

NIH GUIDE

for GRANTS and CONTRACTS

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Vol. 4, No. 7, August 8, 1975

NEW REVIEW CYCLE FOR GRANT APPLICATIONS

A N N O U N C E M E N T

The review schedule below for competing grant applications in the extramural programs of the National Institutes of Health has been recently adopted and is scheduled to be implemented on January 1, 1976. The new schedule was developed so that review cycles will coincide with the change in the Federal fiscal year on October 1, 1976.

| REVISED REVIEW SCHEDULE - <u>EFFECTIVE JANUARY 1, 1976</u> | | |
|--|---|--|
| Receipt Date | Study Section Meeting | Council Meeting |
| Feb. 1 ^{1/} / Mar. 1 ^{2/} | <u>June</u> | <u>September</u> (3rd and 4th weeks) <u>October</u> (1st and 2nd weeks) |
| June 1 ^{1/} / July 1 ^{2/} | <u>October - November</u> (4th week of October - 1st to 3rd weeks of November) | <u>January</u> (4th week) <u>February</u> (1st week) |
| Oct. 1 ^{1/} / Nov. 1 ^{2/} | <u>February - March</u> (4th week of February - 1st to 3rd weeks of March) | <u>May</u> (3rd and 4th weeks) |

1/ Receipt date for renewals (all competing renewals) and new applications for institutional and individual National Research Service Awards, Research Career Development Awards, program projects and centers.

2/ Receipt dates for new and supplemental research project grant applications.

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

Supplements, printed on yellow paper, are published by the respective awarding units concerning new projects, solicitations of sources, and requests for proposals.

The new review cycle will become effective January 1, 1976, making the first receipt dates for competing applications in 1976 on February 1 and March 1. These applications will be reviewed by initial review groups in June 1976, and by National Advisory Councils in September-October 1976. The review cycles will continue as indicated above.

ESTABLISHMENT OF AN NIH GRANTS
PEER REVIEW STUDY TEAM

A N N O U N C E M E N T

The National Institutes of Health (NIH) has established an internal study team to conduct a detailed and comprehensive study of the procedures generally known as "peer review" and make a report of its findings and recommendations to the Director, NIH. The team will focus on the applicability of the peer review process to the NIH awarding instruments and programs, the attributes and problems of alternative review procedures, and the role and character of peer review in the decision-making process at the NIH. In addition to this broad charge, the study team has been asked specifically to assess the impact on and make recommendations relative to peer review and provisions of the Freedom of Information Act, the Federal Advisory Committee Act, and the Privacy Act.

The 15 members of the study team reflect a broad cross section of the NIH and the National Institute of Mental Health (NIMH). It is under the chairmanship of Dr. Ruth L. Kirschstein, Director, National Institute of General Medical Sciences. The study team at this time would be pleased to receive written comments, views, and information from the scientific community or other interested groups or individuals. These may be addressed to Dr. Mathilde Solowey, Executive Secretary, NIH Grants Peer Review Study Team, Room 4A52, Building 31, National Institutes of Health, Bethesda, Maryland 20014.

CANCER CONTROL PROGRAM

A N N O U N C E M E N T

INTRODUCTION

Under the National Cancer Plan, the Division of Cancer Control and Rehabilitation (DCCR) has the principal Federal responsibility for assuring the rapid and effective application of cancer research findings in the prevention, detection, diagnosis, and treatment of cancer and for the rehabilitation and continuing care of cancer patients. It is the ultimate DCCR goal to reduce the incidence, morbidity, and mortality from cancer through a five-pronged effort:

1. Identification of new methods, knowledge, and techniques that may be applicable to control activities.
2. Field testing of potential control knowledge and techniques in limited community field trials to determine their potential for widespread community usage.
3. Evaluation of potentially useful control knowledge and techniques to determine their effectiveness, practicality, acceptability, impact on the disease, and economic or cost-benefits prior to embarking on costly widescale community demonstration and promoting efforts.
4. Demonstration of effective, practical, control knowledge and techniques.
5. Promotion of demonstrated effective, practical knowledge and techniques to assure their rapid widespread utilization in all areas in the nation.

DCCR is concerned with the entire scope of the cancer problem, from the prevention of the disease to the rehabilitation and continuing care of the cancer patient during and after treatment. Program thrusts, therefore, are in three major intervention areas: (1) Prevention; (2) Detection, Diagnosis, and Pre-treatment Evaluation; and (3) Treatment, Rehabilitation and Continuing Care. DCCR activities are supported by either grants or contracts. The most appropriate support mechanism will be determined on an individual project basis. The following activities relate to grants only.

GRANT ACTIVITIES

The grant-supported portion of this national program encompasses all three intervention areas. It is intended: (1) to allow the initiation of new concepts in a more effective utilization of existing procedures and/or techniques, and (2) to provide information on the refinement of established procedures and/or techniques for a more vigorous prosecution of cancer control. The DCCR is not involved in (1) performing regulatory functions,

or (2) the support of delivery of health care per se. The DCCR does not support the usual laboratory and clinical research to develop new techniques and procedures. Since this grant program is not intended to duplicate the contract programs in the DCCR, applications duplicating current RFP's or existing contract programs will be returned. It is in this context, therefore that grant applications directed to the subject matter indicated above will be received and accepted. Because exceptions may exist, it is advisable to consult with the DCCR staff to determine if a proposed study will fit within the above guidelines.

Grants may be utilized as a mechanism for support in the following areas:

A. Prevention

The prevention activities of DCCR are to be concerned with:

1. The application of identified methods and techniques to inform and stimulate health professionals and the public to fully utilize available cancer prevention services. Such projects are to be oriented toward avoiding the occurrence of the disease through prevention efforts, especially methods and techniques for reducing the exposure to carcinogens, and must include the testing and evaluation of all preventive activities proposed.
2. Programs for the development of cessation strategies involved with cigarette smoking and alcohol consumption.
3. Programs for understanding the determinants of consummatory behavior as they relate to cancer prevention strategy.

B. Detection, Diagnosis, and Pre-treatment Evaluation

The DCCR will support investigator-initiated work in this intervention area relative to:

1. The assessment and evaluation of screening/detection systems with special emphasis on determining the appropriate interval of screening procedures and the cost-effectiveness of various screening-detection systems.
2. Studies designed to develop a better understanding of the factors which motivate and/or inhibit primary health care personnel and the public from dealing more appropriately with early detection, diagnosis, and pre-treatment evaluation.
3. Innovative studies designed to improve the techniques and procedures for effective utilization in appropriate settings of professional assistants in the detection/diagnosis of cancer.

4. Studies to re-evaluate presently accepted or evaluate newer methods for pre-treatment evaluation and to promote the development of criteria and standards for pre-treatment evaluation directed toward defining adequate, acceptable, and structured approaches to pre-treatment evaluation of the patient as required to choose the most appropriate treatment regimen.

C. Rehabilitation/Continuing Care

The DCCR will support:

1. Research on the management of pain in cancer patients.
2. Research studies on the psychological and psychosocial aspects of cancer as it affects the patient, the patient's family and health professionals. This area may include:
 - a. The development of new procedures and techniques for counseling cancer patients, their families, and the health personnel dealing with cancer patients, and
 - b. Studies of attitudes and behavior as they relate to the delivery of rehabilitation and continuing care.
3. Research studies on the dietary and nutritional management of cancer patients (especially those patients undergoing aggressive or palliative therapy) including feeding behavior, their alteration by disease and/or treatment and restoration toward normal feeding.
4. Studies for new approaches to the rehabilitation problems of head and neck cancer patients in relation to cosmesis, speech, and swallowing. These approaches may involve new materials and procedures, as well as new uses of existing approaches and procedures.
5. Studies for the development of new physical techniques/procedures to rehabilitate cancer patients with specific deficits (paraplegia, stoma, etc.) to the extent that these techniques are of primary benefit to cancer patients.
6. Studies for the development of new concepts and procedures for the continuing care of cancer patients with the disease in varying states of control.
7. Studies of social factors in relation to the patterns of rehabilitation and continuing care to include level of care received, impact of care and of alternative approaches for the patient, family, and community, including health professionals.

D. Special Community Resource Development

Under this general area of cancer control, applications are to be concerned with the development of community outreach programs through the National Cancer Institute's designated comprehensive cancer centers and multi-protocol clinical cooperative groups.

APPLICATION REQUIREMENTS

Applications should be submitted on PHS grant application form NIH 398 which should be mailed to:

Division of Research Grants
National Institutes of Health
Bethesda, Maryland 20014

Applicants should type "CANCER CONTROL" in the top margin of the application's face page. A covering letter should also identify the application as a response to the Cancer Control Program. A copy of this letter and any inquiries should be directed to:

Dr. Dorothy R. Brodie
Program Director for Grants
Division of Cancer Control and
Rehabilitation, NCI
Blair Building - Room 628
National Institutes of Health
Bethesda, Maryland 20014

Telephone: (301) 427-7990

An application submitted in response to this announcement and so identified provides assurance only that the application will be considered for assignment to this program area and not a commitment for such assignment. DRG in collaboration with funding unit staffs will make assignments to funding units whose program best fits the substantive contents of the application as presented.

NOTICE OF
AVAILABILITY

NOTICE

"Selected Approaches to Gas Chromatography-Mass Spectrometry in Laboratory Medicine," papers of a one-day conference sponsored by the Automation in the Medical Laboratory Sciences Review Committee of the National Institute of General Medical Sciences, are available. This brochure includes seven talks on the basic technology, applications in the clinical laboratory, the interpretation of data, characteristics of electronic outputs, and a discussion of those advanced techniques of GC-MS likely to be of use in the clinical laboratory.

Copies are available from Dr. Robert S. Melville, Chief, Automated Clinical Laboratory Section, Biomedical Engineering Program, NIGMS-NIH, Westwood Building, Room 954, Bethesda, Maryland 20014.

GRANT APPLICATIONS SOUGHT ON
MECHANISMS OF ACTION OF FLUORIDE
NATIONAL CARIES PROGRAM
NATIONAL INSTITUTE OF DENTAL RESEARCH

A N N O U N C E M E N T

The high incidence of dental caries in children throughout the world is well recognized. Although dental caries seldom endangers life, it may be painful, debilitating, and expensive and may contribute to long-term suboptimal health. Although early treatment of carious lesions is valuable and promotes better health, the ultimate goal of the National Caries Program is preventing the occurrence of caries. If prevention is to be effective, a substantial proportion of the population must be reached at an early age.

The most dramatic success in the reduction of incidence, severity, and rate of progression of caries has been due to water fluoridation and to topical applications of fluoride by various methods. The preventive value of topical fluorides is universally accepted. There appears to be merit in most topical fluoride formulations and techniques of application. However, the mechanisms whereby fluoride reduces the occurrence of dental caries are only partially understood.

Fluoride may exert its effect in one or more of several ways: (1) by making the enamel more resistant to acid demineralization; (2) by inhibiting the microbial enzyme systems which convert sugars into acids in the dental plaque, or by affecting the type of extracellular polysaccharides formed; (3) by affecting the colonization of tooth surfaces by cariogenic organisms; (4) by a direct bactericidal or bacteriostatic effect; and (5) by stimulating the remineralization process at the enamel surface. Recent studies suggest that these mechanisms are not mutually exclusive, and that it is possible, and indeed probable, that fluoride works in several ways simultaneously or in ways that have not been discovered yet. Experimental and clinical evidence indicates that the potential of fluoride therapy to prevent and control dental caries is much greater than results currently attained by the majority of preparations and delivery methods in use.

The National Caries Program is encouraging submission of high quality research grant applications proposing investigations which would provide a better understanding of the various mechanisms by which topically applied fluoride exerts its cariostatic effects.

Specific examples of areas of program interest include the following:

Effect of Fluoride on Tooth Physiology Further studies are required to clarify the decreased response to fluoride with tooth age; whether the maturation process and deposition of organic material on the enamel surface interferes with uptake of fluoride by enamel; the selective effect of fluoride on different tooth surfaces; and the effect of fluoride on tooth morphology.

Effect of Fluoride on Fluorapatite Formation - Stability of Fluoride Products Studies are needed to determine whether there is a correlation between increased fluorapatite formation in enamel and a reduction in the occurrence of caries. It is important to correlate the content, distribution, and depth of fluoride penetration in enamel surfaces with caries incidence. Further studies should attempt to identify the fluoride salts that are formed in the enamel surface as a result of topical fluoride treatments and whether the cariostatic effect of solutions that deliver large amounts of fluoride into the enamel (such as ammonium fluoride) is only temporary due to conversion of more tooth mineral into larger amounts of calcium fluoride. In addition, studies should endeavor to measure the fluoride concentrations at frequent intervals to determine how much and how quickly fluoride is lost from the tooth surface.

Effect of Fluoride in Promoting Enamel Remineralization New research in this area should determine the mechanism whereby fluoride promotes remineralization of enamel; whether certain ions retard the progression of carious lesions by encouraging the dissolved enamel mineral to reprecipitate and by preventing hydrolysis of fluoride from the enamel surface. It would be important to find out if the redeposited mineral is more resistant to acid dissolution than sound enamel, and whether it is advantageous to introduce insoluble, non-mineral materials, such as protein together with fluoride, into an incipient carious lesion.

Effect of Fluoride on Response to Other Trace Elements Definitive studies are required to determine the role and mode of action of trace elements such as boron, strontium, molybdenum, vanadium, and others in enhancing or diminishing the cariostatic effect of fluoride in humans.

Effect of Fluoride on Saliva Composition Investigations in this area should clarify whether saliva and plaque fluid contain substances which inhibit or enhance fluorapatite formation in enamel after the teeth receive topical fluoride applications.

Effect of Fluoride on Metal Ion Complexes Additional in vitro and in vivo studies are required to determine the influence of metal ions on the surface properties of hydroxyapatite or tooth materials and their ability to bind topically applied fluoride.

Electrochemical Effects of Fluoride Desorption of pellicle protein and bacteria may be one of the several mechanisms by which fluoride exerts its cariostatic effect in vivo. Fluoride, in low concentrations, appears to desorb albumin and salivary glycoprotein adsorbed to hydroxyapatite in vitro.

The fluoride ions, competing for cationic sites replace acidic protein groups adsorbed to cationic sites on the mineral surfaces. Microorganisms adsorbed to hydroxyapatite may be desorbed in the same way by a similar mechanism. Further studies are required to confirm this hypothesis.

Effect of Ambient Fluoride Further studies are required to elucidate the mechanism of action of ambient fluoride at low concentrations: bacteriostatic, favoring enamel remineralization, neutralizing acids produced by plaque microorganisms or other mechanism or combination of mechanisms. New studies should also determine the optimal concentration of fluoride, frequency of application, and optimum vehicle for allowing fluoride to be present constantly in the oral environment.

Effect on Oral Microorganisms Some studies have demonstrated that fluoride inhibits acid production by oral microorganisms. This effect of fluoride has been interpreted by some as interfering with the transport of glucose into the cells or as altering the composition of the extracellular polysaccharides produced by different strains of Strep. mutans by interfering with the synthesis or release of the glycosyltransferases. There is preliminary information indicating that different oral streptococci have different sensitivities to the same concentration of fluoride. Additional studies should explore: the effect of fluoride concentration on selecting the microbial composition of plaque and on the extent of plaque accumulation, the forms of fluoride in plaque, direct bactericidal/bacteriostatic effect versus metabolic inhibitor effect of fluoride, factors that control the uptake of fluoride by plaque microorganisms, the extent and sites of fluoride accumulations by bacterial cells, and the effect of fluoride on intermediary metabolism.

APPLICATION - REVIEW

Use standard research grant application form NIH 398 and instructions therein. Applicants should indicate in a covering letter that the application is in response to the announcement on "Mechanisms of Action of Fluoride". Mail the application and the letter to the Division of Research Grants, National Institutes of Health, Bethesda, Maryland 20014.

| | |
|-----------------------------|---------------------------------------|
| Applications received by | Results announced by the following |
| October 1 | April |
| March 1 | November |
| July 1 | February |

Applications will be reviewed initially for scientific merit by the DRG study sections and secondly by the National Advisory Dental Research Council.

If additional information is needed prior to submission of a grant application, applicants are invited to contact either Dr. Thomas C. O'Brien or Dr. Raquel Halegua:

Caries Grant Programs Branch
National Caries Program
National Institute of Dental Research
National Institutes of Health
5333 Westbard Avenue, Room 522
Bethesda, Maryland 20014

Telephone: (301) 496-7884

SELECTED BIBLIOGRAPHY

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NIH Guide for Grants and Contracts, Cumulative Contents (continued)

Volume No. 4

Guide No. 1, February 10, 1975

Transportation of Hazardous Materials 1

Guide No. 2, March 14, 1975

Research Career Development Program, Animal Resources Branch, DRR 1

Occupational Health Research Related to Energy Production
and Development 3

Research Grant Support in the Areas of Profound Hearing
Impairment and Auditory Prosthesis 5

National Research Service Awards for Individual
Postdoctoral Fellows 7

Cancer Research Emphasis Grants 8

Guide No. 3, April 25, 1975

Minority Access to Research Careers (MARC Program) 1

Guide No. 4, June 1, 1975

Cancer Research Emphasis Grants (CREG) 1

Guide No. 5, June 9, 1975

Predocctoral and Postdoctoral Trainee and Fellowship Support 1

Release of Information by NIH of Research and
Research Training Grant Records 6

Copyright 8

Citation and Acknowledgment of NIH Grant Support 8

Report of Awards of Contracts 9

NIH Research Career Development Award Program 9

NIH Special Research Career Programs 10

Guide No. 6, July 3, 1975

Health Communications by Satellite 1

Medical Library Resource Project Grants 2

Guide No. 7, August 8, 1975

New Review Cycle for Grant Applications 1

Establishment of An NIH Grants Peer Review Study Team 2

Cancer Control Program 3

Notice of Availability 6

Grant Applications Sought on Mechanisms of Action of Fluoride,
National Caries Program, National Institute of Dental Research 7

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National Caries Program
National Institute of Dental Research
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