NSF 24-561: Foundations for Digital Twins as Catalyzers of Biomedical Technological Innovation

Program Solicitation

Document Information

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National Science Foundation
Directorate for Mathematical and Physical Sciences
    Division of Mathematical Sciences
Directorate for Computer and Information Science and Engineering
    Office of Advanced Cyberinfrastructure

National Institutes of Health
    Office of Data Science Strategy

Food and Drug Administration

Full Proposal Deadline(s) (due by 5 p.m. submitting organization's local time):

June 21, 2024

May 05, 2025

First Monday in May, Annually Thereafter

Table Of Contents

Important Information And Revision Notes

Any proposal submitted in response to this solicitation should be submitted in accordance with the *NSF Proposal & Award Policies & Procedures Guide* (PAPPG) that is in effect for the relevant due date to which the proposal is being submitted. The NSF PAPPG is regularly revised and it is the responsibility of the proposer to ensure that the proposal meets the requirements specified in this solicitation and the applicable version of the PAPPG. Submitting a proposal prior to a specified deadline does not negate this requirement.

Summary Of Program Requirements

General Information

Program Title:

    Foundations for Digital Twins as Catalyzers of Biomedical Technological Innovation (FDT-BioTech)

Synopsis of Program:

    The Foundations for Digital Twins as Catalyzers of Biomedical Technological Innovation (FDT-BioTech) program supports inherently interdisciplinary research projects that underpin the mathematical and engineering foundations behind the development and use of digital twins and synthetic data in biomedical and healthcare applications, with a particular focus on digital, in silico models used in the evaluation of medical devices and the relevance of the developed models in addressing current and emerging challenges affecting the development and assessment of biomedical technologies. The goal of the FDT-BioTech initiative is to catalyze biomedical technological innovation through new foundational development of methods and algorithms relevant to digital twins and synthetic humans.

Cognizant Program Officer(s):

Please note that the following information is current at the time of publishing. See program website for any updates to the points of contact.

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Applicable Catalog of Federal Domestic Assistance (CFDA) Number(s):

- 47.049 --- Mathematical and Physical Sciences
- 47.070 --- Computer and Information Science and Engineering
- 93.310 --- NIH Office of Data Science

Award Information

Anticipated Type of Award: Standard Grant or Continuing Grant

Estimated Number of Awards: 6 to 10

The number of awards will depend on the quality of the received proposals and the budget availability.

Anticipated Funding Amount: $4,000,000 to $5,000,000

$4,000,000 to $5,000,000 in FY24, contingent on availability of funds.

The duration of the awards should be up to 3 years. The award size and duration should be consistent with the project scope.

Collaborative projects from multiple organizations are accepted, according to standard NSF procedures. The total budget (direct and indirect cost) for a collaborative project from multiple organizations must not exceed $1,000,000.

Eligibility Information

Who May Submit Proposals:

Proposals may only be submitted by the following:

- Institutions of Higher Education (IHEs) - Two- and four-year IHEs (including community colleges) accredited in, and having a campus located in the US, acting on behalf of their faculty members. Special Instructions for International Branch Campuses of US IHEs: If the proposal includes funding to be provided to an international branch campus of a US institution of higher education (including through use of subawards and consultant arrangements), the proposer must explain the benefit(s) to the project of performance at the international branch campus, and justify why the project activities cannot be performed at the US campus.

Who May Serve as PI:

There are no restrictions or limits.

Limit on Number of Proposals per Organization:

There are no restrictions or limits.

Limit on Number of Proposals per PI or co-PI: 1

An individual may serve as PI or co-PI on no more than ONE proposal. Participating in a proposal as other senior/key personnel does not count in this limit. Changes in investigator roles post-submission to meet the eligibility limits will not be allowed. **It is the responsibility of the submitters to confirm that the entire team is within the eligibility guidelines.**

Proposal Preparation and Submission Instructions

A. Proposal Preparation Instructions

- **Letters of Intent:** Not required

- **Preliminary Proposal Submission:** Not required

- **Full Proposals:**

  - Full Proposals submitted via Research.gov: *NSF Proposal and Award Policies and Procedures Guide* (PAPPG) guidelines apply. The complete text of the PAPPG is available electronically on the NSF website at: https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg.

  - Full Proposals submitted via Grants.gov: *NSF Grants.gov Application Guide: A Guide for the Preparation and Submission of NSF Applications via Grants.gov* guidelines apply (Note: The *NSF Grants.gov Application Guide* is available on the Grants.gov website and on the NSF website at: https://www.nsf.gov/publications/pub_summ.jsp?ods_key=grantsgovguide).

B. Budgetary Information

- **Cost Sharing Requirements:**

  Inclusion of voluntary committed cost sharing is prohibited.

- **Indirect Cost (F&A) Limitations:**

  Not Applicable

- **Other Budgetary Limitations:**

  Not Applicable

C. Due Dates

- **Full Proposal Deadline(s)** (due by 5 p.m. submitting organization's local time):

  June 21, 2024

  May 05, 2025

  First Monday in May, Annually Thereafter

Proposal Review Information Criteria

Merit Review Criteria:

National Science Board approved criteria. Additional merit review criteria apply. Please see the full text of this solicitation for further information.

Award Administration Information

Award Conditions:

Standard NSF award conditions apply.

Reporting Requirements:

Standard NSF reporting requirements apply.

I. Introduction

Digital twins offer tremendous potential to revolutionize healthcare delivery by enabling data-informed decision-making under uncertainty. The National Academies of Science, Engineering and Medicine (NASEM) published a report in 2023 entitled "Foundational Research Gaps and Future Directions for Digital Twins." This report defines a digital twin as "a set of virtual information constructs that mimics the structure, context, and behavior of a natural, engineered, or social system (or system-of-systems), is dynamically updated with data from its physical twin, has a predictive capability, and informs decisions that realize value". In addition, this report recognizes that in the healthcare sciences such virtual representations of human physiology and pathology have the potential to enable novel pathways for the development and evaluation of new biomedical technologies. Achieving this vision requires a convergent research approach that engages disciplines spanning mathematics, statistics, biomedical engineering, and computational sciences to address the broad range of emerging needs for developing foundational concepts behind digital twins. This anticipated paradigm shift hinges on fundamental scientific and engineering breakthroughs by interdisciplinary teams for developing, validating, and sharing human digital twin frameworks, capable of integrating data from individuals, populations, and devices to catalyze new discoveries and innovation in healthcare systems.

The Foundations for Digital Twins as Catalyzers of Biomedical Technological Innovation (FDT-BioTech) program aims to accelerate innovations in biomedical technologies through development of principled mathematical, statistical, and engineering foundations for digital twins and synthetic human models in healthcare applications. The specific focus of FDT-BioTech is on digital, in silico models that could be used in the evaluation of medical devices and to advance regulatory sciences. The work is also expected to contribute more broadly to the development and implementation of human digital twins. This FDT-BioTech program provides an opportunity to form cohesive collaboration teams including mathematicians, statisticians, biomedical engineers, computer scientists, physicians, and experts from other domains. This collaboration will advance our understanding of foundational mechanisms behind computational representations of physiologic systems; verification, validation, and uncertainty quantification in a biomedical context; transferability, generalizability, and robustness; ethics, security, and privacy; and validation and sharing mechanisms, particularly in terms of regulatory relevance.

II. Program Description

This interagency solicitation is a collaboration between the U.S. National Science Foundation (NSF), National Institutes of Health (NIH) and Food and Drug Administration (FDA). The Foundations for Digital Twins as Catalyzers of Biomedical Technological Innovation (FDT-BioTech) supports innovative and transformative research to advance the mathematical, statistical, and engineering approaches underpinning digital twins in biomedical and healthcare domains ultimately enabling unique tools for innovative evaluation of novel emerging technology that can potentially de-risk therapeutic, biologic, and medical device development and accelerate the introduction of safe and effective medical technologies for improved patient outcomes. Additionally, the emerging concepts of digital twins demonstrate a high potential to revolutionize preclinical and clinical research through reliable in silico investigations, as well as transform clinical practice by providing a framework for patient monitoring, management, and optimal decision making.

Furthermore, collectively, digital twins can be used to develop digital cohorts for accelerating innovation in biomedical technology. For instance, ensembles of digital twin humans could allow for on-demand enrollment of digital cohorts and pipelines for development, tuning, testing, and monitoring in the digital world. Digital study populations can display the variability observed in human populations, including under-represented subgroups and rare conditions, thereby addressing the fundamental problem of algorithmic and other biases which remains inaccessible with current paradigms. Ultimately, leveraging digital models of patients, disease processes, and medical devices is an agile modern approach to

technological development and represents a paradigm shift in the development and evaluation of medical products and new technologies. However, achieving this vision hinges on fundamental advances in mathematics, statistics, computational sciences, and engineering.

Note: Projects may leverage virtual representations at multiple scales including a single physiologic or pathologic system, multiple systems, whole-humans, or populations; and be patient-specific or synthetically-derived. Virtual representations may include artificial intelligence (AI), first-principles, mechanistic, or empirical models. The virtual representations should be capable of interfacing with medical technologies and thus may include virtual representations of medical devices.

The rationale for FDT-BioTech is the current knowledge gaps that obstruct the development and use of digital twins in biomedical and other domains. Filling this gap requires novel crosscutting interdisciplinary approaches, where mathematical and statistical foundations play a pivotal role. Some examples of new developments in the foundation of digital twins with strong potential to spur new advances in biotechnology include but are not limited to the following:

1. **Computational representations of physiological systems at appropriate scales:** The virtual representation of real-world physiology is at the core of a human digital twin. The human body is a dynamic and complex system whose behaviors are extremely difficult to model and predict. Tools to adequately build computational representations are lacking. New mathematical, statistical and machine learning methods are needed to enable novel computationally efficient pathways for the integration of prior information into the systematic combination of physical data and their digital counterparts. These strategies may include hybrid modeling approaches – combining mechanistic models, machine learning, and data-driven models – and surrogate models – statistical data-fit models, reduced order models, and simplified models. Furthermore, these models must be capable of assimilating dynamic multi-modal data at different spatial and temporal scales, dynamically updating and adapting, coupling multiphysics systems, and operating with limited data or accounting for extrapolation. These requirements may necessitate new model management workflows including assessing model evolution and drift. Understanding the tradeoffs associated with model and computational choices will increase confidence in predictive insights and digital twin-informed decision making. Moreover, digital twins not only integrate data streams from their physical twin but also data and outcomes from similar physical counterparts. New mathematical, statistical and machine learning methods are needed that could enable novel computationally efficient pathways for integration of prior information into the systematic combination of physical data and their digital counterparts.

2. **Verification, Validation, and Uncertainty Quantification (VVUQ):** Appropriate verification, validation, and uncertainty quantification (VVUQ) are essential to build confidence and trust in digital twins. The complexity of the digital twin ecosystem may require new and advanced strategies and workflows that consider VVUQ as a continuous process. New data collection technologies (quality, source, structure) may affect algorithm or solution verification. Further, the state of the physical twin will evolve over time; and new strategies are needed to ensure the virtual representation accurately reflects these changes (i.e., adaptive model validation). The current lack of evidence of digital twin predictive capabilities adversely impacts the use of digital twins in the healthcare domain. There is a critical need for understanding the confidence interval of digital twin outputs while accounting for various types of uncertainties including modeling uncertainties, measurement and data uncertainties, and process uncertainties. One benefit of digital twins is the ability to test what-if scenarios, such as the performance of a therapeutic, biologic, or diagnostic device. However, to harness this potential, the outputs from the digital twin should be representative of the physical twin's response (i.e. commutable) even when based on unseen data or extrapolation. New approaches, including but not limited to tools for causal inference, covariate adjustment, extreme value analysis, and neural solvers of partial differential equations, are needed for assessment of the digital twin utility in a broad range of settings.

3. **Transferability, Generalizability and Robustness**: Most digital twins are designed with a particular purpose in mind. To leverage these digital twins for new purposes or scenarios (i.e. testing novel medical technologies), new techniques and tools are required to quantify and improve the transferability of digital twin predictions. There is also a need for techniques to advance the generalizability of evaluation findings on synthetic data from digital twin models to findings on patient data, including performance on various population subgroups. Another fundamental question is associated with the analysis of the robustness of the digital twin models, so that the

medical devices designed and evaluated using digital twins are ensured to exhibit the expected standards of safety and effectiveness.

4. **Ethics, Security, and Privacy**: Ethics, security, and privacy are critical to the success of digital twin ecosystems; and include fidelity and reliability of the models, security and access to data, recognition that data and models built on that data may be biased, and ethical use of the data and model outputs. The current limited understanding of the sources and types of biases has led to considerable concern in the community that synthetic human models, including digital twins, may inadvertently propagate or even further exacerbate current inequalities in healthcare delivery. For example, bias may be introduced in data measurement technologies, data labeling, data sources (i.e. is the data representative of the population, have rare conditions been included, small data sets); as well as models, algorithms, and decision-making processes based on this data. Understanding, measuring, and minimizing potential latent biases require novel or advanced methods of statistical inference as current approaches are underdeveloped. Further, strategies to ensure protection of privacy of individual's data used to develop the DT (at various scale), and equitable impacts and distribution of resources within the context of digital twins are needed. Development of such foundational approaches have potential to accelerate the widespread adoption of digital twins not only in biomedical sciences but also numerous application domains.

5. **Validation and Sharing Mechanisms**: There is a critical need to design computational infrastructure, platforms, and best practices for in silico databanks for medical technology evaluation with pre-defined data sequestration provisions. The lack of methods and platforms with broad involvement of the interdisciplinary scientific community substantially impacts the development, validation, and adoption of digital twins in biomedicine. Furthermore, innovative tools are needed for management, maintenance, service, test data reuse, and auditing of banks of digital twins under privacy- and integrity-preserving federated settings. This in turn will allow for a synergistic acceleration of innovation in a wide range of medical technology areas. Finally, the widespread adoption of digital twins and in silico models for human health will only be realized by more collaborative solutions to sharing and validation of models with established protocols between different digital twin sources as opposed to the status of a disconnected, site-specific collection of digital twin data and human in silico models.

The above list of themes provides examples for possible research initiatives that may be supported by the FDT-BioTech solicitation. Proposals with complementary aims, not listed here, will also be considered. Furthermore, these research themes are clearly not mutually exclusive, and a given project may address multiple themes.

Ethical, Legal, and Social Implications (ELSI): It is essential to recognize ethical, legal, and social implications (ELSI) during the development of human digital twins and synthetic humans. A digital twin ecosystem that does not include ESLI at the start will build inequity into core design and implementation principles perpetuating disparities in health, infrastructure, and resources. All proposals must identify potential ELS implications of the proposed work and outline ways to mitigate negative implications.

This program encourages teams to consider the generalizability of their approaches to other systems, populations, or non-biomedical applications.

In addition to the examples described in this solicitation, the program welcomes submissions of proposals that contain outcomes (methods and models) with a clear dissemination plan, made available as practical, open-source tools that industry can utilize in support of the development of new biomedical technologies. Such tools should be of production quality, shared with the research community, and facilitate interoperability with other tools and data infrastructure. Proposals targeting such tools should include project personnel with cyberinfrastructure development expertise. Furthermore, these tools can include innovative science-based approaches including methodologies and datasets and are meant to support innovators in early stages of development as they prepare toward securing premarket authorization by the FDA. Examples of regulatory science tools published by the Office of Science and Engineering Laboratories, Center for Devices and Radiological Health (OSEL/CDRH/FDA) are available in FDA's catalog of regulatory science tools (Catalog of Regulatory Science Tools to Help Assess New Medical Devices | FDA). Furthermore, FDA will offer opportunities to the FDT-BioTech PIs to discuss and submit their software code implementing the developed methods and algorithms and receive feedback on its relevance to current and emerging regulatory science challenges within the precompetitive space.

This program welcomes the submission of proposals that include the participation of the full spectrum of diverse talent in STEM, e.g., as PI, co-PI, senior/key personnel, postdoctoral scholars, graduate or undergraduate students or trainees. This includes historically under-represented or underserved populations. It also includes diverse institutions including Minority-Serving Institutions (MSIs), Primarily Undergraduate Institutions (PUIs), and two-year colleges, as well as major research institutions. Proposals from EPSCoR (Established Program to Stimulate Competitive Research) jurisdictions are especially encouraged.

Successful projects are anticipated to be collaborative in nature and have at least two senior/key personnels, with participation from both the mathematical sciences and at least one of the domain knowledge disciplines such as the biomedical sciences or computer science with cyberinfrastructure development expertise. In particular, interdisciplinary teams with PI and co-PI from the mathematical sciences, biomedical sciences and computer science with cyberinfrastructure development expertise are encouraged. These requirements will help to ensure that the proposals are truly integrative.

III. Award Information

Anticipated Type of Award: Standard Grant or Continuing Grant

Estimated Number of Awards: 6 to 10

The number of awards will depend on the quality of the received proposals and the budget availability.

Anticipated Funding Amount: $4,000,000 to $5,000,000

$4,000,000 to $5,000,000 in FY24, contingent on availability of funds.

The duration of the awards should be up to 3 years. The award size and duration should be consistent with the project scope.

Collaborative projects from multiple organizations are accepted, according to standard NSF procedures. The total budget (direct and indirect cost) for a collaborative project from multiple organizations must not exceed $1,000,000.

Estimated program budget, number of awards and average award size/duration are subject to the availability of funds.

IV. Eligibility Information

Who May Submit Proposals:

Proposals may only be submitted by the following:

- Institutions of Higher Education (IHEs) - Two- and four-year IHEs (including community colleges) accredited in, and having a campus located in the US, acting on behalf of their faculty members. Special Instructions for International Branch Campuses of US IHEs: If the proposal includes funding to be provided to an international branch campus of a US institution of higher education (including through use of subawards and consultant arrangements), the proposer must explain the benefit(s) to the project of performance at the international branch campus, and justify why the project activities cannot be performed at the US campus.

Who May Serve as PI:

There are no restrictions or limits.

Limit on Number of Proposals per Organization:

There are no restrictions or limits.

Limit on Number of Proposals per PI or co-PI: 1

An individual may serve as PI or co-PI on no more than ONE proposal. Participating in a proposal as other senior/key personnel does not count in this limit. Changes in investigator roles post-submission to meet the eligibility limits will not be allowed. **It is the responsibility of the submitters to confirm that the entire team is within the eligibility guidelines.**

Additional Eligibility Info:

A minimum of two collaborating Senior/Key Personnel, with participation from both the mathematical sciences and at least one of the domain knowledge disciplines such as the biomedical sciences or computer science with cyberinfrastructure development expertise is required. Interdisciplinary teams with PI and co-PI from the mathematical sciences, the biomedical sciences, and computer science with cyberinfrastructure development expertise are encouraged.

V. Proposal Preparation And Submission Instructions

A. Proposal Preparation Instructions

Full Proposal Preparation Instructions: Proposers may opt to submit proposals in response to this Program Solicitation via Research.gov or Grants.gov.

- Full Proposals submitted via Research.gov: Proposals submitted in response to this program solicitation should be prepared and submitted in accordance with the general guidelines contained in the *NSF Proposal and Award Policies and Procedures Guide* (PAPPG). The complete text of the PAPPG is available electronically on the NSF website at: https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg. Paper copies of the PAPPG may be obtained from the NSF Publications Clearinghouse, telephone (703) 292-8134 or by e-mail from nsfpubs@nsf.gov. The Prepare New Proposal setup will prompt you for the program solicitation number.

- Full proposals submitted via Grants.gov: Proposals submitted in response to this program solicitation via Grants.gov should be prepared and submitted in accordance with the *NSF Grants.gov Application Guide: A Guide for the Preparation and Submission of NSF Applications via Grants.gov*. The complete text of the *NSF Grants.gov Application Guide* is available on the Grants.gov website and on the NSF website at: (https://www.nsf.gov/publications/pub_summ.jsp?ods_key=grantsgovguide). To obtain copies of the Application Guide and Application Forms Package, click on the Apply tab on the Grants.gov site, then click on the Apply Step 1: Download a Grant Application Package and Application Instructions link and enter the funding opportunity number, (the program solicitation number without the NSF prefix) and press the Download Package button. Paper copies of the Grants.gov Application Guide also may be obtained from the NSF Publications Clearinghouse, telephone (703) 292-8134 or by e-mail from nsfpubs@nsf.gov.

In determining which method to utilize in the electronic preparation and submission of the proposal, please note the following:

Collaborative Proposals. All collaborative proposals submitted as separate submissions from multiple organizations must be submitted via Research.gov. PAPPG Chapter II.E.3 provides additional information on collaborative proposals.

See PAPPG Chapter II.D.2 for guidance on the required sections of a full research proposal submitted to NSF. Please note that the proposal preparation instructions provided in this program solicitation may deviate from the PAPPG instructions.

The following instructions supplement or deviate from the PAPPG:

Proposal Title: To facilitate timely processing, proposal titles must begin with FDT-BioTech, followed by a colon and the title of the project (i.e. FDT-BioTech: Title). The title of collaborative proposals submitted as separate submissions from multiple organizations should begin with the designation "Collaborative Research: FDT-BioTech:" All proposals in a collaborative project should have the same title. Please note that if submitting via Research.gov, the system will automatically insert the prepended title "Collaborative Research" when the collaborative set of proposals is created.

Project Description: In addition to the requirements specified in the PAPPG, the Project Description should clearly:

- Demonstrate the potential benefits of the proposed work for regulatory sciences.
- Include a separate section with a heading **Ethics, Legal, and Social Implications (ELSI)** that clearly identifies potential Ethics, Legal, and Social Implications (ELSI) in the proposed work and consider ways to mitigate negative implications.
- Explain how the proposed research effectively integrates diverse fields (e.g. mathematics, statistics, computational sciences, biomedical sciences, computer science, cyberinfrastructure development and engineering) to advance the foundation of digital twins.
- Address how the multidisciplinary group of researchers is appropriate to the project, how the team members provide distinct, complementary expertise to the project, and why all fields of expertise are needed to complete the proposed work represented on the team.

B. Budgetary Information

Cost Sharing:

Inclusion of voluntary committed cost sharing is prohibited.

C. Due Dates

- **Full Proposal Deadline(s)** (due by 5 p.m. submitting organization's local time):

    June 21, 2024

    May 05, 2025

    First Monday in May, Annually Thereafter

D. Research.gov/Grants.gov Requirements

For Proposals Submitted Via Research.gov:

To prepare and submit a proposal via Research.gov, see detailed technical instructions available at: https://www.research.gov/research-portal/appmanager/base/desktop?_nfpb=true&_pageLabel=research_node_display&_nodePath=/researchGov/Service/Desktop/ProposalPreparationand For Research.gov user support, call the Research.gov Help Desk at 1-800-381-1532 or e-mail rgov@nsf.gov. The Research.gov Help Desk answers general technical questions related to the use of the Research.gov system. Specific questions related to this program solicitation should be referred to the NSF program staff contact(s) listed in Section VIII of this funding opportunity.

For Proposals Submitted Via Grants.gov:

Before using Grants.gov for the first time, each organization must register to create an institutional profile. Once registered, the applicant's organization can then apply for any federal grant on the Grants.gov website. Comprehensive information about using Grants.gov is available on the Grants.gov Applicant Resources webpage: https://www.grants.gov/web/grants/applicants.html. In addition, the NSF Grants.gov Application Guide (see link in Section V.A) provides instructions regarding the technical preparation of proposals via Grants.gov. For Grants.gov user support, contact the Grants.gov Contact Center at 1-800-518-4726 or by email: support@grants.gov. The Grants.gov Contact Center answers general technical questions related to the use of Grants.gov. Specific questions related to this program solicitation should be referred to the NSF program staff contact(s) listed in Section VIII of this solicitation.

Submitting the Proposal: Once all documents have been completed, the Authorized Organizational Representative (AOR) must submit the application to Grants.gov and verify the desired funding opportunity and agency to which the application is submitted. The AOR must then sign and submit the application to Grants.gov. The completed application will be transferred to Research.gov for further processing.

The NSF Grants.gov Proposal Processing in Research.gov informational page provides submission guidance to applicants and links to helpful resources including the NSF Grants.gov Application Guide, Grants.gov Proposal Processing in Research.gov how-to guide, and Grants.gov Submitted Proposals Frequently Asked Questions. Grants.gov proposals must pass all NSF pre-check and post-check validations in order to be accepted by Research.gov at NSF.

When submitting via Grants.gov, NSF strongly recommends applicants initiate proposal submission at least five business days in advance of a deadline to allow adequate time to address NSF compliance errors and resubmissions by 5:00 p.m. submitting organization's local time on the deadline. Please note that some errors cannot be corrected in Grants.gov. Once a proposal passes pre-checks but fails any post-check, an applicant can only correct and submit the in-progress proposal in Research.gov.

Proposers that submitted via Research.gov may use Research.gov to verify the status of their submission to NSF. For proposers that submitted via Grants.gov, until an application has been received and validated by NSF, the Authorized Organizational Representative may check the status of an application on Grants.gov. After proposers have received an e-mail notification from NSF, Research.gov should be used to check the status of an application.

VI. NSF Proposal Processing And Review Procedures

Proposals received by NSF are assigned to the appropriate NSF program for acknowledgement and, if they meet NSF requirements, for review. All proposals are carefully reviewed by a scientist, engineer, or educator serving as an NSF Program Officer, and usually by three to ten other persons outside NSF either as *ad hoc* reviewers, panelists, or both, who are experts in the particular fields represented by the proposal. These reviewers are selected by Program Officers charged with oversight of the review process. Proposers are invited to suggest names of persons they believe are especially well qualified to review the proposal and/or persons they would prefer not review the proposal. These suggestions may serve as one source in the reviewer selection process at the Program Officer's discretion. Submission of such names, however, is optional. Care is taken to ensure that reviewers have no conflicts of interest with the proposal. In addition, Program Officers may obtain comments from site visits before recommending final action on proposals. Senior NSF staff further review recommendations for awards. A flowchart that depicts the entire NSF proposal and award process (and associated timeline) is included in PAPPG Exhibit III-1.

A comprehensive description of the Foundation's merit review process is available on the NSF website at: https://www.nsf.gov/bfa/dias/policy/merit_review/.

Proposers should also be aware of core strategies that are essential to the fulfillment of NSF's mission, as articulated in *Leading the World in Discovery and Innovation, STEM Talent Development and the Delivery of Benefits from Research - NSF Strategic Plan for Fiscal Years (FY) 2022 - 2026*. These strategies are integrated in the program planning and implementation process, of which proposal review is one part. NSF's mission is particularly well-implemented through the integration of research and education and broadening participation in NSF programs, projects, and activities.

One of the strategic objectives in support of NSF's mission is to foster integration of research and education through the programs, projects, and activities it supports at academic and research institutions. These institutions must recruit, train, and prepare a diverse STEM workforce to advance the frontiers of science and participate in the U.S. technology-based economy. NSF's contribution to the national innovation ecosystem is to provide cutting-edge research under the guidance of the Nation's most creative scientists and engineers. NSF also supports development of a strong science, technology, engineering, and mathematics (STEM) workforce by investing in building the knowledge that informs improvements in STEM teaching and learning.

NSF's mission calls for the broadening of opportunities and expanding participation of groups, institutions, and geographic regions that are underrepresented in STEM disciplines, which is essential to the health and vitality of science and engineering. NSF is committed to this principle of diversity and deems it central to the programs, projects, and activities it considers and supports.

A. Merit Review Principles and Criteria

The National Science Foundation strives to invest in a robust and diverse portfolio of projects that creates new knowledge and enables breakthroughs in understanding across all areas of science and engineering research and education. To identify which projects to support, NSF relies on a merit review process that incorporates consideration of both the technical aspects of a proposed project and its potential to contribute more broadly to advancing NSF's mission "to promote the progress of science; to advance the national health, prosperity, and welfare; to secure the national defense; and for other purposes." NSF makes every effort to conduct a fair, competitive, transparent merit review process for the selection of projects.

1. Merit Review Principles

These principles are to be given due diligence by PIs and organizations when preparing proposals and managing projects, by reviewers when reading and evaluating proposals, and by NSF program staff when determining whether or not to recommend proposals for funding and while overseeing awards. Given that NSF is the primary federal agency charged with nurturing and supporting excellence in basic research and education, the following three principles apply:

- All NSF projects should be of the highest quality and have the potential to advance, if not transform, the frontiers of knowledge.
- NSF projects, in the aggregate, should contribute more broadly to achieving societal goals. These "Broader Impacts" may be accomplished through the research itself, through activities that are directly related to specific research projects, or through activities that are supported by, but are complementary to, the project. The project activities may be based on previously established and/or innovative methods and approaches, but in either case must be well justified.
- Meaningful assessment and evaluation of NSF funded projects should be based on appropriate metrics, keeping in mind the likely correlation between the effect of broader impacts and the resources provided to implement projects. If the size of the activity is limited, evaluation of that activity in isolation is not likely to be meaningful. Thus, assessing the effectiveness of these activities may best be done at a higher, more aggregated, level than the individual project.

With respect to the third principle, even if assessment of Broader Impacts outcomes for particular projects is done at an aggregated level, PIs are expected to be accountable for carrying out the activities described in the funded project. Thus, individual projects should include clearly stated goals, specific descriptions of the activities that the PI intends to do, and a plan in place to document the outputs of those activities.

These three merit review principles provide the basis for the merit review criteria, as well as a context within which the users of the criteria can better understand their intent.

2. Merit Review Criteria

All NSF proposals are evaluated through use of the two National Science Board approved merit review criteria. In some instances, however, NSF will employ additional criteria as required to highlight the specific objectives of certain programs and activities.

The two merit review criteria are listed below. **Both** criteria are to be given **full consideration** during the review and decision-making processes; each criterion is necessary but neither, by itself, is sufficient. Therefore, proposers must fully address both criteria. (PAPPG Chapter II.D.2.d(i). contains additional information for use by proposers in development of the Project Description section of the proposal). Reviewers are strongly encouraged to review the criteria, including PAPPG Chapter II.D.2.d(i), prior to the review of a proposal.

When evaluating NSF proposals, reviewers will be asked to consider what the proposers want to do, why they want to do it, how they plan to do it, how they will know if they succeed, and what benefits could accrue if the project is successful. These issues apply both to the technical aspects of the proposal and the way in which the project may make broader contributions. To that end, reviewers will be asked to evaluate all proposals against two criteria:

- **Intellectual Merit:** The Intellectual Merit criterion encompasses the potential to advance knowledge; and

- **Broader Impacts:** The Broader Impacts criterion encompasses the potential to benefit society and contribute to the achievement of specific, desired societal outcomes.

The following elements should be considered in the review for both criteria:

1. What is the potential for the proposed activity to
    a. Advance knowledge and understanding within its own field or across different fields (Intellectual Merit); and
    b. Benefit society or advance desired societal outcomes (Broader Impacts)?
2. To what extent do the proposed activities suggest and explore creative, original, or potentially transformative concepts?
3. Is the plan for carrying out the proposed activities well-reasoned, well-organized, and based on a sound rationale? Does the plan incorporate a mechanism to assess success?
4. How well qualified is the individual, team, or organization to conduct the proposed activities?
5. Are there adequate resources available to the PI (either at the home organization or through collaborations) to carry out the proposed activities?

Broader impacts may be accomplished through the research itself, through the activities that are directly related to specific research projects, or through activities that are supported by, but are complementary to, the project. NSF values the advancement of scientific knowledge and activities that contribute to achievement of societally relevant outcomes. Such outcomes include, but are not limited to: full participation of women, persons with disabilities, and other underrepresented groups in science, technology, engineering, and mathematics (STEM); improved STEM education and educator development at any level; increased public scientific literacy and public engagement with science and technology; improved well-being of individuals in society; development of a diverse, globally competitive STEM workforce; increased partnerships between academia, industry, and others; improved national security; increased economic competitiveness of the United States; and enhanced infrastructure for research and education.

Proposers are reminded that reviewers will also be asked to review the Data Management and Sharing Plan and the Mentoring Plan, as appropriate.

Additional Solicitation Specific Review Criteria

Regulatory science tools component for medical device evaluation:

The work to be funded by this solicitation must demonstrate the potential benefits for regulatory sciences. Proposals shall include a detailed section of how the proposed computational methods and tools developed under the awards will impact the early de-risking of new technology and contribute to facilitating regulatory evaluations including, for example, frequent interaction with OSEL/CDRH/FDA during the post-award period.

B. Review and Selection Process

Proposals submitted in response to this program solicitation will be reviewed by Ad hoc Review and/or Panel Review.

NSF will coordinate and manage the review of proposals jointly with NIH and FDA. The representatives from NIH and FDA may serve as panel observers. Relevant information about proposals and reviews of proposals will be shared with NIH and FDA as appropriate.

Reviewers will be asked to evaluate proposals using two National Science Board approved merit review criteria and, if applicable, additional program specific criteria. A summary rating and accompanying narrative will generally be completed and submitted by each reviewer and/or panel. The Program Officer assigned to manage the proposal's review will consider the advice of reviewers and will formulate a recommendation.

After scientific, technical and programmatic review and consideration of appropriate factors, the NSF Program Officer recommends to the cognizant Division Director whether the proposal should be declined or recommended for award.

NSF strives to be able to tell proposers whether their proposals have been declined or recommended for funding within six months. Large or particularly complex proposals or proposals from new recipients may require additional review and processing time. The time interval begins on the deadline or target date, or receipt date, whichever is later. The interval ends when the Division Director acts upon the Program Officer's recommendation.

After programmatic approval has been obtained, the proposals recommended for funding will be forwarded to the Division of Grants and Agreements or the Division of Acquisition and Cooperative Support for review of business, financial, and policy implications. After an administrative review has occurred, Grants and Agreements Officers perform the processing and issuance of a grant or other agreement. Proposers are cautioned that only a Grants and Agreements Officer may make commitments, obligations or awards on behalf of NSF or authorize the expenditure of funds. No commitment on the part of NSF should be inferred from technical or budgetary discussions with a NSF Program Officer. A Principal Investigator or organization that makes financial or personnel commitments in the absence of a grant or cooperative agreement signed by the NSF Grants and Agreements Officer does so at their own risk.

Once an award or declination decision has been made, Principal Investigators are provided feedback about their proposals. In all cases, reviews are treated as confidential documents. Verbatim copies of reviews, excluding the names of the reviewers or any reviewer-identifying information, are sent to the Principal Investigator/Project Director by the Program Officer. In addition, the proposer will receive an explanation of the decision to award or decline funding.

VII. Award Administration Information

A. Notification of the Award

Notification of the award is made to *the submitting organization* by an NSF Grants and Agreements Officer. Organizations whose proposals are declined will be advised as promptly as possible by the cognizant NSF Program administering the program. Verbatim copies of reviews, not including the identity of the reviewer, will be provided automatically to the Principal Investigator. (See Section VI.B. for additional information on the review process.)

B. Award Conditions

An NSF award consists of: (1) the award notice, which includes any special provisions applicable to the award and any numbered amendments thereto; (2) the budget, which indicates the amounts, by categories of expense, on which NSF has based its support (or otherwise communicates any specific approvals or disapprovals of proposed expenditures); (3) the proposal referenced in the award notice; (4) the applicable award conditions, such as Grant General Conditions (GC-1)*; or Research Terms and Conditions* and (5) any announcement or other NSF issuance that may be incorporated by reference in the award notice. Cooperative agreements also are administered in accordance with NSF Cooperative Agreement Financial and Administrative Terms and Conditions (CA-FATC) and the applicable Programmatic Terms and Conditions. NSF awards are electronically signed by an NSF Grants and Agreements Officer and transmitted electronically to the organization via e-mail.

*These documents may be accessed electronically on NSF's Website at https://www.nsf.gov/awards/managing/award_conditions.jsp?org=NSF. Paper copies may be obtained from the NSF Publications Clearinghouse, telephone (703) 292-8134 or by e-mail from nsfpubs@nsf.gov.

More comprehensive information on NSF Award Conditions and other important information on the administration of NSF awards is contained in the NSF *Proposal & Award Policies & Procedures Guide* (PAPPG) Chapter VII, available electronically on the NSF Website at https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg.

Administrative and National Policy Requirements

Build America, Buy America

As expressed in Executive Order 14005, Ensuring the Future is Made in All of America by All of America's Workers (86 FR 7475), it is the policy of the executive branch to use terms and conditions of Federal financial assistance awards to

maximize, consistent with law, the use of goods, products, and materials produced in, and services offered in, the United States.

Consistent with the requirements of the Build America, Buy America Act (Pub. L. 117-58, Division G, Title IX, Subtitle A, November 15, 2021), no funding made available through this funding opportunity may be obligated for an award unless all iron, steel, manufactured products, and construction materials used in the project are produced in the United States. For additional information, visit NSF's Build America, Buy America webpage.

C. Reporting Requirements

For all multi-year grants (including both standard and continuing grants), the Principal Investigator must submit an annual project report to the cognizant Program Officer no later than 90 days prior to the end of the current budget period. (Some programs or awards require submission of more frequent project reports). No later than 120 days following expiration of a grant, the PI also is required to submit a final annual project report, and a project outcomes report for the general public.

Failure to provide the required annual or final annual project reports, or the project outcomes report, will delay NSF review and processing of any future funding increments as well as any pending proposals for all identified PIs and co-PIs on a given award. PIs should examine the formats of the required reports in advance to assure availability of required data.

PIs are required to use NSF's electronic project-reporting system, available through Research.gov, for preparation and submission of annual and final annual project reports. Such reports provide information on accomplishments, project participants (individual and organizational), publications, and other specific products and impacts of the project. Submission of the report via Research.gov constitutes certification by the PI that the contents of the report are accurate and complete. The project outcomes report also must be prepared and submitted using Research.gov. This report serves as a brief summary, prepared specifically for the public, of the nature and outcomes of the project. This report will be posted on the NSF website exactly as it is submitted by the PI.

More comprehensive information on NSF Reporting Requirements and other important information on the administration of NSF awards is contained in the *NSF Proposal & Award Policies & Procedures Guide* (PAPPG) Chapter VII, available electronically on the NSF Website at https://www.nsf.gov/publications/pub_summ.jsp?ods_key=pappg.

VIII. Agency Contacts

Please note that the program contact information is current at the time of publishing. See program website for any updates to the points of contact.

General inquiries regarding this program should be made to:

- Yulia R. Gel, MPS/DMS, telephone: (703) 292-7888, email: ygel@nsf.gov

- Zhilan J. Feng, MPS/DMS, telephone: (703) 292-7523, email: zfeng@nsf.gov

- Stephanie George, ENG/CBET, telephone: (703) 292-7825, email: stgeorge@nsf.gov

- Varun Chandola, CISE/OAC, telephone: (703) 292-2656, email: vchandol@nsf.gov

- Ashok Srinivasan, CISE/OAC, telephone: (703) 292-2122, email: asriniva@nsf.gov

- Laura Biven, NIH, telephone: (301)480-4021, email: odssdt@nih.gov

- Fenglou Mao, NIH, telephone: (301)451-9389, email: odssdt@nih.gov

- Aldo Badano, FDA, telephone: (301) 796-2534, email: aldo.badano@fda.hhs.gov

For questions related to the use of NSF systems contact:

- NSF Help Desk: 1-800-381-1532
- Research.gov Help Desk e-mail: rgov@nsf.gov

For questions relating to Grants.gov contact:

- Grants.gov Contact Center: If the Authorized Organizational Representatives (AOR) has not received a confirmation message from Grants.gov within 48 hours of submission of application, please contact via telephone: 1-800-518-4726; e-mail: support@grants.gov.

IX. Other Information

The NSF website provides the most comprehensive source of information on NSF Directorates (including contact information), programs and funding opportunities. Use of this website by potential proposers is strongly encouraged. In addition, "NSF Update" is an information-delivery system designed to keep potential proposers and other interested parties apprised of new NSF funding opportunities and publications, important changes in proposal and award policies and procedures, and upcoming NSF Grants Conferences. Subscribers are informed through e-mail or the user's Web browser each time new publications are issued that match their identified interests. "NSF Update" also is available on NSF's website.

Grants.gov provides an additional electronic capability to search for Federal government-wide grant opportunities. NSF funding opportunities may be accessed via this mechanism. Further information on Grants.gov may be obtained at https://www.grants.gov.

About The National Science Foundation

The National Science Foundation (NSF) is an independent Federal agency created by the National Science Foundation Act of 1950, as amended (42 USC 1861-75). The Act states the purpose of the NSF is "to promote the progress of science; [and] to advance the national health, prosperity, and welfare by supporting research and education in all fields of science and engineering."

NSF funds research and education in most fields of science and engineering. It does this through grants and cooperative agreements to more than 2,000 colleges, universities, K-12 school systems, businesses, informal science organizations and other research organizations throughout the US. The Foundation accounts for about one-fourth of Federal support to academic institutions for basic research.

NSF receives approximately 55,000 proposals each year for research, education and training projects, of which approximately 11,000 are funded. In addition, the Foundation receives several thousand applications for graduate and postdoctoral fellowships. The agency operates no laboratories itself but does support National Research Centers, user facilities, certain oceanographic vessels and Arctic and Antarctic research stations. The Foundation also supports cooperative research between universities and industry, US participation in international scientific and engineering efforts, and educational activities at every academic level.

Facilitation Awards for Scientists and Engineers with Disabilities (FASED) provide funding for special assistance or equipment to enable persons with disabilities to work on NSF-supported projects. See the *NSF Proposal & Award Policies & Procedures Guide* Chapter II.F.7 for instructions regarding preparation of these types of proposals.

The National Science Foundation has Telephonic Device for the Deaf (TDD) and Federal Information Relay Service (FIRS) capabilities that enable individuals with hearing impairments to communicate with the Foundation about NSF programs, employment or general information. TDD may be accessed at (703) 292-5090 and (800) 281-8749, FIRS at (800) 877-8339.

The National Science Foundation Information Center may be reached at (703) 292-5111.

The National Science Foundation promotes and advances scientific progress in the United States by competitively awarding grants and cooperative agreements for research and education in the sciences, mathematics, and

engineering.

To get the latest information about program deadlines, to download copies of NSF publications, and to access abstracts of awards, visit the NSF Website at https://www.nsf.gov

- **Location:**   2415 Eisenhower Avenue, Alexandria, VA 22314

- **For General Information**   (703) 292-5111
  (NSF Information Center)**:**

- **TDD (for the hearing-impaired):**   (703) 292-5090

- **To Order Publications or Forms:**

  Send an e-mail to: nsfpubs@nsf.gov

  or telephone: (703) 292-8134

- **To Locate NSF Employees:**   (703) 292-5111

Privacy Act And Public Burden Statements

The information requested on proposal forms and project reports is solicited under the authority of the National Science Foundation Act of 1950, as amended. The information on proposal forms will be used in connection with the selection of qualified proposals; and project reports submitted by proposers will be used for program evaluation and reporting within the Executive Branch and to Congress. The information requested may be disclosed to qualified reviewers and staff assistants as part of the proposal review process; to proposer institutions/grantees to provide or obtain data regarding the proposal review process, award decisions, or the administration of awards; to government contractors, experts, volunteers and researchers and educators as necessary to complete assigned work; to other government agencies or other entities needing information regarding proposers or nominees as part of a joint application review process, or in order to coordinate programs or policy; and to another Federal agency, court, or party in a court or Federal administrative proceeding if the government is a party. Information about Principal Investigators may be added to the Reviewer file and used to select potential candidates to serve as peer reviewers or advisory committee members. See System of Record Notices, NSF-50, "Principal Investigator/Proposal File and Associated Records," and NSF-51, "Reviewer/Proposal File and Associated Records." Submission of the information is voluntary. Failure to provide full and complete information, however, may reduce the possibility of receiving an award.

An agency may not conduct or sponsor, and a person is not required to respond to, an information collection unless it displays a valid Office of Management and Budget (OMB) control number. The OMB control number for this collection is 3145-0058. Public reporting burden for this collection of information is estimated to average 120 hours per response, including the time for reviewing instructions. Send comments regarding the burden estimate and any other aspect of this collection of information, including suggestions for reducing this burden, to:

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