

NIH GUIDE

for GRANTS and CONTRACTS

U.S. Department of Health and Human Services

Vol. 9, No. 12, October 10, 1980

IN THIS ISSUE:

Request for Research Applications: RFA

NIH-NIEHS-EP-81-1

National Institute of Environmental Health Sciences

Alternative Designs of Standard Cancer Bioassay

Application receipt date--January 5, 1981

Index - NIEHS Page 1

Integration of Autonomic and Somatic Divisions

of the Nervous System, National Institute of

Neurological and Communicative Disorders and Stroke

Index - NINCDS Page 4

Availability of DRR Documents

DRR Program Highlights

Animal Resources Directory

Index - DRR Page 6

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.

ANNOUNCEMENT

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA

NIH-NIEHS-EP-81-1

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

ALTERNATIVE DESIGNS OF STANDARD CANCER BIOASSAY

Application receipt date: January 5, 1981

I. BACKGROUND INFORMATION

In recent years, the number of new agents entering the environment has grown at an unprecedented rate. Concomitant to this growth, there has been an increasing interest in the development of rational procedures for assessing human risks associated with environmental exposures to potentially hazardous agents--procedures that will lead to adequate safeguards of human health. Unfortunately, lack of relevant environmental exposure data for evaluating human health effects has often forced officials charged with regulatory responsibilities to rely on high exposure laboratory animal data in the risk estimation process. In the area of cancer assessment, the main source of such data has been the standard bioassay. In the current format of this bioassay, the two separate dose levels are employed with fifty male and fifty females of two different species of laboratory animals being chronically exposed at each dose level. Concurrent controls are also run, leading to an overall total of six hundred animals. In an effort to maximize the screening sensitivity of the bioassay, the high dose level is often set at the maximum tolerated dose (MTD). Similarly, the lower exposure level is frequently chosen to be half of the MTD.

The original focus of the cancer bioassay was on the detection or assessment of carcinogenic potential. However, these studies are increasingly being used for human risk as well. Typically, animal risk at low doses is extrapolated from the experimental data based on an assumed underlying model, and the corresponding estimated human risk is then calculated. While questions have been raised concerning the

This program is described in the Catalog of Federal Domestic Assistance, Number 13.892, Prediction, Detection and Assessment of Environmentally-caused Diseases and Disorders. 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 52 and 45 CFR, Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency Review.

appropriateness of the current bioassay design for making these estimates of low-dose risk, practical constraints on resources prohibit routine "mega-mouse" experiments involving large numbers of animals at low doses. Thus, there is a need to examine the current bioassay and determine if its design might be altered in a way that would lead to a more meaningful risk assessment without sacrificing its current ability to detect potential carcinogens. In response to this perceived need, the NIEHS is soliciting the submission of research grants to address this issue.

II. GOALS AND SCOPE

The objective of these studies is to stimulate interest in the development of alternative designs of the standard cancer bioassay in order to make the end results more amenable to low-dose extrapolation and risk estimation. In attempting to modify the current bioassay, prospective grant applicants should bear in mind that the overall bioassay is a multi-year, multi-phase process, and that any or all phases of this process are legitimate subjects for investigation in any attempt to modify the bioassay design. However, any proposed alternative design should maintain the cancer screening potential of the current bioassay. Furthermore, grant applicants should probably regard the present overall total of six hundred animals per experiment as an approximate upper bound on experimental size.

III. MECHANISMS OF SUPPORT

Support for this program will be through the National Institutes of Health traditional grant-in-aid following the guidelines established for this type of support mechanism. While it is expected that each successful applicant will plan, direct and carry out the research program, both the programs and any significant modifications must be mutually agreed upon by the participants and the NIEHS.

It is anticipated that a total of \$300,000 will be allocated for this program during the first year; however, award of grants is contingent upon the availability of funds. The project period required to accomplish the aims of the proposal is felt to be two years but meritorious proposals of longer duration will also receive full consideration.

IV. REVIEW PROCEDURE AND CRITERIA

A. Review Procedure

Proposals in response 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 Advisory Environmental Health Sciences Council. Applicants will be informed of the results of the competition as soon as possible after the May 1981 meeting of the Council.

B. Review Criteria

Applications must be responsive to the RFA, and therefore, relevant to the program goals of the sponsoring institute. Those applications considered to be unresponsive to the RFA will be returned to the applicant. Those factors considered to be important for review include: The investigator should be able to demonstrate a knowledge of the various mathematical models/statistical procedures currently employed in low-dose extrapolation, a familiarity with statistical bioassay and experimental design, and some biological background in cancer research. To achieve this background, it may be necessary to adopt a multi-disciplinary research team approach. The application will be judged upon the overall scientific merit, adequacy of the methodology, facilities and resources, commitment of time, and cost effectiveness of the proposal. The sponsoring institution should indicate a commitment of facilities and resources to the program.

V. METHOD OF APPLYING

Applications should be submitted on Form PHS 398, the application form for the traditional research grant. Application kits containing this form and the necessary instructions are available in most institutional business offices or from the Division of Research Grants, NIH. The original and six copies of the application must be received before 5:00 p.m. Eastern time on January 5, 1981. Applications must be sent to:

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

The face page of the application should be labeled "In response to RFA# NIH-NIEHS-EP-81-1". One copy of the application should be sent to:

Dr. Edward Gardner, Jr.
Program Director
Regular Research Programs Section
Scientific Programs Branch
Extramural Program
National Institute of Environmental
Health Sciences
P.O. Box 12233
Research Triangle Park, NC 27709

VI. STAFF CONTACT

Questions relating to this announcement may be directed to: Dr. Edward Gardner, Jr. (address above) or (919) 755-4021.

ANNOUNCEMENT

INTEGRATION OF AUTONOMIC AND SOMATIC DIVISIONS OF THE NERVOUS SYSTEM

NATIONAL INSTITUTE OF NEUROLOGICAL AND COMMUNICATIVE DISORDERS AND STROKE

The Fundamental Neurosciences Program (FNP) of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) encourages the submission of applications for research grants for the investigation of somatic-autonomic mechanisms of neuronal integration. Emphasis is placed on the effects of 1) "visceral afferents" on higher nervous processes and 2) cutaneous stimulation on autonomic activity.

BACKGROUND

The common classification of nerve fibers as visceral or somatic afferent and visceral or somatic efferent, and the separation of the nervous system into somatic and autonomic divisions, have obfuscated their intimate interrelationships in support of tissue function. Somatic activity is almost always accompanied by reactions involving the autonomic nervous system such as vascular adjustments accompanying muscular contraction. The activity of autonomically innervated organs influence diverse central nervous system structures, via visceral afferent pathways.

EXAMPLES

Projects of the following types illustrate this area:

1. Baroreceptor and chemoreceptor ("visceral afferent") influences on cortical activity. Several studies suggest that baroreceptor stimulation is accompanied by changes in cortical activity which may influence non-cardiovascular activities, detectable physiologically and behaviorally.

This program is described in the Catalog of Federal Domestic Assistance, Number 13.854, Fundamental Neurosciences Program. Grants will be awarded under the authority of 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 52 and 45 CFR Part 74. This program is not subject to A-95 Clearinghouse or Health Systems Agency Review.

2. Effects of cutaneous stimulation on autonomic activity (somato-autonomic reflexes). Stimulation of sensory receptors in the skin may be accompanied not only by cardiovascular responses but by changes in the bladder, stomach, or intestines through visceromotor activation.

APPLICATION AND REVIEW PROCEDURES

Applications should be prepared on Form PHS 398 following instructions contained in the application kit. Application kits are available from most institutional business offices or from the Division of Research Grants, NIH. The applications will be judged solely on scientific merit in accord with NIH policy and procedures involving peer review. Initial review will be by the appropriate study section of the Division of Research Grants. Secondary review will be by the National Advisory Neurological and Communicative Disorders and Stroke Council. Applications judged more responsive to program interests of other Institutes will be assigned accordingly.

Deadline dates for the receipt of applications are March 1, July 1, and November 1.

The phrase "**Prepared in response to NINCDS invitation for research grants in autonomic-somatic neurointegration**" should be typed across the top of the first (face) page of the application. The original and six copies of the application should be mailed to the following address:

Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
Bethesda, Maryland 20205

One copy of the application is to be sent to the address below. Also, for further information applicants may contact:

Dr. Herbert C. Lansdell
Fundamental Neurosciences Program
National Institute of Neurological
and Communicative Disorders and Stroke
Federal Building, Room 916
7550 Wisconsin Avenue
Bethesda, Maryland 20205
Telephone: (301) 496-5745

NOTICE

AVAILABILITY OF DRR DOCUMENTS*DRR PROGRAM HIGHLIGHTS*ANIMAL RESOURCES DIRECTORY

A special indepth report highlighting the 1979 research program activities of NIH's Division of Research Resources has been published and is now available. Titled **1979 Program Highlights, Division of Research Resources**, the 32-page report is packaged in a booklet containing 39 photos and charts. The booklet describes each of the Division programs in detail, elucidates the program growth, delineates 1979 results, progress, and achievements, and gives indication of future program directions.

Also available is the second revision of the **Animal Resources Directory**. The new completely revised 56-page publication is designed as a guide for scientists seeking sources of assistance and collaboration involving animals in biomedical research.

The directory identifies animal diagnostic laboratories, animal information projects, animal reference centers, special colony and model study centers, and NIH's major primate research centers currently supported by DRR.

Examples of resources provided by the Animal Resources Program include modern analytical laboratory equipment; surgery, X-ray, and clinical pathology units; improved animal cages and holding facilities; materials and techniques for diagnosis of animal diseases; reference reagents and antisera; animal breeding stations; germfree animals; and selected invertebrate and vertebrate species, including specific genetic strains and models in development.

The directory identifies the resources provided, research emphasis or application, the principal investigator or director, and address and telephone number. A contact person is indicated for each resource.

Included is a geographic index listing the resources by state and within each state. A map shows the locations of the primate research centers and animal diagnostic laboratories throughout the country.

A single free copy of either of these publications may be secured by writing to the Research Resources Information Center, 1776 East Jefferson Street, Rockville, MD 20852 or by request from the Office of Science & Health Reports, Division of Research Resources, National Institutes of Health, Bethesda, MD 20205.