPLYING

A. Format of Application

Applications must be submitted on form PHS 398 (revised 5/80), the application form for research project grants. Application kits are available at most institution business offices, or may be obtained from the Division of Research Grants, NIH. The conventional presentation in form and detail applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (Section IV above) must be fulfilled.

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.

B. Application Procedure

The completed original application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications should be received by November 1, 1982. If applications are received after that date, the applicant will have the

opportunity of having them considered, along with other unsolicited applications, in the next regular review cycle. Also, the Division of Research Grants (DRG) will not accept any application in response to this announcement, which is the same as one currently being considered by any other NIH awarding unit. A copy of the application should also be sent to Dr. Millner at the address shown below.

VI. INQUIRIES

Inquiries may be directed to:

Elaine S. Millner, Dr. P.H.
Special Programs Branch
Division of Cancer Cause and Prevention
National Cancer Institute
Landow Building - Room 8C16
Bethesda, Maryland 20205

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NCI-DCCP-SPB-82-11

BIOCHEMICAL EPIDEMIOLOGY

NATIONAL CANCER INSTITUTE

Application Receipt Date: November 15, 1982

I. BACKGROUND

Although a significant proportion of human cancers are 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 promoting 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 epidemologists and experimentalists, including biochemists, analytical chemists, immunologists, and nutritionists.

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention Research. Awards are under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, as amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

II. GOALS AND SCOPE

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 both 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 assays, examination of chromosomal defects or susceptibility to cell transformation, assays for immunocompetence or analysis of serum levels of vitamins or micronutrients), 2) detection and quantitation of chemical carcinogens or their metabolites 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 should be consistent with the state-of-the-art; feasibility studies or pilot studies are acceptable when developmental research is needed as preparation for a population study.

III. MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health research project grant. Responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. The total project period for applications submitted in response to the present RFA should not exceed three years. The intent is to fund several individual research project grants, with total costs amounting to approximately $1.5 million 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 the National Cancer Institute, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose. Renewal applications will compete with all other unsolicited applications received by the NCI. NIH policies governing regular research project grants will apply to applications received in response to this request.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Procedure

Upon receipt in the Division of Research Grants, applications will be reviewed for responsiveness. If an application is judged to be nonresponsive, the applicant will be contacted and given an opportunity to have it considered along with other unsolicited grants received by NIH for this cycle.

Proposals responsive to this solicitation will be reviewed in competition with each other on a nationwide basis. The initial review will be for scientific merit and will be carried out by an appropriate peer review group. The secondary review for relevance and responsiveness to the announcement will be made by the National Cancer Advisory Board.

B. Review Criteria

Applications should be responsive to the RFA and, therefore, relevant to the program goals of the National Cancer Institute. Those fctors considered to be important for review include a demonstrated knowledge of the applicable science, adequacy of facilities and commitment, availability of subject population when applicable and in-depth knowledge of the state-of-the-art to which the RFA is directed. The application will be judged upon the overall scientific merit, adequacy of methodology, facilities and resources, commitment of time and cost effectiveness of proposal, and quality of collaboration.

V. METHOD OF APPLYING

A. Format of Application

Applications must be submitted on form PHS 398, the application form for research project grants. Application kits are available at most institutional business offices, or may be obtained from the Division of Research Grants, NIH. The conventional presentation in format and detail applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (IV.B) must be fulfilled. Please check "Yes" in item 2 on the front page of your application, followed by the words "PROPOSAL IN RESPONSE TO RFA NIH-NCI-DCCP-SPB-82-11, BIOCHEMICAL EPIDEMIOLOGY."

B. Application Procedures

The completed original application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications should be received by November 15, 1982. If applications are received after that date, the applicant will have the opportunity of having them considered in the next regular review cycle. Also, the Division of Research Grants (DRG) will not accept any application in response to this announcement, that is the same as one currently being considered by any other NIH awarding unit. Two copies of the application should also be sent to Dr. Copley at the address shown below.

VI. INQUIRIES

Inquiries may be directed to:

Dr. Genrose Copley
Special Programs Branch
Division of Cancer Cause and
Prevention
National Cancer Institute
Landow Building - Room 8C-16
Bethesda, Maryland 20205

Telephone: (301) 496-9600

REQUEST FOR RESEARCH GRANT APPLICATION: RFA

NIH-NCI-DCCP-SPB-82-12

"ACCURACY" OF QUESTIONNAIRE DERIVED HISTORIC DIETARY INFORMATION

NATIONAL CANCER INSTITUTE

Application Receipt Date: November 15, 1982

The Division of Cancer Cause and Prevention (DCCP) of the National Cancer Institute (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 (data reflecting past dietary intake) of the same individuals recorded at some earlier point in time.

Grants are awarded to profit and nonprofit organizations and institutions, governments and their agencies, and occasionally to individuals. This type of grant solicitation (the RFA) is used to encourage investigator-initiated research projects in areas of special importance to the National Cancer Program. Applicants funded under the RFA are supported through the customary National Institutes of Health (NIH) grant-in-aid in accordance with Public Health Service (PHS) policies applicable to Research Project Grants including cost-sharing. The RFA solicitation, however, represents a single competition, with a specific deadline for receipt of applications. All applications received in response to the RFA are usually reviewed by the same NIH Initial Review Group (IRG). The specific deadline for the receipt of responses to this RFA is November 15, 1982. Applications should be prepared and submitted in accordance with the aims and requirements of the following sections:

I. BACKGROUND INFORMATION

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

This program is described in the Catalog of Federal Domestic Assistance No. 13.393, Cancer Cause and Prevention Research. Awards are under authorization of the Public Health Service Act, Section 301(c) and Section 402 (Public Law 78-410, amended; 42 USC 241; 42 USC 282) and administered under PHS grant policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

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 carcinogensis, 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 non-institutionalized 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.

II. OBJECTIVES AND SCOPE

The primary objective of this RFA is to encourage studies aimed at assessing the accuracy and validity of historical dietary information obtained by questioning individuals or their surrogates. 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 availability 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.

III. MECHANISM OF SUPPORT

The responses to this RFA will use the traditional NIH grant-in-aid. The RFA identifies the scope of the Institute's interest. It is expected that responsibility for the planning, direction and execution of the proposed research will be solely that of the applicant. 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 the National Cancer Institute, 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.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Procedures

Each application submitted in response to the RFA will be reviewed by: (1) an appropriate initial peer review panel of the Division of Research Grants, National Institutes of Health, for scientific merit and (2) the National Cancer Advisory Board. All applications will be evaluated in competition with each other on a nationwide basis.

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed toward the attainment of the stated programmatic goals. They will be considered in competition with each other for these RFA monies. If the application is judged by the National Cancer Institute not to be responsive, the applicant may have it considered as a traditional R01, along with other unsolicited applications in the next regular review cycle.

The factors considered in evaluating each response to this RFA will be:

1. Scientific merit of research approach, design, and methodology.

2. Research experience and competence of the Principal Investigator and staff in the use of historical dietary information in the conduct of the proposed studies.

3. Adequacy of time (effort) which the Principal Investigator and staff would devote to the proposed studies.

4. Adequacy of existing/proposed facilities and resources (including the availability of appropriate historical dietary data). Applications which specify a proposed use of human specimens need to provide assurance and details concerning the nature, source, and availability of those specimens.

V. METHODS OF APPLYING

A. Format of Application

Applications should be submitted on form PHS 398 (rev. 5/80), the application form for research project grants. Application kits are available at most institution business offices, or may be obtained from the Division of Research Grants, NIH. The conventional presentation in format and detail applicable to regular research grant applications should be followed, and the requirements specified under Review Criteria (IV.B) must be fulfilled. 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.

B. Application Procedure

The completed original application and six (6) copies should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

To ensure their review, applications should be received by November 15, 1982. If applications are received after that date, the applicant will have the opportunity of having them considered, along with other unsolicited applications, in the next regular review cycle. Also, the Division of Research Grants (DRG) will not accept any applications in response to this announcement which is the same as one currently being considered by any other NIH awarding unit. A copy of the application should be sent to Dr. Hjortland at the address shown below.

VI. INQUIRIES

Inquiries may be directed to:

Dr. Marthana C. Hjortland
Special Programs Branch
Division of Cancer Cause and Prevention
National Cancer Institute
Landow Building - Room 8C-18
Bethesda, Maryland 20205

Telephone: (301) 496-9600

PROGRAM RESEARCH INTERESTS IN IMMUNE MECHANISMS OF CUTANEOUS DISORDERS (IMMUNODERMATOLOGY)

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

The National Institute of Allergy and Infectious Diseases is interested in expanding research activities of the Immunology, Allergic and Immunologic Diseases Program concerned with immune mechanisms and hypersensitivity reactions in diseases of the skin. Investigations dealing with involvement of the skin as target tissue by immune humoral and cellular reactants and with cells of the integument serving as natural sources of specific antigens in immune processes are required to further our understanding of immunologic and allergic cutaneous diseases. The development of such studies will depend upon joint investigative endeavors in the disciplinary areas of allergy, dermatology, and immunology (immunobiology, immunochemistry, immunogenetics, and immunopharmacology).

The role of hypersensitivity and immune related inflammatory mechanisms in disorders of the skin as a product of both basic and clinical investigations has become increasingly evident. Additionally, the recognition of the common occurrence and socioeconomic impact of allergic skin diseases has provided the stimulus to further major efforts in relevant dermatology and allergy-immunology research at an increasing number of university sections and medical centers. Clinical immunologists are in a position to take advantage of the ready access of the skin for in vivo studies of both immune mechanisms in the production of local lesions and systemic immunopathologic processes with manifestations at cutaneous sites. The purpose of this announcement is to encourage the interaction of researchers in allergy, dermatology, and immunology in order to advance progress in the prevention, diagnosis, and treatment of immune-mediated skin diseases.

Some areas encompassed by the scope of this program include investigations designed to study allergic phenomena and immune mechanisms in the following conditions:

1. Studies to differentiate allergic skin disorders arising as a result of IgE related mechanisms: cell-mediated immunity/delayed hypersensitivity, and inflammation emerging from activation of the complement cascade and the effects of chemical mediators.

2. Atopic dermatitis: the definition of possible interacting etiologies that influence the development and course of allergic eczema as a multifactorial disorder.

3. Urticaria and angioedema: investigations to detect and define the multiple allergenic, neurogenic, chemical, and microcirculatory factors that result in heterogeneous disorders with identical presentation.

This program is described in the Catalog of Federal Domestic Assistance No. 13.855, Immunology, Allergic and Immunologic Diseases Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency review.

4. Contact hypersensitivity: evaluation of the nature of normal skin cell components converted to antigenic determinants as a result of interaction with sensitizing agents.

5. Infection: immune responses to both pathogenetic and saprophytic flora serving as microbial antigens in immune and hypersensitivity reactions.

METHOD AND CRITERIA FOR REVIEW

Assignment of Application

Applications will be received by the NIH Division of Research Grants, referred to an appropriate study section for scientific review, and assigned to the NIAID for possible funding, unless programmatic considerations indicate more appropriate assignment to an alternative awarding unit. These decisions will be governed by normal programmatic considerations as specified in the DRG referral Guidelines.

Review Procedures

Applications in response to this announcement will be reviewed on a nationwide basis in competition with each other, and in accord with the usual National Institutes of Health peer review procedures. They will first be reviewed for scientific and technical merit by a review group composed mostly of non-Federal scientific consultants (study section). Following study section review, the application will be evaluated for program relevance by the NIAID Advisory Council. The review criteria customarily employed by the National Institutes of Health for regular research grant applications will prevail.

Deadline

Applications will be accepted in accordance with the usual receipt dates for new applications:

March 1 July 1 November 1

Method of Applying

Applications should be submitted on form PHS 398 (Rev. 5/80) which is available in the institution's business office. If not available there, they may be obtained from:

Office of Grants Inquiries
Division of Research Grants
National Institutes of Health
Westwood Building - Room 448
Bethesda, Maryland 20205

The phrase "PREPARED IN RESPONSE TO PROGRAM RESEARCH INTERESTS IN IMMUNE MECHANISMS AND CUTANEOUS DISORDERS (IMMUNODERMATOLOGY)" should be typed across the top of the first page of the application.

The original and six copies of the application should be sent or delivered to:

Application Receipt Office
Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
Bethesda, Maryland 20205

For further information investigators are encouraged to contact:

Robert A. Goldstein, M.D., Ph.D.
Chief, Allergy and Clinical
Immunology Branch
National Institute of Allergy and
Infectious Diseases
Westwood Building - Room 755
Bethesda, Maryland 20205

Telephone: (301) 496-7104

In order to alert the Skin Diseases Program of the NIADDK to the submission of proposals with primary thrust directed to dermatology, you may wish to communicate with:

Alan N. Moshell, M.D.
Director, Skin Diseases Program
Extramural Programs
National Institute of Arthritis, Diabetes,
and Digestive and Kidney Diseases
Westwood Building - Room 405
Bethesda, Maryland 20205

Telephone: (301) 496-7326

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NIAID-82-9

PROGRAM PROJECTS IN LYMPHOCYTE BIOLOGY

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Application Receipt Date: February 15, 1983

I. BACKGROUND INFORMATION

The Immunobiology and Immunochemistry Branch of the Immunology, Allergic and Immunologic Diseases Program of the NIAID supports fundamental studies on the structure and function of the immune system to gain an understanding of immune response mechanisms at their basic cellular and molecular levels as they function in health and disease. Program Projects in Lymphocyte Biology represent an award mechanism which the Branch has employed to meet this objective. Each program project utilizes an integrated multidisciplinary approach for basic biologic studies of immunologically-functional lymphocyte populations. Five such program projects are now supported although support for one is scheduled to conclude in 1984. This request for applications (RFA) is intended to encourage the development of proposals from collaborating investigators and to coordinate the submission and review of new and renewal program project applications, providing an equitable opportunity for both to compete for funds currently available to the Program in this area of research.

II. RESEARCH GOALS AND SCOPE

The ultimate goal of these program projects is the attainment of a complete knowledge of the life history of immunocompetent cells and of the genetic and phenotypic factors that determine their fate and function in vivo and in vitro. The ultimate practical application would be the use of selected cloned lymphocytic cells and their products for the clinical care or reconstitution of immunodeficient individuals, to alleviate allergic states, to provide resistance to life-threatening infections and to correct aberrant or defective immunoregulatory mechanisms.

The scope of these program projects includes studies of every facet of the immune response ranging from the initial step of antigen recognition to the final elaboration of immunologically distinctive products of specific lymphocytes. Research currently supported by this mechanism was designed to greatly expand knowledge of the morphologic and functional heterogeneity of lymphocyte populations and to develop the capability for identification and selection of

This program is described in the Catalog of Federal Domestic Assistance No. 13.855, Immunology, Allergic and Immunologic Diseases Research. Awards will be made under the authority of the Public Health Service Act, Title III, Section 301 (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grant policies and Federal Regulations 42 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency Review.

lymphocyte subpopulations with specific immune reactivity or antigenic composition, for hybridization of such populations and for selective production of specific, biologically-active, lymphocyte products.

Proposals submitted in response to this RFA should consist of a number of integrated component projects utilizing multifaceted experimental approaches and the technical expertise of cell biologists, cellular immunologists, immunochemists, microbiologists, and geneticists. However, the proposal should clearly explain how the planned multidisciplinary approach can be expected to accomplish the stated goal more efficiently and effectively than a series of independent individual grant-supported studies.

Proposals should emphasize new ideas and new initiatives and should be concerned with the acquisition of new knowledge relevant to the immune system and its structure and function. Although proposals are expected to be based primarily on experimental laboratory investigations, the value and place of clinical studies are recognized. Inclusion of patient oriented studies or laboratory procedures utilizing human source materials is acceptable, provided such studies have an immunologic base or draw upon immunologically relevant technology.

Designation of an individual to serve as the program project director should be based upon accomplishment, experience as a senior scientist and ability to assume both leadership of the investigative group and responsibility for scientific, professional, and administrative functions, and commitment of a significant amount of time to the project. Each component project in the proposal should have a designated principal investigator, also with a demonstrable record of accomplishment in one of the basic science disciplines or clinical specialties relevant to the particular subject of investigation.

III. MECHANISM OF SUPPORT

Program project grants are awarded to an institution in behalf of a program director for the support of a broadly based, multidisciplinary, long-term research program which has a specific major objective or basic theme. A program project generally involves the organized efforts of groups of investigators, members of which conduct research projects related to the overall program objective. The grant can provide support for the projects and for certain core resources shared by individuals in a program where the sharing facilitates the total research effort. Each component project supported under a program project grant is expected to contribute to and be directly related to a common theme; the projects should demonstrate an essential element of unity and interdependence.

This program does not provide support for nonresearch components, such as a clinical referral service or a clinical laboratory service function.

Grant funds may be utilized to support the research activities of scientific and professional personnel, administration, consultation services, central support services, equipment, supplies, travel, and publications costs. Support for research-related cost of patient involvement and medical care may be authorized. Since the Program cannot provide funds for new construction, adequate physical facilities must be available for the primary needs of the project. However, moderate alterations or renovations to enhance clinical or laboratory facilities may be allowed if they are necessary to meet objectives of the proposal.

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.

II. OBJECTIVE AND SCOPE

The primary objective of this RFA is to define the pharmacological role of nicotine in selected animal model(s), or humans, exposed to cigarette smoke under chronic conditions. The proposed work should address precursor states which have indications of being related 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).

III. MECHANISM OF SUPPORT

This RFA will use the traditional National Institutes of Health grant-in-aid. Responsibility for the planning, direction, and execution of the proposed research will be that of the applicant. 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. 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 plan of the National Cancer Institute, the award of grants pursuant to this RFA is contingent upon the availability of funds for this purpose.

IV. REVIEW PROCEDURES AND CRITERIA

A. Review Method

All applications submitted in response to this RFA will be reviewed by: (1) a review group of the Division of Research Grants, NIH; and (2) the National Cancer Advisory Board. All applications will be evaluated on a competitive basis.

B. Review Criteria

Applications must be responsive to this RFA, in the sense of being directed toward the attainment of the stated programmatic objective. If the application is judged by the National Cancer Institute not to be responsive to the RFA, the applicant will have the opportunity of having his application considered along with other unsolicited applications received by the National Institutes of Health in the review cycle which is current at that time.

The factors to be considered in evaluating the proposals which are responsive to this RFA are:

1. Scientific merit of proposed research, design and methodology.
2. Research experience and competence of the Principal Investigator and staff.
3. Availability and adequacy of time which the Principal Investigator and staff would devote to the proposed studies.
4. Adequacy of existing/proposed facilities and resources.
5. Probability of the investigator obtaining goals which are set forth in the application.

V. METHODS OF APPLYING

Applications should be submitted on form PHS 398, which is available at most institutional business offices, or may be obtained from the Division of Research Grants, NIH. 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:

Division of Research Grants
National Institutes of Health
Westwood Building - Room 240
5333 Westbard Avenue
Bethesda, Maryland 20205

Applications must be received by the National Institutes of Health by November 1, 1982. The Division of Research Grants (DRG) will not accept any application in response to this announcement that is the same as one currently being considered by any other NIH awarding unit. 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
Division of Research Grants
Westwood Building - Room 2A16
Bethesda, Maryland 20205

VI. INQUIRIES

Inquiries may be directed to:

Dr. Thomas B. Owen
Special Programs Branch
Division of Cancer Cause
and Prevention
National Cancer Institute
Landow Building - Room 8C18
Bethesda, Maryland 20205

Telephone: (301) 496-9600

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