
Original Article

NIH assistance for new therapeutic development: NIH-RAID Pilot Program

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ABSTRACT The National Institutes of Health (NIH) wishes to alert the biotech/medical research community to an opportunity to obtain assistance in the development of new therapeutic agents. The NIH Roadmap has established a pilot programme, the NIH-Rapid Access to Interventional Development (RAID) Pilot, to make available, on a competitive basis, critical resources needed for the development of new small-molecule or natural product-derived therapeutic agents. This programme, part of the Translational Research component of Reengineering the Clinical Research Enterprise, uses resources of NCI's Developmental Therapeutics Program. Services provided depend upon the project and strength of the preliminary data. Services potentially available include bulk supply, GMP manufacturing, formulation, assay development suitable for pharmacokinetic testing, and animal toxicology. Assistance can also be provided in the regulatory process. Currently, animal efficacy studies and synthesis of recombinant proteins, monoclonal antibodies, or reagents for gene therapy are not supported. The NIH-RAID Pilot will, however, consider requests for services to support later-stage preclinical development of monoclonal antibodies, recombinant proteins, and gene therapy agents. Additionally, the NIH-RAID Pilot will now consider requests for the manufacture of small-molecule or natural product material for any clinical study. Proposals must originate from academic or non-profit investigators, but collaboration with industry partners is encouraged.

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BRIDGING THE 'VALLEY OF DEATH'

The National Institutes of Health (NIH) traditionally has supported the most

meritorious basic research into the causes and processes of disease, frequently identifying promising avenues of therapy development. Typically, however, it can be difficult for investigators to obtain funding from pharmaceutical companies and venture capitalists, as these sources have become more averse to taking a chance on raw technology and are more interested in drugs that have demonstrated at least some promise in a small clinical trial. This has left more promising ideas unable to pass through what some experts have called the 'valley of death' between basic discovery and commercial development. The NIH has recognised this gap in the process of drug development, and has expanded significantly its support of translational research.

The NIH Roadmap for Medical Research,¹ launched in 2004, is a series of initiatives designed to address fundamental knowledge gaps, develop transformative tools and technologies, and/or foster innovative approaches to complex problems. Funded through the NIH Common Fund, these programmes cut across the missions of individual NIH Institutes and Centers (ICs) and are intended to accelerate the translation of research to improvements in public health. They synergise the work of many NIHICs, and collectively represent a unique effort that no single or group of institutes and centres or other entity can do, but are the responsibility of the NIH as a whole. The Office of Portfolio Analysis and Strategic Initiatives, in collaboration with all NIH ICs, oversees programmes funded by the Common Fund. Additional information about the NIH Roadmap and Common Fund can be found at <http://nihroadmap.nih.gov>.

Among the Roadmap initiatives is the NIH-Rapid Access to Interventional Development (RAID) Pilot Program,² which is designed to complement public-private partnerships in pursuing high-risk ideas or therapies for uncommon disorders that frequently do not attract private sector investment. Where private sector capacity is

limited or not available, public resources can bridge the gap between discovery and clinical testing so that more efficient translation of promising discoveries may take place. To help address this need, the NIH established a pilot programme to make available, at no charge, certain critical resources needed for the development of new therapeutic agents. The NIH-RAID Pilot Program reduces some of the common barriers between laboratory discoveries and clinical trials for new therapies. Projects in both the early and late stages of pre-clinical development are suitable for NIH-RAID applications. The NIH-RAID Pilot will accept requests through 2011. It is important to note that the programme can consider significantly higher numbers of proposal than have been received so far.

NIH-RAID PILOT PROGRAM SERVICES

The main tasks that are supported by the NIH-RAID Pilot are as follows:

- Synthesis of small molecules in bulk
- Synthesis of oligonucleotides
- Chemical synthesis of peptides
- Scale-up production
- Development of analytical methods
- Isolation and purification of naturally occurring substances
- Pharmacokinetic/ADME studies including bioanalytical method development
- Development of suitable formulations
- Manufacture of drug supplies
- Range-finding initial toxicology
- IND-directed toxicology
- Product development planning and advice in IND preparation
- Later-stage preclinical development of monoclonal antibodies, recombinant proteins, and gene therapy agents.

The tasks necessary will vary from project to project. In some cases the NIH-RAID Pilot will support only one or two key steps for early-stage preclinical development; in other cases it may be possible to provide assistance

with most of the development tasks needed to file an IND.

In addition to the services described above, a compelling need exists for research involving biologics: complex, large molecules that are often created by recombinant DNA technology. The research and development costs associated with biologics are high because biologics are structurally complex and difficult to manufacture. The NIH-RAID Pilot recently announced the acceptance of requests for services to support later-stage preclinical development of monoclonal antibodies, recombinant proteins, and gene therapy agents.³ Although the programme is currently not able to offer support for preparation of monoclonal antibodies and recombinant proteins, proposals are accepted for the manufacture of non-GMP viral and non-viral gene vectors as well as GMP-grade adeno-associated virus and lentivirus vectors.⁴ As this work is usually very expensive and project-specific, applicants requesting the manufacture of gene vectors are strongly encouraged to contact the NIH-RAID Pilot Program Office before submitting an application. Potential applicants may also be advised to discuss such projects with programme staff of institutes with missions related to the proposed project.

The output of NIH-RAID Pilot activities, both products and information, will be made fully available to the originating investigator for support of additional studies or of an IND application and performance of clinical trials. Data and product will be transferred to the applicant under the terms of an NIH-RAID Pilot Material Transfer Agreement. For those projects approved for production of a clinical batch, the final vialled drug product will be delivered in a single shipment. The NIH-RAID Pilot cannot distribute drug product in multiple shipments or on a per patient basis.

In vitro or animal efficacy information is a key to formulating a proposal. For the most part, efficacy investigation is not within the scope of the NIH-RAID Pilot Program, and

other sources of funding should be sought by the investigator. Requests for test compound supply for efficacy investigation, however, may be considered on a case-by-case basis. In addition, the NIH-RAID Pilot Program is not intended to support human subject research, aside from provision of clinical lot production of test compounds.

NIH-RAID PILOT PROGRAM ELIGIBILITY

The NIH-RAID Pilot Program services are available at no cost to academic and not-for-profit investigators, but these investigators are free to collaborate with corporate partners. It is expected that each application will have a project leader with an academic appointment in an institution with an NIH-assured Institutional Review Board or involve formal collaborations with a staff member of such an institution. Ideas arising solely from a corporate source without academic collaborators are not eligible at present, and proposals from for-profit organisations will not be accepted. Nevertheless, it is recognised that partnerships with for-profit entities are critical in the development process, and products may be licensed to for-profit partners and still be eligible for the NIH-RAID Pilot. Project leaders are also free to negotiate with companies for additional licensing opportunities while the NIH-RAID Pilot projects are under way. For awarded projects, representatives of the for-profit partner may attend meetings with the Developmental Therapeutics Program staff, but the primary point of communication will be the project leader. The NIH is considering new mechanisms of direct support of drug development efforts within the small business community, but no decision has been made public at this time. Any announcement to this effect would be published in the NIH Guide to Grants and Contracts.⁵

NIH-RAID is open to both domestic and non-US applicants, provided the applicant meets all the other eligibility criteria.

APPLICATION AND REVIEW

The NIH-RAID Pilot is not a grant programme. Successful projects will gain access to the government's contract resources, as well as the assistance of the NIH in establishing and implementing a product development plan. Funds to support individual projects will come both from Roadmap funds and from individual institutes, with institutes assuming the bulk of support in the specific disease areas germane to their mission. This co-sponsorship is critical because of the resource and expertise needs and because the NIH-RAID Pilot cannot support the full developmental pipeline; an institute partnership may therefore be important for subsequent translational efforts.

To obtain access to NIH-RAID Pilot resources, applications must be submitted electronically through Grants.gov.⁶ Applications are screened to determine whether the resources requested are appropriate for this programme. Applications are then reviewed for scientific merit by a review group assembled by the NIH Center for Scientific Research. The results of that evaluation along with supplemental information from the lead investigator will guide final institute and Roadmap resource allocation. Three application receipt dates are announced each year, generally January, May, and September.

INTELLECTUAL PROPERTY RIGHTS

It is expected that originating parties will have acquired or be in the process of acquiring intellectual property protection before involvement of the NIH-RAID Pilot. All intellectual property relevant to the project needs to be fully described in the application.

Most NIH-RAID Pilot tasks will be accomplished by the use of contracts in the Developmental Therapeutics Program of the

NCI.⁷ Normally, NCI will not acquire intellectual property rights to inventions made by its employees with research material under NIH-RAID, unless the originating investigator and NCI agree that to do so would be in the best interest of the project. If the NCI does file a patent application, the originating investigator will be given the opportunity to negotiate for an exclusive license.

SUMMARY

The NIH-RAID Pilot Program is designed to facilitate access of academic centres and investigators to opportunities for therapeutic development arising from their research. The NIH considers translational research to be of high priority, and significant resources are available, for which investigators are strongly encouraged to apply. For-profit partners are welcome to participate in approved projects along with the academic institution, and their expertise and ability to conduct ancillary work can be valuable to the project. Applications for development of therapeutics for any disorder are eligible, but funding decisions will be based on project merit, available funds, and NIH Institute priorities. Potential applicants are encouraged to discuss their research with NIH-RAID Pilot Program staff. Contact information is available on the Program web page.²

NOTES

1. See <http://nihroadmap.nih.gov/>.
2. See <http://nihroadmap.nih.gov/raid/>.
3. See <http://grants.nih.gov/grants/guide/notice-files/NOT-RM-08-005.html>.
4. See <http://grants.nih.gov/grants/guide/notice-files/NOT-RM-08-025.html>.
5. See <http://grants.nih.gov/grants/guide>.
6. See <http://www.grants.gov/index.jsp>.
7. See http://dctd.cancer.gov/ProgramPages/DTP_OngoingInitiatives_Drug_Development.htm.