NIH GUIDE

For Grants and Contracts

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The NIH Guide announces scientific initiatives and provides policy and administrative information to individuals and organizations who need to be kept informed of opportunities, requirements, and changes in extramural programs administered by the National Institutes of Health.

Vol. 20, No. 31
August 16, 1991

NOTICES

NOTICES OF AVAILABILITY (RFPs and RFAs)

ONGOING PROGRAM ANNOUNCEMENTS

NOTICES

HUMAN LIVER FOR SCIENTIFIC INVESTIGATION

P.T. 34; K.W. 0780000, 0780025

National Institute of Diabetes and Digestive and Kidney Diseases

The Liver Tissue Procurement and Distribution System (LTPADS) is an NIH

service contract to obtain human liver from regional centers for distribution to scientific investigators throughout the United States. These regional centers have active liver transplant programs with human subjects approval to provide portions of the resected pathologic liver for which the transplant is performed. Human pathologic liver prepared according to the investigator's specifications provides the opportunity to verify if animal liver investigations are relevant to human liver pathophysiology. The preparation of these livers has been excellent for the usual molecular biologic techniques. Therefore, the National Institute of Diabetes and Digestive and Kidney Diseases is primarily interested in soliciting requests from investigators interested in studying pathologic liver specimens. Examples would include a particular metabolic disorder or disease entity or the general process of cirrhosis. A limited supply of "normal" liver specimens may also be requested but the turn around time for completion of large requests for "normal" liver is much longer than for most pathologic liver specimens.

Further information and request forms may be obtained from:

Harvey L. Sharp, M.D.
Principal Investigator, LTPADS
c/o Elizabeth Webster
Box 279 UMHC
University of Minnesota Hospitals
Minneapolis, MN 55455
Telephone: (612) 624-1133

SMALL GRANTS FOR INNOVATIVE TECHNOLOGY

PA: PA-90-28

P.T. 34; K.W. 0710035

National Center for Research Resources

There is a change in the review schedule for applications submitted to the NCRR Small Grants for Innovative Technology program, previously announced in the August 24, 1990, NIH Guide for Grants and Contracts, Vol. 19, No. 31. In the previous announcement, a schedule for accelerated review was described. Starting with the October 1, 1991, application receipt date, and until further notice, all applications will be reviewed on the schedule given below:

Annual Receipt Date	Initial Review Group meeting	NCRR Council review	Earliest Date for funding
February 1	June-July	Sept.-Oct.	December
October 1	Feb.-March	May-June	August

Further information and special application instructions are available from:

Biomedical Research Technology Program
National Center for Research Resources
National Institutes of Health
Westwood Building, Room 8A11
Bethesda, MD 20892
Telephone: (301) 496-5411

NOTICES OF AVAILABILITY (RFPs AND RFAs)

ENHANCEMENT OF GENINFO DATABASE SYSTEM

BAA/RFP AVAILABLE: BAA/RFP NLM 92-101/AJM

P.T. 34; K.W. 1004017, 1002019

National Library of Medicine

The National Center for Biotechnology Information (NCBI) was established by Public Law 100-607 in November 1988 as a division of the National Library of Medicine. The Center has been given the responsibility to (1) create automated systems for storing and analyzing knowledge about molecular biology, biochemistry, and genetics; and (2) support, assist, and enhance existing public information resources for biotechnology, such as nucleic acid and protein sequence databanks, and other related research information resources. In accordance with this mandate, NCBI will assume responsibility for GenBank, the NIH DNA sequence database, in September 1992.

To provide sequence information to the scientific community, the NCBI is developing the GenInfo database, an integrated nucleic acid and protein sequence database based on the published literature and direct author submissions. GenInfo also contains elements that serve as links to information in other sequence databases.

The need for integration of molecular biology databases has been widely recognized and the NCBI is committed to facilitating the interconnection of databases of sequence, structural, genetic, bibliographic, and other factual information. The design approach aims to modularize the database development process and focus on the necessity for stability and comprehensiveness in a foundation database. The design concept and the representation of the data in a standard data description language will facilitate access to the underlying data by specialized databases that can provide value-added views of all or part of the data.

In order to support a range of database development efforts that depend upon the specialized experience of investigators, the NCBI announces that it will be issuing a Broad Agency Announcement inviting proposals related to enhancing the coverage of GenInfo and developing specialized value-added databases that would link to and enhance the GenInfo system of molecular biology databases. The Broad Agency Announcement is a research and development contract mechanism that provides for investigator-developed statements of work within the scope of a broad range of activities defined by the NCBI. Offerors may submit proposals in one or more of the five categories listed below. The research categories for which proposals are sought are: design and implementation of specialized collections of biological sequence and other genomic data; integrated views of data in the GenInfo Database, e.g., non-redundant subsets, merged sequence sets; enhancement of the GenInfo Backbone Database with additional annotation of biological data; application of standardized nomenclature (e.g., taxonomies, gene names) to molecular biology data; enhancement of connectivity among biological resource databases by cross-referencing or explicit linkages.

It is anticipated that the award(s) from this announcement will be multi-year, cost-reimbursement type contract(s).

The Broad Agency Announcement will be issued on September 23, 1991. Responses will be due by February 24, 1992. Written requests for a copy of Broad Agency Announcement number BAA/RFP NLM 92-101/AJM should be sent to:

Mr. Anthony Murray
National Library of Medicine
Office of Acquisitions Management
8600 Rockville Pike
Building 38A, Room B1N17
Bethesda, MD 20892

PRECLINICAL EVALUATION OF INTERMEDIATE ENDPOINTS AND THEIR MODULATION BY CHEMOPREVENTIVE AGENTS

MASTER AGREEMENT RFP AVAILABLE: NCI-CN-15390-51

P.T. 34; K.W. 0740018, 0755018, 0715035

National Cancer Institute

The National Cancer Institute has a requirement for a contractor to conduct animal cancer model studies of biomarkers and intermediate endpoints that might be used in human clinical trials in order to examine, in detail, the biomarker modulating effects of selected chemopreventive compounds. The studies shall improve biomarker sensitivity specificity, assay methodology, and sample handling. The emphasis will be on efficient studies aimed at providing more quantitative and more validating intermediate endpoints for future human clinical trials. This acquisition is for a five-year Master Agreement and is in support of the Division of Cancer Prevention and Control located in Bethesda, MD. The Request for Proposals (RFP) will be available on or about August 22, 1991, and proposals will be due approximately September 30, 1991.

Copies of the RFP may be obtained by sending a written request citing the RFP No. NCI-CN-15390-51, to:

Ms. Christine L. Ptak
Contract Specialist
Research Contracts Branch, PCCS
National Cancer Institute
Executive Plaza South, Room 635
Bethesda, MD 20892
Telephone: (301) 496-8603

PHASE II CLINICAL TRIALS OF NEW CHEMOPREVENTIVE AGENTS

MASTER AGREEMENT RFP AVAILABLE: NCI-CN-15391-51

P.T. 34; K.W. 0740018, 0755015, 0715035

National Cancer Institute

The National Cancer Institute is interested in establishing a Master Agreement pool with the objective of encouraging cancer chemoprevention clinical trials that use biochemical and biological markers as intermediate endpoints. The application of biological markers to clinical prevention trials carries great promise in relation to ultimate cancer prevention. When neoplasia itself is used as an endpoint in studies of this type, a very large number of subjects tested for long durations is often required. The emphasis in Phase II clinical trials will be on small, short-term, efficient studies that will determine the dose of a given chemopreventive agent that exhibits a pharmacodynamic effect on an intermediate endpoint and then to do a dose response study to determine the minimum dose at which this biological effect is observed and to confirm the maximum safe dose. The second state of the Phase II study will involve a randomized blinded trial in a small group of subjects whose endpoint will be a measurable biological effect of the agent versus the placebo. This acquisition is for a five-year Master Agreement and is in support of the Division of Cancer and Prevention and Control located in Bethesda, MD. The Request for Proposals (RFP) will be available on or about August 22, 1991, and proposals will be due approximately September 30, 1991.

Copies of the RFP may be obtained by sending a written request, citing the RFP No. NCI-CN-15391-51, to:

Ms. Christine L. Ptak
Contract Specialist
Research Contracts Branch, PCCS
National Cancer Institute
Executive Plaza South, Room 635
Bethesda, MD 20892

BREAST CANCER DIAGNOSIS, MANAGEMENT, AND SEQUELAE IN OLDER WOMEN

RFA AVAILABLE: CA/NR/AG-91-24

P.T. 34, II; K.W. 0715035, 0745020

National Cancer Institute
National Center for Nursing Research
National Institute on Aging

Letter of Intent Receipt Date: September 16, 1991
Application Receipt Date: November 27, 1991

PURPOSE

This Request for Applications (RFA) invites applications for research directed at breast cancer management in women ages 65 and over. Applications must address diagnostic evaluation, treatment, or follow-up of older patients with breast cancer. Major objectives are (1) to identify factors that impact on appropriate diagnosis and state-of-the-art cancer care for this age group; and (2) to develop and test interventions to enhance appropriate oncologic care.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Breast Cancer Diagnosis, Management, and Sequelae in Older Women, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report:

Stock No. 017-001-0473-1) through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by for-profit or nonprofit organizations, either public or private.

MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) grant-in-aid (R01). Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. Except as otherwise stated in this RFA, awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement.

This RFA is a one-time solicitation. Generally, future unsolicited competing continuation applications will compete with all investigator-initiated applications and be reviewed by a Division of Research Grants study section. However, should the National Cancer Institute (NCI), the National Center for Nursing Research (NCNR), or the National Institute on Aging (NIA) determine that there is a sufficient continuing program need, a request for competitive continuation applications will be announced. The total project period for applications submitted in response to the present RFA may not exceed three years. The anticipated award date will be July 1, 1992.

FUNDS AVAILABLE

Approximately $2,100,000 in total costs per year for three years will be committed to specifically fund applications submitted in response to this RFA. Three to four awards by NCI, two awards by NCNR, and at least one award by NIA are anticipated.

This level of support 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, NCNR, and NIA, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

RESEARCH OBJECTIVES

Specific objectives are (1) to identify barriers to appropriate diagnosis and treatment of symptomatic breast cancer in this age group; and (2) to design and test interventions directed at eliminating defined barriers.

Projects concerning breast cancer diagnosis must address patient attitudes towards symptoms, access to specialized oncologic care, or physician practices in diagnosis and/or staging elderly patients. Treatment projects must focus on physician attitudes and practices in recommending treatment, impact of comorbid medical problems on therapy, patient-physician interactions in decision-making, supportive care during cancer treatment, or early and late sequelae of disease and treatment. Screening/early detection projects in asymptomatic women and terminal care or hospice interventions for elderly women receiving only comfort measures are excluded.

STUDY POPULATIONS

Potential populations include breast cancer patients ages 65 and older, their families, their physicians, and other health care professionals involved in their care. There must be no upper age limit for patient populations.

SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

REVIEW CONSIDERATIONS

Applications will be evaluated according to specific review criteria for scientific and technical merit by an appropriate peer review group convened by the Division of Extramural Activities, NCI.

APPLICATION PROCEDURES

The most recent revision of the research grant application form PHS 398 (revised 10/88) must be used in applying for these grants. Applications must be received by November 27, 1991; those received after that date will be returned. Further information regarding application procedures and application forms may be obtained from the NCI Program Director named below.

LETTER OF INTENT

Prospective applicants are asked to submit, by September 16, 1991, a letter of intent to:

Susan G. Nayfield, M.D., M.Sc.
Program Director
Community Oncology and Rehabilitation Branch
National Cancer Institute
Executive Plaza North, Room 300
Bethesda, MD 20892
Telephone: (301) 496-8541

INQUIRIES

Direct inquiries regarding programmatic issues to:

Susan G. Nayfield, M.D., M.Sc.
Program Director
Community Oncology and Rehabilitation Branch
National Cancer Institute
Executive Plaza North, Room 300
Bethesda, MD 20892
Telephone: (301) 496-8541

Direct inquiries regarding fiscal matters to:

Ms. Eileen M. Natoli
Team Leader, Grants Administration Branch
National Cancer Institute
Executive Plaza South, Room 242
Bethesda, MD 20892
Telephone: (301) 496-7800

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Number 93.399, Cancer Control. Awards will be made under the authority of the Public Health Service Act, Title IV, Section 301 (Public Law 78-410, 42 U.S.C. 241, and Section 412, as amended by Public Law 99-158, 42 U.S.C. 258a-1) and administered under PHS grants policies and Federal regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

BREAST CANCER EDUCATION SUMMITS AT NCI-DESIGNATED COMPREHENSIVE CANCER CENTERS

RFA AVAILABLE: CA-91-27

P.T. 04; K.W. 0715035, 0502017, 0403004

National Cancer Institute

Application Receipt Date: October 11, 1991

PURPOSE

The purpose of this Request for Applications (RFA) is to provide support for the planning, implementation, and evaluation of Breast Cancer Education Summits. The summits are intended to convey information and educational materials about breast cancer to community organizations and businesses and to stimulate these organizations and businesses to establish breast cancer education and screening programs in the community. The aim is to motivate these organizations and businesses to reach women in the community, to inform them about the risks of breast cancer and the methods to achieve early detection, and how to seek the best treatment. The summit is intended ultimately to reach all women in the community with special emphasis on women at high risk for breast cancer and populations that are medically underserved and/or hard to reach. Special attention must be given to encouraging the establishment of readily available, low-cost, high-quality mammograms for underserved populations, such as at the worksite.

The regional summits must follow the model of the national summits, including educational sessions, and panel discussions featuring successful community-based programs and worksite screening efforts.

It is expected that the grants awarded under this RFA will be used to partially fund planning, implementation and evaluation of the summit conference. The summits will be co-sponsored by the National Cancer Institute (NCI) and other non-profit organizations. Centers are encouraged to obtain additional funding from local sources for any costs not met by this grant.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000", a PHS-led national activity for setting priority areas. This RFA, Breast Cancer Education Summits at NCI-Designated Comprehensive Cancer Centers, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents. Government Printing Office, Washington, D.C. 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Eligibility for this RFA is limited to NCI-Designated Comprehensive Cancer Centers.

MECHANISM OF SUPPORT

The administrative and funding mechanism to be used to support these summits will be the Conference Grant Award (R13). Applicants will be responsible for the planning, direction and execution of the proposed project. Except as otherwise stated in this RFA, awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement, DHHS Publication No. (OASH) 90-50,000, revised October 1, 1990.

This RFA is a one-time solicitation.

FUNDS AVAILABLE

Approximately $150,000 in total costs will be committed to specifically fund applications submitted in response to this RFA. It is anticipated that five to six awards will be made. No more than $25,000 direct costs will be distributed to a single Cancer Center.

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 NCI, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

SPECIAL REQUIREMENTS

Applications will be selected for funding based on merit of the applications. However, location of the Cancer Centers will also be considered to assure balanced geographic distribution of the five or six summits, allowing the broadest coverage of the U.S. population.

Applicants must budget for a one-day meeting to be held at NIH in Bethesda, MD, soon after grants are awarded to discuss the summits. The Cancer Centers that receive grants will negotiate timing of their summit meeting with NCI to ensure that the summits are well spaced within the time frame of February 1992 to September 1992.

The funds and resources provided by the NCI must be used for information and education purposes only and not for additional fund-raising activities.

APPLICATION PROCEDURES

The research grant application form PHS 398 (revised 10/88) must be used in applying for these grants. These forms are available at most institutional business offices; from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441; and from the NCI Program Director named below. Applicants may find information on the requirements for conference grants and supplemental instructions for application form PHS-398 in the publication on "Support of Scientific Meetings," U.S. Department of Health and Human Services, August 1988, 8 pp.

that may be obtained from the Office of Grants Inquiries and the Grants Management contact noted below.

INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues and requests for the full RFA to:

Linda Anderson
Office of Cancer Communications
National Cancer Institute
Building 31, Room 10A24
9000 Rockville Pike
Bethesda, MD 20892
Telephone: (301) 496-6641

OR

Linda M. Muul, Ph.D.
Special Assistant to OCC
Program Director, Cancer Centers Branch
Division of Cancer Biology, Diagnosis and Centers
National Cancer Institute
Executive Plaza North, Room 308
Bethesda, MD 20892
Telephone: (301) 496-8531

Inquiries regarding fiscal matters are to be directed to:

Robert E. Hawkins
Grants Administration Branch
National Cancer Institute
Executive Plaza South, Room 243
Bethesda, MD 20892
Telephone: (301) 496-7800 Ext. 13

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No 93.397. Cancer Centers Support Awards are made under authorization of the Public Health Service Act, Title IV, Sections 305(a), 410, 411 and 414, Part A (Public Law 78-410, 42 U.S.C. 241 as amended, Public Law 100-607, 42 U.S.C. 285, 285a; Public Law 99-500) and administered under PHS grants policies and Federal Regulations at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

NATIONAL COOPERATIVE DRUG DISCOVERY GROUPS

RFA AVAILABLE: CA-91-19

P.T. 34; K.W. 0715035, 0740020, 0755025, 0755020

National Cancer Institute

Letter of Intent Receipt Date: September 15, 1991
Application Receipt Date: November 13, 1991

In FY 1983 and 1984, the National Cancer Institute (NCI) requested applications for National Cooperative Drug Discovery Groups (NCDDGs) whose goal was the discovery of improved cancer treatment on the basis of novel mechanisms of drug action. In 1986, the program requested applications focused on exploitation of specific and unique characteristics of lung and colon cancer. The NCDDG approach to modern anticancer treatment discovery was broadened further in August 1987 by Requests for Applications (RFAs) inviting applications for the creation and evaluation of both general mechanism of action-based and specific disease-oriented anticancer treatments as well as for the development of innovative preclinical models for determining antitumor selectivity. In FY 1988, NCI invited applications for the establishment of Groups whose goal was the selection, isolation, and evaluation of novel anticancer treatments from natural sources. All four RFAs were reissued in FY 1989. The present RFA is a combined reissuance of the general mechanism of action-based and specific disease-oriented RFAs.

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included or adequately represented in the study populations for clinical studies, a specific justification for this exclusion or inadequate representation must be provided. Applications without such documentation will not be accepted for review.

SUMMARY

The National Cancer Institute (NCI) announces the availability of an RFA for the funding of NCDDGs to stimulate the scientific community to discover new treatments or strategies for the cure of cancer. This program is designed to assist leading investigators in diverse scientific disciplines to interact as a unit regardless of their individual institutional affiliations or prior direct involvement in cancer related research. The purpose is to mobilize, with NCI support, the outstanding talents required for exploitation and extrapolation of leads from fundamental studies to the discovery of improved cancer treatments. An NCDDG is envisioned as being composed of a Principal Investigator (PI) and a number of Program Leaders who will conduct interdependent and synergistic preclinical laboratory programs. Areas of research will be broad and could include a variety of scientific disciplines such as biochemistry, cell biology, pharmacology, medicinal chemistry, and immunology. An NCDDG may be made up of scientists in academic, non-profit research, and commercial organizations.

Awards will be made as cooperative agreements. Assistance via cooperative agreement differs from the traditional research grant in that the cooperative agreement funding mechanism anticipates substantial NCI staff programmatic participation during performance. However, the applying Group must define its objectives in accord with its own interests and perceptions of approaches to the discovery of improved cancer treatment. The role of NCI as a member of the Group is described in the RFA. The NCI Coordinator from the Grants and Contracts Operations Branch, Developmental Theapeutics Program, Division of Cancer Treatment, will marshall the appropriate resources to assist and stimulate the realization of Group objectives. Active participation of industry is encouraged because it will allow this segment of the scientific community to contribute its considerable intellectual and material resources.

The PI's institution will be responsible for the Group application. Awards will be made to the applicant institution on behalf of the Group as a whole and not to individual Laboratory Programs within the Group. The PI's institution will provide a Central Operations Office for the Group and will be responsible for the performance of the entire Group and be accountable for the funds awarded.

The NCI plans to make multiple awards for project periods of up to four years and has set aside $4,000,000 for the initial year's funding.

For further information and a copy of the RFA contact:

George S. Johnson, Ph.D.
Grants and Contracts Operations Branch
Developmental Therapeutics Program
Division of Cancer Treatment
National Cancer Institute
Executive Plaza North, Room 832
Bethesda, MD 20892
Telephone: (301) 496-8783

Questions of an administrative nature not directly related to the programmatic aspects of the RFA may be directed to:

Ms. Mable Lam
Grants Management Specialist
Grants Administration Branch
National Cancer Institute
Executive Plaza South, Suite 242
Bethesda, MD 20892
Telephone: (301)-496-7800, Ext. 48

This program is described in the Catalog of Federal Domestic Assistance No. 93.395, Cancer Treatment Research. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

EDUCATION PROGRAMS IN CANCER PREVENTION AND CONTROL

RFA AVAILABLE: CA-91-20

P.T. 34; K.W. 0715035, 0502017, 0745027, 0795003, 0745020

National Cancer Institute

Letter of Intent Receipt Date: September 15, 1991
Application Receipt Date: November 13, 1991

PURPOSE

The National Cancer Institute (NCI) invites grant applications to support educational programs aimed at developing investigators with new research skills focused on the design and implementation of cancer prevention and/or control intervention research. A major goal of this Request for Applications (RFA) is to broaden the research infrastructure of cancer prevention and control by increasing the number of well-trained scientists in the field. A parallel goal is to develop a cadre of clinical oncologists proficient in the use of public health approaches and behavioral techniques for the development and/or implementation of interventions designed to prevent cancer and to increase the early detection and diagnosis of cancer. Another objective is to orient health professionals already schooled in areas of public health, the behavioral and social sciences, nursing, and biostatistics toward careers in cancer prevention and control research by providing them with basic knowledge in cancer biology, prevention and control, and the skills necessary for intervention trials.

A sufficient number of prevention-oriented scientists and practitioners carrying out such interventions on a national scale could make a significant contribution to the reduction of cancer incidence and mortality. There should also be an emphasis on providing the specialized skills needed for interventions in the underserved, elderly, and minority populations that have high cancer incidence and mortality rates.

These cross-disciplinary educational programs are likely to involve active collaborations or special arrangements between institutions and/or departments such as those with Cancer Center Support Grants (P30), schools of public health, departments of community and preventive medicine, and other departments and institutions that have the necessary expertise and resources to fulfill the objectives of this RFA.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Education Programs in Cancer Prevention and Control, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0 or Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic non-profit organizations, whether public or private, such as universities, colleges, hospitals, and laboratories. Applications involving minority and women students and investigators are encouraged.

MECHANISM OF SUPPORT

Support for this program will be through the National Cancer Institute Cancer Education Program (R25). Applicants will be responsible for the planning, direction, and execution of the proposed project. Awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement.

This RFA is a one-time solicitation. Generally, future unsolicited competitive continuation applications will compete with all investigator-initiated applications. However, should the NCI determine that there is a sufficient continuing program need, a request for competitive continuation and/or new applications will be announced. The total project period for applications submitted in response to the present RFA may not exceed five years. The earliest award date will be July 1, 1992.

FUNDS AVAILABLE

For FY 1992, $2,500,000 in total costs will be available for approximately ten awards. This funding level is dependent upon the receipt of a sufficient number of applications of high scientific merit. Although this program is provided for in the financial plans of the NCI, the award of grants pursuant to this RFA is also contingent upon the availability of funds for this purpose.

PROJECT DESCRIPTION

This education program requires the integration of many diverse elements such as: (1) a core curriculum covering topics in cancer biology, cancer prevention, public health, and behavioral sciences; (2) peer-reviewed, faculty-held cancer prevention and control research projects; (3) the availability of appropriate patient study populations and data bases; and (4) the availability of appropriate laboratory and clinical facilities. Principal Investigators and applicant organizations must demonstrate the ability to organize and administer this type of interdisciplinary cancer-oriented program whose structure may require linkage to other academic and programmatic components of the parent and/or collaborating institutions.

Proposed programs must provide requisite educational skills in cancer prevention and control through course work, seminars, 'hands-on' intervention-type projects, and other research experiences. Depending upon the proposed program's educational objectives, faculty, research, target student population, and other available resources, applicants may propose a predoctoral and/or postdoctoral type program. Graduates of the program must have some knowledge of cancer biology, including topics such as models of carcinogenesis and short-term intervention end-points that would allow for monitoring the efficacy of various interventions. They must also have some familiarity with the clinical aspects of the major cancer sites. Finally, they must understand the research methodologies of key prevention related disciplines such as epidemiology and the behavioral sciences, methodologies for the identification of high-risk groups, and some exposure to theories of health education and prevention and control.

Research graduates must be able to formulate hypotheses and design and conduct research on the effectiveness of interventions in populations, while practitioner graduates must be able to apply the results of research studies to appropriate populations.

SPECIAL REQUIREMENTS

A multidisciplinary Cancer Education Committee is essential to the overall administration of a Cancer Education Program. It must consist of experts representing basic, behavioral, and clinical disciplines concerned with cancer and its prevention. Schools and departments participating in joint applications must be represented on the committee. Evidence must be provided of the committee's function, structure, composition, and frequency of meetings.

SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of women and minorities in study populations. If women or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

APPLICATION PROCEDURES

The most recent revision of the research grant application form PHS 398 (rev. 10/88) must be used in applying for these Cancer Education (R25) awards. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441.

Applications must be received by November 13, 1991. Consult the RFA for complete application procedures.

LETTER OF INTENT

Although not required, a letter of intent may be submitted by September 15, 1991, and include a descriptive title of the proposed educational program, the name and address of the Principal Investigator, names of other key personnel,

participating institutions, and the number and title of the RFA. The letter of intent is to be sent to:

Dr. Robert Adams
Cancer Training Branch
Division of Cancer Biology, Diagnosis and Centers
National Cancer Institute
Executive Plaza North, Room 232
Bethesda, MD 20892
Telephone: (301) 496-8580
FAX: (301) 402-0181

INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged and are to be directed to Dr. Robert Adams or Dr. Vincent Cairoli at the above address. The opportunity to clarify any issues or questions from potential applicants is welcome. The program official will be pleased to mail the complete RFA to all who request it.

Direct inquiries regarding programmatic issues to:

Dr. Robert C. Adams
Cancer Training Branch
National Cancer Institute
Executive Plaza North, Room 232
Bethesda, MD 20892
Telephone: (301) 496-8580
FAX: (301) 402-0181

Direct inquiries regarding grants management issues to:

Mr. Robert Hawkins
Grants Administration Branch
National Cancer Institute
Executive Plaza South, Room 242
Bethesda, MD 20892
Telephone: (301) 496-7800, extension 13

For information regarding the Division of Cancer Prevention and Control intramural Cancer Prevention Fellowship Program, contact:

Dr. Douglas L. Weed
Director, Cancer Prevention Fellowship Program
Division of Cancer Prevention and Control
National Cancer Institute
Executive Plaza South, Room T41
Bethesda, MD 20892
Telephone: (301) 496-8640

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.398, Cancer Research Manpower. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

PHASE I TRIALS OF NEW CYTOTOXIC AND BIOLOGIC AGENTS IN CHILDREN WITH CANCER

RFA AVAILABLE: CA-91-22

P.T. 34; K.W. 0755015, 0715035, 0740020, 0710100

National Cancer Institute

Letter of Intent Receipt Date: September 11, 1991
Application Receipt Date: November 26, 1991

PURPOSE

The Division of Cancer Treatment (DCT), National Cancer Institute (NCI), invites cooperative agreement applications (U01) from consortia of institutions, including DCT Clinical Trials Cooperative Groups, wishing to perform: (1) Phase I clinical trials of new cytotoxic, biologic, and

differentiation-inducing agents in children with advanced refractory cancer; (2) appropriate detailed laboratory studies of new cytotoxic agents to include pharmacokinetics of the parent compound and its important metabolites as well as additional studies when appropriate (e.g., intracellular activation kinetics); and (3) appropriate laboratory correlative studies for new biologic and differentiation-inducing agents.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This Request for Applications (RFA), Pediatric Phase I Trials of New Cytotoxic and Biologic Agents in Children with Cancer, is related to the priority area of cancer. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary report: Stock No. 017-001-0043-1) through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325 (telephone 202-783-3238).

ELIGIBILITY CRITERIA

Non-profit organizations and institutions and governments and their agencies are eligible to apply. For-profit organizations are also eligible unless specifically excluded by legislation. Both domestic and foreign applicants may apply.

Each awardee will be known as a Pediatric Phase I Clinical Trials Group (PPICTG). A PPICTG must be a consortium of medical institutions that agree to work together with a Principal Investigator and a single administrative focus; however, each PPICTG will be funded by a single cooperative agreement. Each PPICTG will be expected to accrue 40-50 patients per year. Each applicant institution must have a coordinating center/operations office responsible for coordination of protocol development and submission, study conduct, quality control and study monitoring, collection of data, data management and analysis, adherence to requirements regarding investigational drug management and federally mandated regulations, and protocol and performance reporting of data from the Phase I trials. Each applicant institution is responsible and accountable for both the use of the funds provided and for the performance of the cooperative agreement supported activity.

MECHANISM OF SUPPORT

Awards will be made as cooperative agreements (U01) that create an assistance relationship with substantial programmatic involvement of NCI staff during the performance of the project. This mechanism is used when the NCI wishes to stimulate investigator interest and proposes to advise or assist in an important and opportune area of research. Applicants will be responsible for the planning, direction, and execution of the proposed project. NCI participation, through the staff of the Cancer Therapy Evaluation Program, will provide assistance in the nature of information regarding NCI priorities and ongoing efforts elsewhere in the scientific community and will provide advice (through the protocol review process) regarding methodology, feasibility, and adherence to regulatory requirements mandated by the role of the NCI as a drug sponsor.

FUNDS AVAILABLE

The NCI anticipates making two awards for the project period of up to four years. A total of $750,000 in total costs is expected to be setaside for the initial year's funding. Although this program is provided for in the financial plans of the NCI, the award of cooperative agreements pursuant to this RFA is also contingent upon the availability of funds appropriated for fiscal year 1992.

STUDY POPULATIONS

SPECIAL INSTRUCTIONS FOR INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES.

For projects involving clinical research, NIH requires applicants to give special attention to the inclusion of females and minorities in study populations. If females or minorities are not included in the study populations for clinical studies, a specific justification for this exclusion must be provided. Applications without such documentation will not be accepted for review.

APPLICATION PROCEDURES/LETTER OF INTENT

This RFA is a one-time solicitation with a specified deadline of November 26, 1991, for receipt of applications. Prospective applicants are asked to submit by September 11, 1991, a letter of intent that includes a descriptive title of the proposed research, the name and address of the Principal Investigator, the names of other key personnel, the participating institutions, and the number and title of the RFA in response to which the application is being submitted. Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, it is requested in order to provide an indication of the number and scope of applications to be reviewed.

The letter of intent is to be sent to Dr. Malcolm Smith at the address noted below.

This is an abbreviated version of the RFA. A copy of the complete RFA describing the research goals and scope, the cooperative agreement mechanism, the review criteria, and other requirements necessary for potential applications and is available from:

Dr. Malcolm Smith
Cancer Therapy Evaluation Program
Division of Cancer Treatment
National Cancer Institute
EPN, Room 741
Bethesda, MD 20892
Telephone: (301) 496-2522
FAX: (301) 480-4663

Inquiries concerning this RFA are encouraged and are to be directed to Dr. Smith at the above address and telephone number.

For fiscal and administrative manners, contact:

Ms. Mary Niemiec
Grants Management Specialist
National Cancer Institute
EPS, Room 242
Bethesda, MD 20892
Telephone: (301) 496-7800 ext. 52
FAX: (301) 496-8601

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No 93.395, Cancer Treatment Research. Awards are made under the authorization of the Public Health Service Act, Title IV Sections 301, 410, and 411, Part A (Public Law 78-410, 42 USC 241 as amended, Public Law 99-158, 42 USC 285a) and administered under PHS grants policies and Federal Regulations at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

CANCER EDUCATION PROGRAMS IN PAIN MANAGEMENT

RFA AVAILABLE: CA-91-25

P.T. 34; K.W. 0715150, 0715035, 0502017, 0415001, 0710030

National Cancer Institute

Letter of Intent Receipt Date: November 1, 1991
Application Receipt Date: December 6, 1991

PURPOSE

The National Cancer Institute (NCI) invites grant applications to support education activities in pain management, rehabilitation, or psychosocial issues affecting cancer patients and their families. These cancer education programs are intended to facilitate the dissemination and application of information regarding state-of-the-art procedures for effective pain control, for improving the rehabilitation of cancer patients and their reentry into the workplace, and for using psychosocial knowledge and techniques to promote the well-being of cancer patients.

Applicant institutions with expertise in oncology, nursing, psychology, sociology, and other relevant disciplines must be able to establish interdisciplinary educational programs in one or more of the target areas of cancer pain management, cancer rehabilitation, or psychosocial issues affecting cancer patients and their families. Short training courses,

workshops, lectures, small discussion groups, demonstrations, hands-on experiences, when suitable, or other useful formats will be employed either locally or regionally to disseminate proper knowledge and skills. It is hoped that these educational and training activities will in turn further prompt physicians and other health professionals to apply effective and innovative procedures and techniques in these subject areas that will be of material benefit to the quality of life of cancer patients and their families.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Cancer Education Programs In Pain Management, is related to the priority area of health promotion: educational and community-based programs. Potential applicants may obtain a copy of "Healthy People 2000," (Summary Report: Stock No. 017-001-00473-1 or Full Report: Stock No. 017-001-00474-0) through the Superintendant of Documents, Government Printing Office, Washington, D.C. 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic non-profit organizations, whether public or private, such as universities, colleges, hospitals, laboratories, units of State or local governments, and eligible agencies of the Federal Government. Applications from minorities and women are encouraged.

MECHANISM OF SUPPORT

Support for this program will be through the National Cancer Institute Cancer Education Program (R25). Applicants will be responsible for the planning, direction, and execution of the proposed project. Awards will be administered under PHS grants policy as stated in the Public Health Service Grants Policy Statement.

FUNDS AVAILABLE

For FY 1992, $800,000 in total costs will be available for approximately ten awards. The project period will be for up to three years. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. The earliest feasible start date for the initial award will be July 1, 1992. Although this program is provided for in the financial plans of the NCI, the award of grants pursuant to this RFA is contingent upon the availability of funds for this purpose.

SPECIAL REQUIREMENTS

Applicants are requested to identify clearly in the application the following aspects of the proposed initiative: (1) the content and scope of the educational activities; (2) the specific populations to be educated and their availability; (3) the procedures to be used to announce these educational activities and to recruit participants; (4) the qualifications of the faculty member(s) who would conduct the program(s); (5) the potential benefits to cancer patients and their families likely to arise as the result of these educational programs; (6) the methods of evaluation of the program outcomes; and (7) the specific plans to disseminate aspects of the educational activities that prove to be effective.

APPLICATION PROCEDURES

The most recent revision of the research grant application form PHS 398 (rev. 10/88) must be used in applying for these Cancer Education (R25) awards. These forms are available at most institutional business offices and from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Room 449, Westwood Building, 5333 Westbard Avenue, Bethesda, MD 20892, telephone (301) 496-7441.

Applications must be received by December 6, 1991. Consult the full RFA for complete application procedures and for the optional submission of a letter of intent.

INQUIRIES

Written and telephone inquiries concerning the objectives and scope of this RFA and inquiries about whether or not specific proposed educational activities would be responsive to this RFA are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcomed. The

program official named below will be happy to mail the complete RFA to all who request it.

Direct inquiries regarding programmatic issues to:

Dr. Robert C. Adams
Cancer Training Branch
National Cancer Institute
Executive Plaza North, Room 232
Bethesda, MD 20892
Telephone: (301) 496-8580
Fax: (301) 402-0181

Direct inquiries regarding grants management issues to:

Mr. Robert Hawkins
Grants Administration Branch
National Cancer Institute
Executive Plaza South, Room 242
Bethesda, MD 20892
Telephone: (301) 496-7800, extension 13

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance Number 93.398, Cancer Research Manpower. Awards are made under the authorization of the Public Health Service Act, Title IV, Part A, Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285 and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

ONGOING PROGRAM ANNOUNCEMENTS

BASIC RESEARCH IN PERTUSSIS

PA: PA-91-84

P.T. 34; K.W. 0715125, 0740075, 0755020

National Institute of Allergy and Infectious Diseases

PURPOSE

The National Institute of Allergy and Infectious Diseases invites investigator-initiated research grant applications to support our efforts to scientifically and systematically address issues surrounding the safety of the current whole-cell pertussis vaccine. Several areas related to Bordetella pertussis remain poorly understood, and the development of optimal vaccines for pertussis requires more complete understanding of the pathogenesis of the disease, the mode of infectivity, the role of individual bacterial components in the disease process, and the mechanism of resistance to disease. To determine the pathogenesis of pertussis, additional work is needed to define the roles of individual bacterial components in the disease process and the mechanisms of resistance to disease. These efforts would be enhanced by the development of animal models and in vitro assays to assess the associated biologic activities. Additional efforts will also be necessary to define the role(s) of secretory immunity in the development and maintenance of protection against B. pertussis. Support will be through individual research grants.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000", a PHS-led national activity for setting priority areas. This Program Announcement (PA), Basic Research on Pertussis, is related to the priority areas of immunization and infectious diseases, and maternal and infant health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325 (telephone 202-783-3238).

BACKGROUND

The final test of any specific immunization program is its effect in the community on the morbidity and mortality of the particular disease. Although

efficacious pertussis vaccines are in widespread use, their safety has been questioned. If new, safe vaccines are to be developed, additional research will be required in many areas including pertussis diagnosis, antigen analysis, pathology, immunity, and epidemiology.

Unlike pertussis disease, which appears to confer life-long immunity, pertussis vaccines confer only partial and relatively transient protection. A high degree of protection persists for three to seven years, then decreases until little protection is evident after about 12 years. Adults who had childhood pertussis and who are re-exposed demonstrate variable antibody levels to antigens that do not correlate with clinical protection. During a recent outbreak of pertussis the number of years since the last administration of vaccine correlated with clinical disease and provided evidence for waning immunity. Individuals who received their last immunization within three years of the outbreak experienced a 21 percent attack rate compared to a 95 percent attack rate in those who had an interval greater than 12 years.

The number of individuals susceptible to pertussis is increasing in the United States. The number of young adults without prior immunizations or with diminished post-vaccination immunity is growing. Individuals older than six years of age are not vaccinated routinely because pertussis morbidity in older children is not considered significant. The reported annual incidence of disease increased from 1010 cases in 1976 to 3275 cases in 1985 as this population of young adult post-pertussis vaccine susceptibles grew. A large number of susceptible newborns and infants live in the U.S. and epidemiologic studies repeatedly implicate adults in the transmission of pertussis to infants. However, adults with clinical pertussis usually are not diagnosed.

There also is a change in the pattern of age group susceptibility to pertussis in the U.S. Prior to 1950, pertussis was a disease of infancy or early childhood. In the 1950's, with widespread vaccine use, most young and school-aged children had vaccine-induced immunity and most adults retained disease-induced immunity. These two pertussis-immune populations predominated until the late 1970's and were responsible for the marked decline in the reported annual incidence of disease. Currently, the population of susceptible young adults with waning vaccine-induced immunity is increasing, and the adult population with post-infection immunity is diminishing.

For these reasons the maximum benefit toward control of pertussis using present day vaccines may have been achieved. Unless a better vaccine is developed, an increase in disease incidence can be expected with the growth of the two reservoirs of susceptible individuals (non-immunized and previously vaccinated children with diminishing immunity). The improved vaccine must produce lasting immunity or must be well tolerated to allow booster administration. Although the conventional whole-cell pertussis vaccine is efficacious, a concern remains regarding reactogenicity due to either cell-associated antigens and/or other reactogenic substances with no role in immunity. Local and systemic adverse reactions have reduced the acceptance of whole-cell vaccine for use in infants and children and have stimulated research for safer vaccines. Clearly, the development of a pertussis vaccine that has low reactogenicity and that provides lasting immunity is highly desirable.

Reliable diagnostic methods would benefit studies on the epidemiology of pertussis and would aid research in pathology, immunology, and vaccine development. Unfortunately, current methods of pertussis diagnosis are relatively insensitive or non-specific, costly, and labor intensive. The laboratory diagnosis is complicated by difficulties encountered in demonstrating B. pertussis by culture or serologic techniques. During the initial stages of the infection, symptoms are absent or are not pathognomonic for pertussis. When diagnostic symptoms appear and a clinical suspicion of pertussis exists, B. pertussis cells in nasopharyngeal secretions are decreased in number and hard to demonstrate. Another complicating factor is that adults and infants younger than six months of age often present pertussis atypically, and the whoop that facilitates diagnosis is often lacking. There is a need, therefore, for new diagnostic methods that are rapid, simple, sensitive, and specific. The new methods also should be cost-effective and practical for use in state health departments, clinical laboratories, and developing countries.

The development of new pertussis vaccines will require additional research on mediators of disease and potential immunogens. Although many of the biological activities of B. pertussis have been documented, the responsible moieties require further study. Most of the identified bacterial components are part of the cell envelope. Some of the important molecules include endotoxin, agglutinogens, filamentous hemagglutinin (FHA), pertussis toxin (PT), adenylate cyclase, tracheal cytotoxin, dermonecrotic toxin, and 69kD outer membrane protein (OMP). The biochemical analysis of the antigens,

immunogens, or toxins of the bacterial cell that stimulate protective immunity and the characterization of the immunological responses they elicit are critical areas of investigation.

Many questions remain unanswered about the mechanisms by which the host mounts an effective immune response against pertussis. The levels and types of antibodies that protect against infection or illness must be determined. Immunity may result from localized secretory response to bacterial surface antigens, but little is known about the mechanisms of mucosal immunity in local disease. Although significant pathological changes occur at the localized site of infection, there are few reports on pertussis antibody in nasal secretions. There have been two studies that correlated the presence of secretory antibody with increasing time after onset of symptoms and with decreasing culture positivity. These results support the diagnostic value of secretory antibody. Additional studies on the cellular and humoral immunity of the host in response to colonization by B. pertussis are necessary.

Another issue in pertussis immunology is the concern that transplacental antibody may blunt the immune response to pertussis vaccine administered to children below the age of six months. It has been reported that the concentration of transplacentally transferred pertussis antibodies present in newborns to equal or exceed that in their mothers. However, most four-month-old infants had no measurable antibody to PT or FHA. The infants with high pre-immunization PT antibody titers had significantly lower post-immunization titers after administration of the conventional whole-cell vaccine than did infants given the newer acellular vaccine. It is not known whether this greater response to acellular vaccine is due to greater immunogenicity of PT in the acellular product, the absence of other components of the whole-cell vaccine in the acellular product, or other unidentified factors.

Two additional potentially important areas of vaccine immunization research are linked to studies on passively acquired immunity. One investigation would determine if infants can be protected by boosting the passive humoral immunity acquired from the mother. The other would study if it is beneficial to select the time of the initial dose of the vaccine so that induced immune responses in infants correspond to the disappearance of maternally acquired antibody.

Immunologic research on pertussis also would benefit from the development of animal models to study local/mucosal immunity following disease.

RESEARCH GOALS AND SCOPE

Specific foci for research may include, but are not limited to:

- o The genetic and biochemical character of virulence factors
- o Basic mechanisms of pathogenesis, including the means by which the organism establishes and maintains colonization and maintains its phenotype in the virulent phenotype
- o The role of virulence factors in disease pathogenesis
- o Correlations between pathogenesis and the various clinical manifestations of disease, such as the characteristic cough
- o The role of virulence factors in the induction of antibody formation
- o The role of antibodies in recovery and protection
- o The role of cell-mediated and mucosal immunity
- o The development of an animal model to study disease pathogenesis and immune response
- o The development of rapid diagnostic methods appropriate for diagnosis in the field
- o The development of diagnostic methods appropriate for use in vaccinees, persons taking antibiotics, and infants
- o The feasibility of an aerosolized or oral vaccine directed at the production of mucosal immunity
- o Biological markers pertaining to correlates of immunity

MECHANISM OF SUPPORT

The support mechanism for this research will be the individual research grant (RO1) and the First Independent Research Support and Transition (FIRST) Award (R29). The number of awards to be made is dependent upon receipt of a sufficient number of applications of high scientific merit and upon availability of funds.

SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Section 2, A-D of the Research Plan AND summarized in Section 2, E, Human Subjects. Applicants/offerors are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resource for conducting the proposed research. In such a case, a letter of agreement from either the GCRC program director or Principal Investigator must be included with the application.

APPLICATION PROCEDURE

Applications must be submitted on the grant application form PHS 398 (Rev. 10/88) and will be accepted on any of the three receipt dates for research grant applications, February 1, June 1, and October 1.

Application kits are available at most business and grants/contracts offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, Westwood Building, Room 449, National Institutes of Health, Bethesda, Maryland 20892, telephone (301) 496-7441.

On the first (face) page, item 2, of the application, the word "yes" must be checked and the title and number of the announcement typed in the space

provided: BASIC RESEARCH IN PERTUSSIS, PA-91-84.

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

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

REVIEW PROCEDURES

Applications will receive institute and initial review group (IRG) assignment on the basis of established Public Health Service referral guidelines. Applications will be reviewed for scientific and technical merit by an IRG convened by the Division of Research Grants, NIH. Following IRG review, the applications will receive a second-level review by an appropriate Council/Board. Applications will compete for available funds with all other approved applications assigned to the institute.

REVIEW CRITERIA

The standard review criteria will be used to assess the scientific merit of applications. The IRG will be reviewing the adequacy of protection of human subjects, the humane care of animals, and biosafety conditions. In clinical research studies, reviewers also will be evaluating the adequacy of the inclusion of women and minorities in the study populations.

STAFF CONTACT

Investigators are encouraged to contact:

David L. Klein, Ph.D.
Program Officer, Respiratory Diseases Branch
Division of Microbiology and Infectious Diseases
National Institute of Allergy and Infectious Diseases
Westwood Building, Room 750
Bethesda, MD 20892
Telephone: (301) 496-5305

For fiscal and administrative matters contact:

Kathy Phillips
Grants Management Specialist
Division of Extramural Activities
National Institute of Allergy and Infectious Diseases
Westwood Building, Room 726
Bethesda, MD 20892
Telephone: (301) 496-7075

This program is described in the Catalog of Federal Domestic Assistance No. 93.856, Microbiology and Infectious Disease Research. Grants will be awarded 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 grants policies and Federal Regulations at 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or a Health Systems Agency review.

ROLE OF XENOBIOTIC RECEPTORS IN TOXICOLOGY

PA: PA-91-85

P.T. 34; K.W. 1007009, 0760075, 0760015, 1002008

National Institute of Environmental Health Sciences

Application Receipt Dates: February 1, June 1, October 1

The National Institute of Environmental Health Sciences (NIEHS) invites grant applications through a Program Announcement (PA) for basic studies on the role of xenobiotic receptors in toxicology. This type of solicitation is issued to encourage investigator-initiated research projects in areas of special programmatic interest to the National Institutes of Health (NIH). Applicants funded under the PA are supported through traditional research grants in accordance with Public Health Service (PHS) policies applicable to research grants. It is noted that only research project (R01) and First Independent Research Support and Transition (FIRST) Award (R29) grant applications will be considered in response to this PA.

BACKGROUND

The NIEHS is the principal NIH component for support of basic research on environmental factors that contribute to human health problems and disease. Major emphasis by NIEHS is placed upon research examining those physical and chemical substances to which humans are exposed in their general environment as a result of human activities such as modern technologies and industrial and commercial processes. Of particular inportance to the accomplishment of the mission of the NIEHS is research to define the mechanisms through which environmental agents exert their effects.

One of the classic hypotheses is that environmental chemicals cause diseases such as birth defects and cancer by direct alteration of DNA. This then results in mutations and subsequent abnormalities in gene expression. However, an increasing number of chemicals fail to fit this "genetic" model and, therefore, additional mechanisms to explain the phenomena must exist and remain to be elucidated. Furthermore, many other mechanisms to explain the biological consequences of other toxic chemical exposures are badly needed because direct chemical reactions or toxic antagonisms have not been found.

A recent development within the field of molecular biology/toxicology has given impetus for the development of other theories that may offer alternative explanations of chemical toxicity. Recently, it has been demonstrated that certain foreign chemicals, the peroxisome proliferators, interact with specific types of receptor proteins (Issemann and Green, Nature, Vol. 347: 645-649, 1990). Some receptor proteins, members of the erbA receptor superfamily, function as transcription factors regulating gene expression. Although these receptors were initially identified through the binding of compounds known to be important for cell growth, differentiation, and development (.e.g., steroid hormones, thyroid hormones), it has now been demonstrated that the peroxisome proliferators also bind to receptor proteins in this family and elicit the expression of a number of gene products. Interestingly, an endogenous biological molecule that naturally binds to these receptors has yet to be discovered and the exact biological role of these receptors is not known. Hence these receptors have been referred to as "orphan" receptors.

Another receptor that appears to fit in this category is the Ah receptor that binds halogenated aromatic hydrocarbons such as dioxin. All, or nearly all, of the responses produced by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds are thought to be mediated by the Ah receptor. This receptor is believed to be in the same erbA superfamily and functions as a regulator of gene expression. Furthermore, heat shock protein synthesis and P450 enzyme activation, both important in tissue response to xenobiotic exposure, have been correlated with Ah receptor binding and steroid receptor binding. Therefore, the activation of genes encoding P450, as well as other drug metabolizing enzymes by these effectors, might be an important step upstream in the regulatory process for controlling the steady state levels of the various transcription activating factors in response to toxic insult. This provides evidence that other xenobiotic receptors may exist.

The identification of these receptors could provide a molecular explanation for xenobiotic toxicity and contribute to a better understanding of the mechanisms of toxicity. The NIEHS is interested in stimulating research in this new field of molecular biology and exploring new approaches to the mechanisms of chemical toxicology.

RESEARCH OBJECTIVES AND SCOPE

This announcement is issued to encourage and foster investigator-initiated basic and applied research on the possible roles of xenbiotic receptors in toxicology. Specifically the NIEHS is interested in supporting research to:

- Identify other receptors for the erbA or other gene families that bind xenobiotics. For example, TCDD or peroxisome proliferators binding to a receptor.

- Identify the effects on gene expression such as increased product synthesis or activity. The P450 activity increase resulting from receptor binding by TCDD or peroxisome proliferator chemicals is one of the responses that has been observed. Alternatively, there could be a decrease in endpoint activity directly or through expression of new compounds that have inhibitory effects. Other ramifications may also develop that need to be explained.

- Identify the effects of the gene products within a specific biological system. As an example, P450s synthesizing bio-organic

growth effector molecules as a result of TCDD binding to a receptor.

The overall objective of this PA is to encourage investigator-initiated grant applications in this new and emerging field of molecular toxicology that explore the concept that receptors specific for xenobiotics directly mediate the effect of a class of chemicals. This new approach should provide an alternative to previous concepts regarding the mechanisms of chemical toxicity that are not directly related to genotoxicity. Multi-investigator projects that bring together molecular biologists and toxicologists to address any of the number of toxic expressions that can result from receptor binding are encouraged.

The NIEHS is not interested in supporting research to identify or define the mechanisms of action of the endogenously produced biological molecules that bind to these receptors. These types of applications are more appropriately supported by other Institutes. However, the NIEHS is interested in investigations of how exogenous chemicals react with these receptors and the resulting physiological and biochemical sequelae.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This PA, Role of Xenobiotic Receptors in Toxicology, is related to the priority area of environmental health. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325 (telephone 202-783-3238).

SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDIES.

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group, together with a rationale for its choice. In addition, general and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Section 2, A-D of the Research Plan AND summarized in Section 2, E, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognize that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial /ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks. Hispanics). The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

MECHANISM OF SUPPORT

The mechanism of support for this activity will be the individual research grant - research project grant (R01) or the First Independent Research Support and Transition (FIRST) Award (R29) as applicable.

APPLICATION AND REVIEW PROCEDURES

Applications will be accepted in accordance with the usual receipt dates for new research grant applications: February 1, June 1, and October 1. The earliest possible award dates will be approximately nine months after the respective receipt dates. Applications received too late for one cycle of review will be held until the next receipt date.

Applications will be received by the NIH Division of Research Grants (DRG) and referred to an appropriate study section for scientific and technical merit review. Institute assignment decisions will be based on programmatic considerations as specified in the NIH Referral Guidelines. The review criteria customarily employed by the NIH for research grant applications will prevail. Following the initial scientific review, the applications will be evaluated by the appropriate Institute advisory council.

METHOD OF APPLYING

Applications must be submitted on form PHS 398 (revised 10/88) that is available in the business or contracts offices at most academic and research institutions and from the DRG Westwood Building, Room 240, Bethesda, MD 20892, telephone (301) 496-7441. To identify the application as a response to this announcement, check "yes" in Item 2 on the face page of the application and enter the title "Role of Xenobiotic Receptors in Toxicology, PA-91-85."

The original and six copies of the application must be directed to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

Inquires related to this PA may be directed to:

Dr. Michael J. Galvin
Program Administrator, Scientific Programs Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709
Telephone: (919) 541-7825

Grants management inquiries may be directed to:

David L. Mineo
Chief, Grants Management Branch
Division of Extramural Research and Training
National Institute of Environmental Health Sciences
P. O. Box 12233
Research Triangle Park, NC 27709
Telephone: (919) 541-1373

This program is described in the Catalog of Federal Domestic Assistance Numbers 93.112, Characterization of Environmental Health Hazards, and 93.113, Biological Response to Environmental Health Hazards. Awards are made under the authority of Section 487, Public Health Service Act as amended (42 USC 288) and administered under PHS Grants Policies and Title 42 of the Code of Federal Regulations, Part 66. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.