

MECHANISMS OF SUPPORT

Medical research activities at NIH are funded through a variety of mechanisms of support including grants, cooperative agreements, and contracts. Research is either intramural or extramural. Intramural research is defined as research conducted within NIH facilities by NIH scientists. Extramural research is defined as research performed at institutions outside of NIH, including academic institutions, medical colleges, state and local governments, independent research organizations, and private industry.

The major funding instruments used by NIH to fund extramural research are financial assistance award grants, cooperative agreement grants, and acquisition awards or contracts. Grants are the most common funding mechanism. These are generally initiated by the investigator. They are used to support scientific research or training. NIH also supports cooperative agreements. These are assistance awards which involve a substantial programmatic NIH role in the project. Research and development contracts are awarded for specific scientific inquiry directed toward particular areas of research needed by NIH. There is significant NIH staff involvement with these contracts.

Within each of the mechanisms of support, NIH strives to manage its public funds prudently. The NIH requires that appropriate steps be taken to ensure high quality results, to establish safeguards to prevent conflicts of interest, to ensure the integrity of the scientific research community and the integrity of research results, and to require that minorities, women, and children be included in study populations, as appropriate.

All grants are identified as either competing (for NIH support) or non- competing continuations (receiving support previously committed). A competing application may be new (Type 1), a competing continuation or renewal (Type 2) or a competing supplement (Type 3).

A new application is the original application requesting NIH support for a specific project. If the application competes successfully, a Type 1 award for a specific amount will generally be made for 12 months. A research grant provides a commitment of support for an average of four years of funding. Thus, after the competing year, the grantee receives noncompeting continuations each year for the specified length of the grant. Nearly three-quarters of funding allocated to RPGs supports noncompeting (Type 5) continuations. Administrative supplements (Type 3), which account for a small proportion of RPG support, provide additional funds to ongoing grants, for administrative adjustments, or to provide a few months of orderly phase-out for large RPGs.

Near the end of committed support, an investigator may submit a competing continuation application (Type 2) requesting up to five additional years of funding. The average cost per year of the renewed grant is likely to increase over the previous grant due to several factors: expansion may occur after preliminary investigations have led to promising

results and well-established conclusions; and, once the direction of the research is clear and justifiable, the research investment is often expanded to explore specific areas of research including the exploration of new variables.

The majority of applications for grant support originate with individual investigators who develop proposals for research or research training within an area of interest to NIH. Principal investigators of research project grants are generally Ph.D.s or M.D.s with an outstanding background in biomedical research at a university, medical school, not-for-profit research institution or for-profit biomedical research organization. In addition, NIH publicizes two types of announcements to stimulate submissions in areas of high priority or special concern:

- ***Program Announcements (PAs)***, describe new, continuing or expanded program interests of an Institute or Center (IC), or announce the availability of a new mechanism of support and an approximate level of support; and,
- ***Requests for Applications (RFAs)***, are solicitations that invite grant applications in a defined scientific area to accomplish a scientific program purpose for the IC at a specified funding level.

Peer Review of Research Grant Applications

When an investigator in the extramural scientific community seeks grant funds for support of a specific research project, a detailed application must be prepared that will be subject to peer review. Most grant applications submitted to the NIH are reviewed through a two-tier system.

The first level of review is performed by a scientific review group (SRG), often called a study section or review committee. These groups are composed of primarily non-government scientists expert in the subject areas of the applications under review. The main purpose of this initial review is to evaluate the scientific and technical merit of applications. Initial review at the NIH is performed either by the Center for Scientific Review (CSR) or by Institutes' or Centers' study sections. Most investigator-initiated applications are reviewed by CSR.

Referral staff review the contents of tens of thousands of applications each grant cycle and, using written guidelines, assign applications to appropriate review groups and Institutes or Centers. Applications received in response to special announcements or to meet specific program needs are likely to be peer reviewed by the Institutes or Centers.

A CSR study section is composed generally of 18 to 20 individuals from among the active and productive researchers in the biomedical community, to serve for multi-year terms. The goal is to have the group's combined knowledge span the diversity of the subject matter assigned to the study section for review, and to have gender, minority and geographic diversity. To ensure this expertise, the study section's membership is frequently supplemented by temporary members and written outside opinions and in some instances, Special Emphasis Panels (SEPs) are formed on an ad-hoc basis to review applications requiring special expertise, or due to special circumstances. In addition to assessing scientific and technical merit, initial reviewers assign numerical scores that reflect these assessments for those applications recommended for consideration for funding. They also review, and when necessary comment on, the appropriateness of proposed procedures for the protection of human subjects, the treatment of animals, and protection of the environment.

To be considered for funding, a grant application must be favorably recommended in initial review and must also pass the second level of review, the concurrence of the National Advisory Council of the Institute or Center to which it has been assigned. In some cases Council review is not required when the amount of funds requested does not exceed \$50,000 in direct costs per year. Councils and Boards review the recommendations from the Scientific Review Group and associated matters and may make recommendations about funding priorities. Councils have major roles in providing advice and guidance on the research and programmatic activities of the Institute or Center.

Council or Board recommendations are based not only on considerations of scientific and technical merit, as judged in the initial review, but also on the relevance of the proposed study to an Institute's programs and priorities. Councils include senior scientists with broad experience, as well as public members with general knowledge of and interest in the mission of the Institute or Center. Actual funding decisions are made by the Institute or Center.

The following are the major mechanisms of support for medical research:

Research Project Grants (RPGs)

Funding investigator-initiated grants continues to be a high priority. The use of research project grants (RPGs) as a mechanism of support covers the entire medical research continuum, from basic scientific research at the molecular and cellular levels to studies of human beings in both healthy and diseased states. Most grant applications originate with

individual investigators who develop proposals for research in their area of interest. Research project grants are awarded to institutions on behalf of a principal investigator to support medical research activities in the areas that represent both the specific interests and competence of the principal investigators and also the NIH Institutes' identified program needs.

The NIH uses several RPG activities to support the best research applications from the most talented researchers. The most common, the traditional R01, accounts for the majority of both total and competing RPGs awarded. The R01 supports a single project with a principal investigator. Another frequently used award is the program project (P01), a multiproject grant, which supports a variety of broad-based multi-disciplinary projects conducted by numerous investigators working on various aspects of a specific major research objective or theme. Along with the R01 and P01 grants, there are other RPG awards used for specific circumstances. Some of these are:

- ***Method to Extend Research in Time (MERIT) Awards (R37)*** - Grants awarded to long-term researchers of superior competence and productivity.
- ***Academic Research Enhancement Award (AREA) (R15)*** - To support small scale research at primarily baccalaureate degree granting institutions.
- ***Small Grants (R03)*** - To provide research support specifically limited in time and amount for initiating studies that are generally for short-term or pilot projects.
- ***Research Project Cooperative Agreements (U01)*** - To support projects with a senior principal investigator in an area representing their specific interests and competencies. There is substantial NIH staff involvement in the project.
- ***Small Business Innovative Research (SBIR) (R43, R44) and Small Business Technology Transfer (STTR) (R41, R42) Awards*** - To support small businesses conducting research and development projects that may lead to commercial products or services. A setaside of 2.65% for SBIRs and 0.15% for STTRs determines the minimum funding level. NIH also supports SBIR and STTR contracts.
- ***Exploratory/Developmental Grants (R21)*** - To support and encourage development of new research activities in categorical program areas.

Research Centers

Research Center grants are awarded to extramural research institutions to provide support for long-term, multi-disciplinary programs of medical research. They also support the development of research resources, aimed to integrate basic research with applied research and transfer activities, and promote research in the areas of clinical applications with an emphasis on intervention including prototype development and refinement of products, techniques, processes, methods, and practices. A description of centers follows:

- ***Specialized/Comprehensive Centers*** - Supports a full range of research and development from very basic to clinical. The spectrum of activities comprises a multidisciplinary attack on a specific disease entity or medical problem area.
- ***Clinical Research Centers*** - Supports clinical research in a specialized environment where each center is a discrete unit of research beds separated from the general care ward with specialized equipment and expert personnel necessary to provide a controlled environment and assist in the rapid transfer of basic research results to patient care.
- ***Biotechnology Research Centers*** - Supports regional and national access to the sophisticated research instrumentation and technology needed to solve medical and clinical research problems that are beyond the purview of conventional means. These expensive resources are shared by investigators on NIH grants, which results in considerable savings to the government.
- ***Comparative Medicine*** - Supports the development of mammalian and nonmammalian models for research, or to make animal or biological materials resources available to all qualified investigators.
- ***Research Centers in Minority Institutions (RCMI)*** - Supports the development and enhancement of the research infrastructure of predominantly minority institutions that grant doctoral degrees in the health professions or in a health-related science, to enable them to become more competitive in seeking NIH and PHS research project grant support.

Other Research

Other Research comprises a number of activities, including:

- ***Research Career Programs (K awards)*** - Designed to provide increased career opportunities in medical research to scientists of superior potential. The program provides support for young investigators who desire advanced development and scientists who need experience to qualify for senior positions. Included within this category are the following awards: Research Career Development Awards, Clinical Investigator Awards, including the K23, K24 and K30 awards for clinical researchers, Academic Investigator Awards, Career Transition Awards, Special Emphasis Research Career Awards, and Physician/Scientist Development Awards.
- ***Education Programs (R25)*** - Grants awarded to schools of medicine, dentistry, public health, and nursing (with Ph.D. programs) and to teaching hospitals affiliated with medical schools. The grantee institutions develop and adopt curricula in the area of education, information, training, technical assistance, coordination, or evaluation.
- ***Cooperative Clinical Research*** - Grants awarded to multiple institutions where investigators are asked to follow common research protocols, because there are insufficient numbers of subjects available at a single institution to conduct a major clinical trial. NIH staff is substantially involved in the management of these awards.
- ***Biomedical Research Support (Shared) (S10)*** - Grants awarded to NIH-supported institutions to fund instrumentation needs, to support pilot studies, and to improve research resources.
- ***Minority Biomedical Research Support (MBRS)*** - Designed to increase the number and quality of ethnic minority biomedical research scientists by strengthening the capability of eligible institutions to conduct quality research in the health sciences and to support undergraduate students in biomedical research at minority institutions.
- ***Other Research Related Grants*** - Various small grants, including scientific review and evaluation, small instrumentation and conference grants.

Research Training

The Ruth L. Kirschstein National Research Service Awards (NRSA) program serves to replenish the Nation's corps of biomedical and behavioral research investigators. Through institutional awards and individual fellowships, NIH supports both basic and applied research training in the biomedical and behavioral sciences. Institutional awards provide the foundation for the manpower development effort by supporting the national capacity for excellent, up-to-date training in a variety of institutional settings. They enable NIH to aid institutions in maintaining vigorous and effective research training programs and, in particular, to support research training programs in areas of national need. Decisions on the number of research trainees to be supported by NIH are based upon assessment of program needs and opportunities by the NIH Institutes, and the NIH Director, recommendations of the National Academy of Sciences (NAS) and other groups, and the availability of funds.

- Ruth L. Kirschstein National Research Service Awards (NRSAs) support trainees and fellows at a predoctoral and postdoctoral level through grants to individuals and institutions such as medical schools and universities.
- A trainee or fellow receives a stipend for full-time concentrated study and may elect, under supervision, an individual research focus.
- Funds are awarded for predoctoral and postdoctoral stipends and for tuition where warranted, with a modest allocation to the institution to defray training-related expenses not covered by tuition.
- NRSAs also include funds for travel, fees, indirect costs, and other expenses.
- Stipend levels constitute the largest dollar portion of NRSAs.

Research and Development Contracts

The NIH awards research and development (R&D) contracts to non-profit and commercial organizations for scientific inquiry directed towards particular areas of research and development. Their purpose is to utilize advances in knowledge and technology to search for solutions to specific questions. Contract performance is closely monitored by NIH to help ensure accomplishment of project goals for the benefit of or use by the awarding Institute or Center.

There are fundamental distinctions between acquisition and assistance arrangements. A contract is a legal instrument that is used to reflect a relationship between the Federal Government and the recipient whenever the principal purpose of the transaction is to acquire goods or services for the direct benefit or use of the Government. In competitive situations, the Government states the work to be undertaken or the problem to be solved in Request for Proposals (RFPs), or a sealed bid Invitation For Bids (IFBs). Respondents compete for a common requirement open to all offerors/bidders. Proposals are evaluated using technical and business evaluation criteria and generally involve negotiations. Bids are awarded to the bidder who is responsible and offers the lowest overall price.

Intramural Research

Through the intramural research program, the NIH conducts basic and clinical research at its on-campus research facilities in Bethesda, Maryland, and at off-campus locations such as the Gerontology Research Center in Baltimore, Maryland; Research Triangle Park, North Carolina; the Rocky Mountain laboratories in Hamilton, Montana; and Phoenix, Arizona. The fundamental research performed by intramural scientists provides the basis upon which advances in medical and dental care are built. An important byproduct of research productivity is the cadre of young physicians and basic scientists who are trained in the techniques and approaches of the intramural scientists. One of the unique features of the NIH intramural research program is the close proximity of many of its research laboratories to the Clinical Center, a 240-bed research hospital on the NIH campus. This provides an opportunity for bridging the gap between basic and clinical science by carrying basic laboratory research to the bedside. NIH intramural scientists serve as a resource to academia and industry, providing expertise, materials and collaborative opportunities.

Cooperative Research and Development Agreements (CRADAs)

Public-private research collaboration has been a critical component of NIH intramural research efforts. Cooperative Research and Development Agreements (CRADAs), created in the 1986 Federal Technology Transfer Act, enhanced and facilitated this collaboration by providing a forum through which NIH scientists and commercial firms could expedite the transfer of expertise and technology from NIH laboratories to encourage the development of improved health care products, processes, and services. A CRADA is an agreement between one or more NIH laboratories and one or more non-federal parties under which the NIH laboratories provide personnel, services, facilities, equipment, or other resources with or without reimbursement (but not funds to non-federal parties) and the non-federal parties provide funds, personnel, services, facilities, equipment, or other resources toward the conduct of specified research or development efforts which are consistent with the missions of the laboratory. CRADAs confer intellectual property rights on NIH inventions. Ultimately, the non-federal partner is responsible for commercialization of the new product, process or service.

CRADAs have been proven to be a cost-effective way for companies to leverage their own research and development efforts. In turn, the stewardship of public funds for support of medical research is maintained and national economic and social interests are strengthened.

Research Management and Support (RMS)

The Research Management and Support (RMS) activity provides support for leadership, program guidance, planning and evaluation for the overall management of NIH programs. Major categories of support include:

- Program support for salaries and expenses for Institute or Center Directors, their administrative staffs (financial management, personnel management, etc.), and scientific program managers. In addition to administering, managing, and reviewing research grants, research training, and research and development contract portfolios, staff is responsible for developing research initiatives in areas of scientific promise. These areas have great potential for the development of disease intervention and health promotion strategies.
- The RMS supports Department of Health and Human Services activities such as

Program Evaluation, the Program Support Center and special projects. These costs are shared by all Public Health Service agencies.

- Other costs provide support for a number of non-administrative programs that supplement and are integral to both the intramural and extramural research studies supported by NIH. Examples follow: public health education, information dissemination activities, epidemiological studies, international collaborative efforts, and science education activities.

Cancer Prevention and Control

Under the Cancer Prevention and Control Program, the National Cancer Institute (NCI) conducts basic and applied research through both the intramural and extramural mechanisms of support. The major focus of the program is the development of strategies to effectively translate knowledge gained from prevention and control research into health promotion and disease prevention activities to reduce the incidence of mortality and morbidity from cancer. The program concentrates on intervention research to validate preventive regimens related to diet, chemoprevention, smoking cessation and prevention, as well as interventions to improve public health and to provide knowledge about cancer and the means to control this disease.

Extramural Construction

The extramural construction mechanism includes funds appropriated for the extramural research facility construction needs of institutions that conduct NIH-funded research through awarding of grants and/or contracts.

In the 1993 NIH Revitalization Act, a shift from designated to general construction authority was mandated to the Director, NIH. Previously, the Director, NIH, acting through the National Center for Research Resources (NCRR), had designated authority for the construction of AIDS facilities. These limitations were removed in the 1993 authorizing legislation when the NIH Director's authority was expanded to include the construction of extramural biomedical and behavioral research facilities across a wide spectrum of research programs.

National Library of Medicine

The National Library of Medicine (NLM), the world's largest library of the health sciences, collects, organizes, disseminates, and preserves biomedical literature in all forms, regardless of country of origin, language, or historical period. NLM's goal is to provide effective biomedical information service to all health professionals as they strive to improve public health. The Library's collection is widely available: it may be consulted at the NLM facility on the NIH campus in Bethesda, Maryland; items may be requested on interlibrary loan; and the extensive NLM bibliographic databases may be searched via the World Wide Web by health professionals and others around the world. NLM's largest database, MEDLINE, contains millions of references and abstracts to medical journal articles. Researchers and the public search MEDLINE hundreds of millions of times each year.

The NLM is mandated to conduct research into biomedical communications (the Lister Hill National Center for Biomedical Communications) and molecular biology (the National Center for Biotechnology Information); to award grants in support of health science libraries and medical informatics research and training; and to create specialized information service in such areas as health services research, environmental health, AIDS, hazardous substances, and toxicology.

Office of the Director

The mission of the Office of the Director (OD) is to provide leadership, focus and direction to the NIH research community. The OD is responsible for the development and management of intramural and extramural research and research training policy, the review of program quality and effectiveness, and the administration of centralized support activities essential to the operation of NIH. Major objectives of the Office are displayed below:

- Direct the development and management of extramural research and training programs;
- Implement and coordinate intramural research policy and programs, develop and coordinate intramural training and recruitment, and provide overall direction to the intramural research program;
- Administer Loan Repayment and Scholarship programs;

- Plan, coordinate, and evaluate the NIH intramural and extramural AIDS research effort;
- Serve as the centralized locus for various AIDS-related policy and operating functions, and represent the Director, NIH, on AIDS-related matters.

The OD also encourages and fosters NIH research and research training efforts in the prevention and treatment of disease through the establishment of program coordination offices that complement and supplement research directions and areas of emphasis conducted within the NIH Institutes and Centers (ICs). While the OD provides the overall direction, coordination and oversight of these programs, the ICs manage the actual research operations. Brief descriptions of these program coordination offices follow:

- The Office of Research on Women's Health (ORWH) serves as the focal point for women's health research at NIH. ORWH establishes NIH goals and policies for research related to women's health, and assures that research conducted and supported by NIH appropriately addresses women's health issues. ORWH also encourages and develops programs and opportunities to encourage women in the pursuit of biomedical research careers.
- The Office of Behavioral and Social Sciences Research (OBSSR) furthers the mission of NIH by emphasizing the role that behavioral and social factors and their interaction with biomedical variables play in health. The three main goals of the Office are to enhance behavioral and social sciences research and training; integrate a biobehavioral perspective across NIH; and improve communication among health scientists and with the public.
- The Office of Dietary Supplements (ODS) responsibilities include: evaluating the role of dietary supplements in the prevention of disease; evaluating the role of dietary supplements in physical and mental health; improving scientific methodology as related to the study of dietary supplements; and informing and educating scientists, health care providers, and the public about the benefits and risks of dietary supplements.
- The Office of Rare Diseases (ORD) supports activities that stimulate and coordinate research on rare diseases and conditions which each affect fewer than 200,000 persons in the United States. ORD works to improve the understanding of the approximately 6,000 conditions that are considered "rare", including providing information on ongoing research to patients and their families, patient support groups, physicians, researchers, and the general public.

- The Office of Science Education (OSE), coordinates science education activities at the NIH and develops and disseminates model science education programs that support understanding of basic scientific concepts, health information, and medical research findings, to promote scientific literacy in the U.S. OSE develops and coordinates innovative, high quality science education programs that bring cutting-edge science and the latest medical research findings to K-16 classrooms throughout the U.S. and the general public.

Buildings and Facilities (B&F)

The NIH Buildings and Facilities program is responsible for the design, construction, improvement, and major repair of clinical and laboratory buildings and supporting facilities essential to the conduct of the mission of the NIH. The B&F appropriation supports two major needs of the NIH biomedical research endeavor: the design and construction of new facilities for NIH research programs; and the continuing repair and improvement of existing facilities.