Systems Biology Data Platform Leveraging the Accelerating Medicines Partnership

Research Opportunity Announcement

Overview Information

Participating Organization(s)	National Institutes of Health (NIH)
Components of Participating Organizations	This Other Transaction (OT) Research Opportunity Announcement (ROA) is to support the *Systems Biology Data Platform (SysBio) Leveraging the Accelerating Medicines Partnership (AMP)* program. This research opportunity will be administered by the NIH Division of Program Coordination, Planning, and Strategic Initiatives (DPSPCI) Office of Strategic Coordination (OSC), also known as the Common Fund.
Research Opportunity Title	Systems Biology Data Platform Leveraging the Accelerating Medicines Partnership (OT2)
Activity Code	This funding opportunity will use the Other Transactions Authority (OTA) governed by 42 U.S. Code § 282 (n)(1)(b). OT awards are not grants, cooperative agreements or contracts and use an OTA, provided by law. Policies and terms for individual OTs may vary between awards. Each award is therefore issued with a specific agreement, which is negotiated with the recipient and may be expanded, modified, partnered, not supported, or later discontinued based on program needs, changing research landscape, performance and or availability of funds.
Research Opportunity Announcement (ROA) Number	**OTA-24-008**
Related Notices	
Research Opportunity Purpose	The purpose of this announcement is to invite applications from eligible organizations to establish the Systems Biology Data Platform (SysBio) Leveraging the Accelerating Medicines Partnership (AMP). Award(s) made through this announcement will provide technical and administrative coordination and support to enable broad use of the data sets and knowledge generated by the different initiatives funded by AMP, potentially in combination with other complementary data sets. The recipient(s) will work collaboratively with the AMP data platforms and the NIH Institutes, Centers and Offices that support them, to coordinate the activities needed to integrate data from across the AMP ecosystem. The end product of SysBio will be a platform that provides a single access point for querying data across the different tissues and conditions studied in the participating AMP projects.
Key Dates	**Release Date of this Research Opportunity Announcement:** March 13, 2024 **Letters of Intent (LOI) Due Date:** April 3, 2024, by 5:00 PM local time of applicant organization. *LOIs are not required to be eligible to submit a full application. However, submitting an LOI is strongly recommended*.

	Application Due Date: May 15, 2024, by 5:00 PM local time of applicant organization. *Late applications to this ROA will not be accepted.* **Award Negotiations:** to begin on or about June 12, 2024. Applicants are expected to respond to written inquiries and attend videoconferences or teleconferences as requested. **Earliest Start Date:** August 1, 2024 **Informational Webinar**: Webinar information will be posted on https://commonfund.nih.gov/venture/sysbio

Agency Contacts

NIH encourages inquiries concerning this announcement and welcomes the opportunity to answer questions from potential applicants.

Scientific Contacts	Anthony Kirilusha, Ph.D. Program Leader Office of Strategic Coordination (OSC) Division of Program Coordination, Planning, and Strategic Initiatives Office of the Director (OD), NIH Email: anthony.kirilusha@nih.gov and sysbio@od.nih.gov
Financial/Agreements Officer Contact	Erna Petrich Team Lead, Other Transactions Agreements Officer Office of Strategic Coordination (OSC) Division of Program Coordination, Planning, and Strategic Initiatives Office of the Director (OD), NIH Email: DOTM@nih.gov (Subject line must include the words “SYSBIO”)

Background:

This initiative is funded through the NIH Common Fund, which supports cross-cutting programs that are expected to have an exceptionally high impact. All Common Fund initiatives invite investigators to develop bold, innovative, and often risky approaches to address problems or to seize new opportunities that offer the potential for rapid progress.

This initiative is part of the Venture Program, a new effort within the Common Fund to support novel, short-term, bold initiatives that have the potential for significant impact in biomedical and behavioral research. Venture initiatives are innovative and nimble, introducing additional flexibility for the Common Fund to tackle a wider variety of research topics. Venture initiatives embrace scientific risk and have strong potential to accelerate science rapidly. These short-term initiatives will be supported for a maximum of 3 years and will include clearly defined goals and milestones to facilitate rigorous measurement of research progress. Each Venture initiative is expected to produce specific deliverables, which can be new knowledge, methods, technologies, or devices.

The purpose of this announcement is to invite applications from eligible organizations to establish the

Systems Biology Data Platform (SysBio) Leveraging the Accelerating Medicines Partnership (AMP). Award(s) made through this announcement will support SysBio by providing technical and administrative coordination and support to enable broad use of the data sets and knowledge generated by the different initiatives funded by AMP and, potentially, other complementary data sets. The recipient(s) will work collaboratively with the AMP data platforms and the NIH Institutes, Centers and Offices that support them, to coordinate the activities needed to integrate data from across the AMP ecosystem. The end product of SysBio will constitute a platform to enable the research community to query data across the different tissues and conditions studied in the different AMP projects from a single access point.

Given the evolving landscape in interoperability projects, and the emerging tools and best practices, this ROA sets out the intended goals for SysBio, and specifies the identified requirements for achieving them. However, the expectation is that applications will provide a roadmap for SysBio that balances these goals with what is feasible, or will become feasible, within the time and budget constraints. The actual scope and tasks, including milestones, will be negotiated before awards are made and periodically reviewed afterward. Funds may be increased, extended, reallocated, recuperated or terminated in cases where unexpected findings, bottlenecks or roadblocks may modify plans or prevent completion of a project attempting to develop the Systems Biology Data Platform Leveraging AMP. Certain milestones may be designated as "go/no-go" milestones and must be successfully achieved by the specified timepoint for project continuation; failure to meet "go/no-go" milestones will be the basis for project termination. See Section 11 about special award terms and additional information.

The Accelerating Medicines Partnership (AMP) is a public-private partnership, including NIH, the FDA, the Foundation for NIH, industry and advocacy organizations. The goal of AMP is to improve the development of new diagnostics and treatments for chronic diseases.

The current AMP projects include:

- Alzheimer's disease 2.0, a successor to AD 1.0 Biomarkers in Clinical Trials
- Autoimmune and Immune-Mediated Diseases (AIM), a successor to AMP Rheumatoid Arthritis and Lupus
- Bespoke Gene Therapy Consortium (BGTC)
- Common Metabolic Diseases (CMD), a successor to Type 2 Diabetes
- Heart Failure
- Parkinson's disease (PD)
- Schizophrenia (SCZ)

A specific objective of AMP is to identify and validate new targets for treatment. To this end, many of the AMP projects have developed data sets of analyses of the target tissues of different diseases, often 'omics-type data. They have created a remarkably rich collection of 'omics' data and patient characteristics across disease-relevant tissue from a variety of chronic diseases.

Most of the AMP projects are focused on understanding diseases in humans, and most attempt to link abnormalities at the molecular and cellular level with patient characteristics and outcomes. Thus, the AMP data sets include both multiple types of 'omics-level data of blood and disease tissues and the characteristics of the patients from whom the tissue was derived (some tissue samples were obtained post-mortem). The emerging data suggest complex mechanisms of diseases, with different mechanisms apparent in individuals with the same clinical diagnosis. In addition, simple observations of high-level reports of the results have revealed multiple, unexpected commonalities between subsets of patients with different diagnoses. The premise of this initiative is that the comparison of mechanisms across

diseases will reveal causative pathways, providing new ways to understand and, critically, treat diseases and the development of a new taxonomy of disease, based on specific mechanisms active in an individual, as well as clinical presentation.

While the AMP data sets cover a range of diseases and tissues, they are siloed in disease-specific platforms built on different standards, making cross platform data discovery and integration difficult. The goal of this project is to create a federated systems biology data ecosystem (Systems Biology Data Platform (SysBio) Leveraging the Accelerating Medicines Partnership (AMP)) as a single access point that allows for discovery, queries, and analysis of data across the AMP data sets. Ultimately, the vision is that an investigator can explore mechanistic hypotheses across different tissues in different diseases, identify subsets of patients with different diseases with shared mechanisms, and link those to patient phenotypes. The objective of SysBio is to facilitate the comparative analysis of the 'omics data across the different tissues and diseases analyzed in the individual AMP projects. In a broader perspective, SysBio will initiate the infrastructure to develop an integrated view of human disease by allowing inclusion of molecular, phenotypic, clinical, and patient reported outcomes data.

SysBio will be the first step in providing a platform for such cross-disease queries. It will provide a prototype, based on a limited set of objectives. Variables to be considered include the types of data to be included (e.g., an initial focus on transcriptomics); the extent of developing a set of sample-related metadata (e.g., metadata related to the sample acquisition, processing and analysis or related to the person from whom it was obtained); required processing and quality control steps (e.g., raw versus pre-processed); outputs (e.g., gene expression matrix or network analysis); etc. SysBio is expected to be modular, with these different aspects built on the infrastructure and data model. The ultimate goal is a platform for an integrated systems analysis of mechanisms that are either shared or specific to different diseases. During the three-year project period, SysBio will focus on developing a prototype resource with an initial focus on queries of specific genes, molecules, and cells across diseases and tissues.

AMP projects are supported by, at last count, 16 NIH Institutes and Centers, and thus represent an NIH-wide resource. SysBio will support a highly efficient and effective biomedical research data infrastructure by connecting the data generated by the AMP programs. By creating a single portal to access the different data platforms, SysBio will improve the FAIR-ness (findability, accessibility, interoperability, and reusability) of NIH-sponsored large-scale datasets. The primary goal of SysBio is to provide a platform that enables scientific use cases that require data from multiple AMP programs. However, interoperability with existing NIH data ecosystem resources is a priority in the design and implementation of SysBio. To the greatest extent possible, SysBio will align with policies and interoperability standards utilized in other NIH data resources, such as the Common Fund Data Ecosystem (CFDE) and the NIH Cloud Platform Interoperability (NCPI) effort. Extending the available harmonized data to include sources outside of AMP is a stated goal of SysBio, especially in years 2 and 3.

In summary, SysBio focuses on multi-omics data sets, which are complex and dynamic, driven by rapid advances in computer and data sciences, and rapidly evolving demands from the biomedical research community. The complexity of the SysBio initiative is further driven by the diversity of data and management practices of the participating platforms. With the goal of maintaining technical cohesion among the participating platforms while solving cutting-edge interoperability and cloud engineering problems, SysBio requires a management and oversight structure that balances the need for a deliberate and strategic approach to implementing critical capabilities (e.g., Researcher Auth Service (RAS)) with the advantages of quickly seizing opportunities presented by emerging use cases and novel technologies. SysBio will also need to adapt to bring additional data repositories into the federated ecosystem as required by the identified priority use cases. Doing so will require the ability to adapt technical (and social) solutions that balance the needs of the researchers with the core missions of the participating repositories and relevant data privacy and security concerns.

Objective Review: NIH will convene an appropriate review group to evaluate applications. See the Objective Review section of this opportunity for further details.

Eligibility: See the Eligibility section of this opportunity.

Application budget: The Common Fund may allocate up to $4,800,000 per year total costs (direct + F&A) for up to three years. The award(s) are contingent upon NIH appropriations and the submission of a sufficient number of meritorious applications. Should multiple awards be made under this solicitation, how funds may be split between awards has not been predetermined and will depend on (1) the objectives proposed by the applicants and how well they fit within the goals of SysBio, (2) the quality of the applications received, (3) availability of funds, and (4) programmatic priorities, but the total for all costs for all awards will be no more than $4,800,000 per year for up to three years.

The application budget should reflect the proposed activities and personnel. The OT mechanism allows for significant flexibility to make budget adjustments as needed to meet NIH's programmatic priorities. Award levels may increase or decrease over time based on funding availability, establishment or termination of (sub-)awards, recipient performance, and other programmatic priorities. It is anticipated that funds will be allocated on a yearly basis.

Cost sharing is not required but may be proposed. However, including a cost share will not impact an applicant's chances of selection.

Anticipated number of Awards: The Common Fund anticipates making one award to carry out the specified tasks, but OT provides the flexibility to make two awards that would each focus on specific tasks.

Award Project Duration: Project duration is anticipated to be up to three (3) years, subject to program needs and availability of funds. Research activities and the associated milestones may be shortened or extended as needed within that period. The OT award will be issued for one year initially and, with mutual agreement, modified and extended annually for two more years. Workplans for research activities and the associated milestones will be negotiated with the NIH OT Program Official and the NIH OT Agreements Officer/Specialist annually at a minimum.

Authority: Other Transactions awards will be made pursuant to current authorizing legislation, including Section 402(n) of the Public Health Service Act, 42 U.S.C. 282(n), as amended.

Outline of this Opportunity

1. SysBio Requirements
2. Eligible Organizations
3. Eligibility Requirements
4. Multiple Principal Investigators and Partnerships among Applicant's Institutions
5. Project Manager/Director Requirement
6. Financial and Risk Assessment
7. Cost Sharing
8. Developing Applications
9. Objective Review
10. Application Timeline
11. Special Award Terms and Information

1. Systems Biology Data Platform (SysBio) Leveraging the Accelerating Medicines Partnership (AMP) – Requirements

The requirements outlined below are those that will be needed to produce the Systems Biology Data Platform Leveraging the Accelerating Medicines Partnership. These are separated into four functions. All applicants must address all four functions. For each of the four functions, a series of tasks are listed, which are anticipated as necessary for operation of the platform. Applicants may provide alternatives but must indicate how these would replace the listed tasks. The expectation is that SysBio will be built in a modular framework, so that the initial requirements will be scaled as data sets, harmonization protocols, and analytic tools are added.

The development work to establish SysBio shall be pursued under the management and oversight of the Common Fund Other Transactions Program Official (OTPO), with scientific and strategic guidance from the SysBio Working Group (WG) composed of NIH staff and SysBio team leads. Given the rapidly evolving landscape of data science and data ecosystems, at the NIH and elsewhere, the milestones proposed and agreed upon during the initial application process are likely to evolve and require adjustment as the SysBio effort moves forward.

SysBio will leverage data from multiple AMP programs and potentially from other NIH and non-NIH sources. Those data will be subject to the governance rules of the host platform. The SysBio platform itself (including the search portal and the cloud-based workspace), as well as any derived data generated to enable SysBio functionality, will be owned and administered by the NIH.

Function 1: Project Management and Coordination

SysBio will require project management. The expectation is that the project will require different teams to accomplish the different functions and coordination between them will be essential. In addition, the AMP ecosystem is complex and includes, at a minimum, the following partners and collaborators:

- The investigators involved in the individual AMP projects.
- The NIH staff involved in management of the AMP awards.
- The funding partners, including industry and advocacy organizations.
- The Foundation for NIH (FNIH), which manages the Executive Committee, which provides oversight for all AMP projects.
- The data management, storage, and access platform unique to each AMP project.
- The community of researchers using data generated by the participating AMP projects.

Consequently, deep coordination of the effort between all of these stakeholders will be required (with assistance from NIH and FNIH staff). Successful launch of SysBio will also require communication about plans and capabilities with the external research community.

Specific anticipated tasks include:

1.a Administrative functions. SysBio will require support for meetings of different teams and working groups. Outputs from those and other documents will require management and dissemination. This task requires organizing SysBio meetings, establishing meeting agendas, capturing and distributing meeting minutes, and tracking follow-up action items. Additionally, a document tracking system must be established to maintain project documentation, such as a summary of activities and key decisions that can be used to report on SysBio progress to the NIH leadership.

1.b Project management and coordination. Channels for internal communication with the project teams will be required as well tracking of the progress of the teams. In addition, coordination is required with the AMP ecosystem, including AMP data platforms, staff at NIH Institutes and Center that are involved in AMP projects, and NIH Offices, including the Office of Data Science Strategy and the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) Office of Strategic Coordination (OSC). Anticipated channels and frequency of communications should be specified. This task also involves tracking milestones and deliverables for SysBio, as well as ensuring that progress reports and other required materials are submitted in a timely manner and are complete. A dashboard must be established to enable SysBio leadership to track milestone progress, delays, and emerging risks or opportunities.

1.c External communication. Develop and deliver presentations to external (to the NIH) audiences for awareness of SysBio and its capabilities. The target audiences will include, but are not limited to, federal agencies, industry, academic and industry researchers, professional societies, and patient advocacy groups. Presenting at conferences and scientific meetings will be required. Additional outreach efforts may include social media, newsletters, workshops (either in-person or virtual), and hackathons (either in-person or virtual). The outreach efforts must be coordinated with the Common Fund and NIH partner platforms.

1.d Termination and transition plan. Applicants must provide a plan that accounts for the possibility of discontinuation of support for SysBio, as well as for transitioning the support, development, and operations of SysBio to a new source. The plan should address the following criteria:

- Information security, including confidentiality, integrity, and availability of data and systems.
- Data transfer process for data created for and stored in the SysBio platform.
- Relevant records, information, and capabilities to effect termination and/or transfer of SysBio support to a new source.
- Deposition of public data into a publicly accessible repository in the event of discontinuation of support.
- Any other provisions deemed necessary by applicant.

Function 2: Data Security

A fundamental purpose of AMP is broad distribution of data while maintaining data security and adhering to use requirements established by consent of the participants. Each AMP project has data contribution and use agreements which establish the requirements and policies for controlled data access. An overarching goal of SysBio is to streamline data access through a secure environment that maintains data privacy. Given the expected modular framework for SysBio, the data security needs may evolve with time. For example, access may initially only be provided to derived data that are not identifiable, but the number and type of datasets hosted by the SysBio Data Platform may evolve with time. Because the SysBio platform and any derived data generated to make the platform functional will be owned and administered by the NIH, guidance for protection of data, such as the Federal Information Security Act (FISMA), must be followed (see Function 2.c below).

2.a Streamline access control mechanisms. Developing a protocol for controlling access to protect identifiable information will be required. A description of how the applicant developed similar protocols in the past (if applicable) is desirable, although not required. SysBio will leverage the work initiated by the NIH Data Science Policy Council and the Scientific Data Council working group on controlled data access coordination. The working group made recommendations on streamlining controlled access mechanisms and re-identification risks. Because these recommendations are not public, they will be shared with the awardee as a part of the kick-off process and will be used in the initial assessment of

opportunities to streamline the AMP projects' controlled access data policies.

2.b Implement single sign-on. The NIH Researcher Auth Service (RAS) provides a consistent process for systems registration through researcher authentication and data authorization. Implementation of the RAS protocol will be necessary to facilitate access to data across the AMP projects. The applicant may propose other solutions that fulfill the single sign-on requirement and are compatible with RAS.

2.c Maintain FISMA compliance. The Awardee's information systems, electronic or hard copy, which contain Federal data need to be protected from unauthorized access consistent with the Federal Information Security Management Act (FISMA) (https://grants.nih.gov/grants/policy/nihgps/html5/section_4/4.1.9_federal_information_security_management_act.htm) and the NIST SP 800-53 standards. A valid authority to operate (ATO) is required to operate within the NIH/OD environment and/or process federal data.

- If the Awardee's system has a valid ATO, the Awardee will need to provide NIH/OD with an assurance package containing the following:
    - Security Assessment Report (SAR) – an independent or third-party security controls assessment consistent with NIST SP 800-53 rev 5, including input from vulnerability and compliance scans as well as penetration tests.
    - Attestation Statement – a document produced either through an independent or third-party assessment that validates that the system is operating in compliance with applicable security controls baselines.
    - Plan of Action and Milestones (POA&M) – a document that captures all identified system security weaknesses, vulnerabilities, and deficiencies related to security and privacy controls.
- If the Awardee's system does not have a valid ATO, the Awardee will need to work with NIH/OD to provide an Assessment & Authorization (A&A) package containing, at a minimum, the following:
    - Security System Plan (SSP) – a document that details the approach to IT security, including an overview of the system environment and in compliance with NIST SP 800-18, Guide for Developing Security Plans for Federal Information Systems, and applicable HHS and NIH policies.
    - Security Assessment Report (SAR) – an independent or third-party security controls assessment consistent with NIST SP 800-53 rev 5, including input from vulnerability and compliance scans as well as penetration tests.
    - Attestation Statement – a document produced either through an independent or third-party assessment that validates that the system is operating in compliance with applicable security controls baselines.
    - Plan of Action and Milestones (POA&M) – a document that captures all identified system security weaknesses, vulnerabilities, and deficiencies related to security and privacy controls.
    - Contingency Plan and Contingency Plan Test – this documents information related to contingency planning for the system. It must be in compliance with NIST SP 800-34, Contingency Planning Guide for Federal Information Systems, and applicable HHS and NIH policies.
- Once a valid ATO is in place for the Awardee's information systems, the system will need to comply with continuous monitoring requirements that will be jointly agreed to by the awardee and NIH/OD. Typically, this consists of:

- Quarterly vulnerability and compliance scan reports.
- Quarterly updated POAMs.
- Annual controls assessment, penetration test reports, and attestation statements.

2.d Compliance with guidance for the use of generative AI. The SysBio Platform must follow HHS guidance on the use of generative AI. Currently available generative AI tools provided by private and public companies offer limited insight into their security posture and cannot provide assurance about the behavior and outputs of the system. External generative AI tools are defined as those not developed and maintained by the applicant for the explicit and exclusive purpose of supporting SysBio. Specifically:

- Personally Identifiable Information (PII) must never be shared with or used in conjunction with external generative AI.
- Consented clinical research or controlled access data must never be shared with or used in conjunction with external generative AI.
- Pre-publication information must never be shared with or used in conjunction with external generative AI.
- External generative AI must not be used as a proxy for software development.

Function 3: Data Harmonization

The central challenge of SysBio is harmonizing data generated by the different AMP projects. Thus, close collaboration between SysBio and the different AMP projects and data platforms will be essential. The CF and other NIH staff involved in SysBio and in AMP will assist in this, but coordination, as specified above in 1.b, will be required.

While each AMP has data derived from different conditions and tissues, the goal of SysBio is the ability to query across these. Each step in the process from sample acquisition and processing to data generation on an analytic technology platform contains multiple variables. The raw data (e.g., sequence data) usually undergoes quality control and then is converted to derived data (e.g., relative gene expression) for statistical analysis, with each of these steps again containing multiple options.

The degree of harmonization required will depend on the questions to be asked. For the purposes of SysBio, with the modular framework, an initial set of use cases will be based on transcriptomic data, focused on simple queries of relative gene expression across tissues. These queries will be based on harmonized single-cell RNA-seq data, in combination with other relevant transcriptomic data available through the participating AMP programs. For this purpose, an initial, limited subset of transcriptomic data available across AMP would be identified and used for harmonization. In some cases, previously derived data might be available, but re-deriving data using a standardized algorithm might be necessary. The decision on whether to re-derive or use existing data will be made based on a combination of factors, including the presence and number of publications referencing the existing data, the quality of the data, the need to re-derive in order to accommodate harmonization, thus expanding the potential usefulness of the data, and other factors that may arise during the data and metadata cataloguing effort. The use of digital object identifiers (DOIs) will be evaluated as a potential solution for facilitating “data freezes”. Currently available software can enable comparison of disparate data sets. However, some cases (e.g., comparison of bulk and scRNAseq) might require generation of small “linker” data to map both together.

A parallel challenge is harmonizing the relevant metadata. Ultimately, one would want to compare molecular mechanisms with clinical presentation and outcomes. For purposes of SysBio, the focus of this 3-year pilot would be to harmonize the metadata associated with specific samples and their

processing, rather than harmonizing metadata about the participants that contributed the samples. Nevertheless, some minimal information (e.g., age, sex, diagnosis, live or post-mortem) about the participant will be needed in the context of the pilot.

3.a AMP file inventory and identification of key datasets. Survey the AMP platforms for the types of files used to represent the relevant transcriptomic data. This includes the syntax for naming and organizing files. Data to be used to develop the pilot of the SysBio Data Platform should be selected based on the source of samples, availability of relevant transcriptomic data, their quality, and the processing approach used to derive transcript-level expression values. Initially, this is likely to involve data from a limited number of AMP projects and, hence, tissues and conditions. Consideration should also be given to data sets outside of AMP if they are available, are complementary to the tissues and conditions of the selected AMP projects and can be effectively harmonized with AMP data. AMP data sets are dynamic, such as adding additional samples or longitudinal outcomes to currently ongoing projects. The applicant must consider a cadence of updates to ensure that the harmonized data provided by the SysBio Data Platform remain current. The proposed updates must balance costs versus timeliness.

3.b AMP metadata inventory. Compile a catalogue of the metadata collected in the different AMP projects. This includes both metadata related to specific samples and metadata about the individual from whom the sample was obtained, as well as naming conventions, if available. As needed, create a unified naming convention based on the data gathered from the participating AMP projects.

3.c Development of the SysBio data model. Develop a solution that enables queries across the AMP datasets. The solution may involve mapping of the conventions used in the different AMPs to a unified syntax and ontology, which would provide the structure for queries across AMP data sets. The applicant must consider how this solution can be scaled to include additional AMP and non-AMP datasets beyond those that will be included in the 3-year pilot phase. Use of existing standards (e.g., UMLS, OMOP, FHIR, SnowMED) should be considered, but is not required if the applicant articulates a compelling alternative approach.

3.d Tools for mapping metadata. Manual recoding of metadata is time-consuming and expensive. Tools will be required to automate mapping between variables in the different AMP data sets, possibly using natural language processing and/or Generative Artificial Intelligence (GenAI) methods. The metadata that would need such mapping will be limited for the pilot phase. However, the applicant must consider how this process can be scaled to include most metadata related to a specific tissue sample analysis as well as patient phenotypes and outcomes.

3.e Production of harmonized data. The expectation is that a common workflow will be defined that permits production of harmonized data sets from AMP projects and other sources. A possible sequence would be to import raw data (e.g., fastq files) to a temporary workspace. These would be aligned, and then raw counts derived and normalized. Relative gene expression (for transcriptomics data) would then be calculated, either per sample for bulk RNA seq or per cell for scRNAseq or nucRNAseq. Whether this derived data would be stored in the SysBio platform or remain on the individual AMP platforms will be an implementation decision likely driven by the size and nature of the harmonized data sets and by the relevant data access and governance mechanisms.

Function 4: Establish the SysBio Platform

The platform incorporates the elements defined in Functions 1-3. As above, the expectation is that an initial search portal prototype will be built by the end of the second year, followed by the public release of the full platform by the end of the third year. The exact functionality that will be available at the time of public release will be determined by negotiations between the SysBio team and NIH Common Fund (CF) staff, with input from the AMP collaborators.

The initial platform must have the ability to report relative gene expression on a per sample basis, for

bulk RNAseq, or for each cell in each sample, for samples derived from different AMP projects (hence from different tissues and conditions). The report will be based on user inputs for searching and selection of which samples to compare. Note that this capacity only requires harmonized derived data. An important goal is to enable inclusion of additional 'omics data, such as metabolomics or epigenetics, in the future. Additionally, the SysBio Data Platform must have tools for analysis of networks or mechanistic pathways across the queried samples. Finally, it must provide the ability to search for files and download (within limits) files, including raw data, into a temporary workspace, where the data can be operated on.

4.a Create the portal. The primary requirement is to deploy a portal that allows users to search the harmonized data by querying for specific genes, molecules or cells. The portal must allow the user to authenticate themselves, must provide basic visualization tools for viewing the results of the data queries (including a summary of the data relevant to the query), must connect to the cloud-based workspace once it's deployed (4.c), and must allow the user to export the results of their queries. Access to the portal must be secured to the appropriate standard as per requirement 2.c. The portal must have sufficient documentation and training options to accommodate new users. The portal must also have the ability to collect and respond to user feedback, to troubleshoot, and to implement critical features identified by users that are needed for the portal to be a useful scientific resource.

4.b Implement a file search function. As described in section 3, key data sets from different AMP projects, and potentially elsewhere, will be selected to be included in the SysBio platform (3.e). The files in these data sets must be harmonized using a standardized workflow to create a derived data set, which must also include relevant, harmonized metadata that was associated with the initial data files (3.f). An API must be developed to search the metadata catalogue (3.b) to identify specific subsets of the derived files, based on selected metadata, that an investigator would like to query. These user-defined subsets of derived files should be usable in the cloud-based workspace, with the potential to temporarily store them there. (4.c). At a minimum, the files should be searchable by tissue/cell type (as appropriate), and condition. Ability to search by gene and other parameters should also be considered.

4.c Develop and deploy a cloud-based workspace. In addition to deploying the SysBio Portal, a cloud-based workspace must be developed that allows users to work with data identified through the file search function of the portal (4.b) and to use standard processing pipelines that were used to generate the harmonized datasets (3.e). Other processing and visualization tools may be developed as needed to support the scientific use of the SysBio Platform. The cloud workspace must:

- Provide users the ability to set up an account through which they can cover the associated cloud compute costs.
- The cloud workspace must have a mechanism for depositing cloud credits into a user's account (with authorization from the NIH), and must address and maintain security controls that are equivalent to FISMA-moderate (NIST. 800-53).
- Allow users to search for AMP datasets (likely via the Portal's search features) and to import the desired data files and metadata into the workspace. Because AMP programs generate large amounts of controlled access data, the cloud workspace must be able to interface with dbGAP and other relevant controlled-access repositories.
- Be compatible with the single sign-on solution implemented under 2.b.
- Where practical, allow the ability to transfer data and workflows between the SysBio cloud workspace and cloud workspace environments provided by other NIH-supported entities, including, but not limited to: All of Us, Common Fund Data Ecosystem (CFDE), NIH Cloud Platform Interoperability program (NCPI), the National Center for Biotechnology Information (NCBI), Sequence Read Archive (SRA), and Help End Addiction Long-term (HEAL).
- Allow users to securely import and use custom-developed and third-party tools and workflows.

The environment should, at a minimum, support the import and integration of tools developed in Python, R, JAVA, and OWL. Integration of Jupyter notebooks is highly desirable, as is support for workflow languages (e.g., WDL, CWL, SnakeMake).

- Develop a cloud credits program that allows for the use of NIH-funded credits, with controls to prevent overspending. This includes providing, in collaboration with the NIH program staff, a transparent and easily accessible mechanism for users to apply for free cloud credits to be used while working in the SysBio cloud workspace.
- Offer relevant training to users and have the ability to collect and respond to user feedback, to troubleshoot, and to implement critical features identified by users that are needed for the cloud workspace to be a useful scientific resource.

A desirable feature will be to allow the user to import their own relevant dataset for co-analysis with AMP data retrieved through the SysBio Portal.

4.d Adapt or develop data query and result visualization tools. The API developed for the portal should allow investigators to query specific genes, molecules, or cells in the specified subsets of derived data, which the user has defined (4.c). The results of the analysis can be presented as a data matrix or heat map of genes or molecules, either per sample or per cell per sample. While such tools exist now, the added complexity here will be the reporting on the basis of tissue and condition. Once a prototype is functional, the capacity to visualize network analyses must be added.

4.e Add datasets and connectivity. Once the prototype is functional, the awardee will work with AMP platforms to include updated or new data and to identify complementary data sets from other sources. This includes the potential to link queries to other ecosystems, such as the Common Fund Data Ecosystem or the NIH Cloud Platform Interoperability project.

2. Eligible Organizations

Non-domestic (non-U.S.) Entities (Foreign applicants) **are not** eligible to apply.

Non-domestic components of domestic organizations **are not** eligible to apply.

Foreign components, as defined in the *NIH Grants Policy Statement*, **are** allowed.

Any public or private non-domestic entity is ineligible to apply for this program as a primary applicant. Additionally, any non-domestic components of U.S. Organizations are ineligible to apply for this program as a primary applicant. Public or private non-domestic entities and non-domestic components of U.S. Organizations are eligible to be listed as sub-contractors/recipients, so long as, they are not excluded from applying for Federal programs throughout the U.S. Government (unless otherwise noted) and from receiving certain types of Federal financial and nonfinancial assistance and benefits.

Applicant organizations may submit more than one application, provided that each application is scientifically distinct. Individuals not affiliated with an organization, or who want to submit an application independently of their current organization, **may not** apply.

The following entities are eligible to apply under this ROA:

Higher Education Institutions

- Public/State Controlled Institutions of Higher Education
- Private Institutions of Higher Education

The following types of Higher Education Institutions are always encouraged to apply for NIH support as Public or Private Institutions of Higher Education:

- Hispanic-serving Institutions
- Historically Black Colleges and Universities (HBCUs)
- Tribally Controlled Colleges and Universities (TCCUs)
- Alaska Native and Native Hawaiian Serving Institutions
- Asian American Native American Pacific Islander Serving Institutions (AANAPISIs)

Nonprofits Other Than Institutions of Higher Education

- Nonprofits with 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Nonprofits without 501(c)(3) IRS Status (Other than Institutions of Higher Education)
- Faith-based or Community-based Organizations
- Regional Organizations

For-Profit Organizations

- Small Businesses
- For-Profit Organizations (Other than Small Businesses)

Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- American Indian/Native American Tribal Governments (Federally Recognized)
- American Indian/Native American Tribal Governments (Other than Federally Recognized)
- Eligible Agencies of the Federal Government
- U.S. Territory or Possession

Other

- Independent School Districts
- Native American Tribal Organizations (other than federally recognized tribal governments)

3. Eligibility Requirements

A successful SysBio application will include teams of individuals with expertise in the following:

- Hands-on working experience in biomedical data and knowledge resources and their use.
- Understanding of the needs of biomedical research and the wider user community in finding, accessing, and using biomedical data and knowledge.
- Development and management of scalable data resources and tools suitable for working with

biomedical data.

- Portal development and management using best research software development practices, and experience in developing platforms with good user experience/user interface features (UX/UI).
- Management and security of personally identifiable research data (e.g., genomics, other -omics, phenotypic and clinical data, imaging).
- Multi-cloud computing.
- Interoperability solutions (e.g., APIs or other microservices, data standards and ontologies, portable workflow languages).
- Computer and personally identifiable data security (e.g., single sign-on, multi-factor authentication and authorization, audit logging, data de-identification, privacy preserving computation).
- Administration and project management of complex research projects involving federated teams.

NOTE: Specific data and/or knowledge integration projects may involve the use of human data, and must comply with all applicable laws and policies, including IRB review.

4. Multiple Principal Investigators and Partnerships among Applicants' Institutions

More than one individual may be named as Principal Investigator (PI) in the application. One individual must be identified as the contact PI. The contact PI and all other individual PIs must each commit at least 10% level of effort to the proposed project. The contact PI must be employed by or affiliated with the applicant organization. ***If a multiple Principal Investigator (MPI) application is submitted, an MPI Leadership plan is required as a part of the overall Leadership Plan (see Section 8.3 below).***

Partnerships among institutions with investigators having complementary skills and expertise to meet the requirements of this ROA are not required but are encouraged.

5. Project Manager/Director (PM/PD) Requirement

NIH expects the proposed project to include an individual that will serve as the PM/PD for the project, with the appropriate scientific expertise and project management responsibilities, who would support the PI(s) with project management and organizational oversight. Such individual should commit at least 50% level of effort to the project.

6. Financial and Risk Assessment

Applicants may be subject to financial analysis and risk assessment conducted by NIH staff.

7. Cost Sharing

Cost Sharing is not required but may be proposed. Those proposing to develop commercial applications or who are using other state or government resources may consider identifying a cost share percentage. Applicants may voluntarily choose to propose a financial plan that includes non-federal resources. The budget submission must clearly identify and justify the use of these resources. Any voluntary cost share must be supported in the application by including a letter of support from the providing organization(s)/individual(s). Inclusion of cost sharing will have no influence in application selection.

8. Developing Applications

8.1 Application Submission Instructions

Complete applications must be submitted under **OTA-24-008** via NIH eRA Commons ASSIST no later than the "***Application Due Date***" shown at the top of this notice, by 5 PM local time of applicant organization.

Late applications submitted to this ROA will not be accepted.

For further information, please consult the FAQ page: https://commonfund.nih.gov/venture/sysbio/faqs

Questions about the scientific scope of this announcement should be addressed to the scientific contact – Dr. Anthony Kirilusha (NIH/OSC): anthony.kirilusha@nih.gov

Letters of Intent (LOIs), due by the "***Letters of Intent Due Date***" shown at the top of this notice, are strongly recommended but not required.

NIH may also share, with PI's and recipient's business official's approval, applications between or among other applicants to ensure optimal configuration of funding, partnerships, and activities. For more details on the review process, see the **Objective Review** section below.

8.2 Letter of Intent

Interested applicants may submit a Letter of Intent (LOI) of no more than 5 pages with sections outlining the following:

- A page that lists key personnel, including their full name, title, affiliation, and e-mail address (1 page).
- A Project Information Summary page (2 pages) as described below for the full application, which includes the name and email addresses for the Contact PI and the Recipient Business Official/Signing Official.
- A brief description of how the PI(s), their institutional affiliations, and teams meet the eligibility requirements stated above (1 page).
- An overview of the planned activities and approach (1 page maximum).

LOIs will be reviewed by NIH staff only to assess eligibility and to identify conflicts of interest for potential reviewers. ***NIH will not be providing feedback about the scientific and technical content for improvements***. Letters of intent must be submitted by email as a single collated PDF attachment to sysbio@od.nih.gov . LOIs submitted by other means may not be considered.

8.3 Full Application

Applications will be accepted only from entities listed in the Eligible Organizations section of this Announcement, who meet the criteria listed in the Eligibility Requirements. Applications submitted from organizations not included in the Eligibility section will not be reviewed. Applications must be prepared and submitted using NIH's eRA ASSIST. Complete applications must be submitted by the Authorized Business Official. The organization must be registered in eRA Commons with one person designated as the contact principal investigator (PI) and one person designated as the Signing Official (SO). Registration process can take a long time, so applicants should begin the registration process as soon as possible.

Failure to complete registrations in advance of the due date is not a valid reason for a late submission. The Signing Official's signature certifies that the applicant has the ability to provide appropriate

administrative and scientific oversight of the project and agrees to be fully accountable for the appropriate use of any funds awarded and for the performance of the OT award-supported project or activities resulting from the application.

Application Format: Applications must be prepared using 11-point font with 1" margins and be single-spaced. Use of graphics and images is allowed, although applications deemed to be using images to bypass the font and margin requirements may be administratively withdrawn. The use of hyperlinks is strictly prohibited.

Full applications must include the following components (page limit in parenthesis):

- **Abstract** (1 page): Provide a summary of the planned activities and approaches and key achievable goals.
- **Specific Aims** (1 page): Provide a narrative describing the rationale and significance of the planned project.
- **Project Information Summary** (2 pages): Provide the information about (note: do not upload this into the "Cover Letter Attachment" field in the ASSIST form but provide it as part of the Attachments section in the form):
  - Project Title
  - Number and title of this Research Opportunity Announcement
  - Principal Investigator(s) first and last name, title, institution, mailing address, email address, and phone number. If multiple Principal Investigators are named, the Contact Principal Investigator must be clearly identified.
  - Name and address of the submitting organization and department, if any, with the organizational Unique Entity Identifier (UEI) number and employment identification number (EIN) provided.
  - Recipient Business Official/Signing Official first and last name, title, institution, mailing address, email address and phone number.
  - Proposed budgets per year for 3 years (direct, indirect and total costs).
  - Proposed project period dates.
  - Full names (last name, first name) of all key personnel, institutional affiliation, title, e-mail address, and percent effort.
  - Confirmation that the work does not involve human subjects or vertebrate animals.
  - Agreement that any or all parts of the application can be shared among other applicants.
- **Project Plan** (12 pages): A full description of the planned activities and approaches to the four functions outlined in the SysBio requirements including:
  - A list of goals and the potential impact of the work to be done if it were successfully implemented. The goals should be broken down into short-term (first year) and long-term (second and third year) categories.
  - Advantages and strengths of the proposed approaches.
  - Examples illustrating the experience and past successes of the project team and team members in similar infrastructure building projects.
  - Discussion of potential risks and alternative plans for resolving them.
  - Plans for partnering with AMP programs and with other sources of NIH-supported data (e.g., the Common Fund Data Ecosystem), including support of working groups.

- Termination and Transition Plan (2 pages): Applicants must provide a termination and transition plan that addresses the requirements listed in Section 1, Function 1.d of this ROA:
  - Information security, including confidentiality, integrity, and availability of data and systems.
  - Data transfer process for data created for and stored in the SysBio platform.
  - Relevant records, information, and capabilities to effect termination and/or transfer of SysBio support to a new source.
  - Deposition of public data into a publicly accessible repository should support for SysBio be discontinued.
  - Any other provisions deemed necessary by applicant.
- **Leadership Plan** (3 pages):
  - Organizational and reporting structure, and personnel responsibilities.
  - Relevant past performance for the team working in and leading large projects and across teams (labs, companies, consortia) and any prior experience of the team working together.
  - Describe how the proposed team meets the eligibility requirements stated above.
  - Multiple Principal Investigator (MPI) Leadership Plan, if applicable.
- **Milestones and Deliverables** (10 pages): The expected project duration is 3 years. Provide a table that lists detailed milestones and deliverables for the first year and high-level milestones and deliverables for years 2 -3. See Section 8.5 below for additional information on how this document should be prepared. A Gantt chart to illustrate the dependencies between the project milestones and project schedule should be provided and identified risks and their mitigation plans should be discussed.
- **Key Personnel List** (1 page): Provide a list of PI(s), PM/PD, Key Personnel, and other significant contributors. For each key person, please provide their first name, last name, title, affiliation, e-mail address, and proposed level of effort.
- **Biosketches** (3 pages per individual): Provide a biosketch of each named key individual appearing in the Key Personnel List. The information in the biosketch should include the name and position title, education/training (including institution, degree, date (or expected date), and field; list of positions and employment in chronological order (including dates); list of relevant publications, proposed level of effort and a personal statement that briefly describes the individual's role in the project and why they are well-suited for this role. Providing successful examples from past work on similar infrastructure building projects as appropriate to illustrate the relevant experience is desired. The format used for an NIH grant application is acceptable: https://grants.nih.gov/grants/forms/biosketch.htm.
- **Other Support** (3 pages per individual)**:** Provide Other Support for all key personnel using NIH grant application format as found here: **https://grants.nih.gov/grants/forms/othersupport.htm**
- **Budget and Budget Justification** (no page limitation): All applications should provide detailed budget information for planned activities and partnerships, as further described in Sections 8.4.
- **Equipment and Facilities** (2 pages): Provide the information about the equipment and other physical resources available to the project team to adequately complete the project milestones.
- **Institutional Letter of Support** (2 pages): A letter of support from the applicant organization indicating institutional commitment to the project (e.g., commitment of space, institutional resources, equipment, administrational support, in kind contributions, etc.). The applicant organization must be willing to enter into a negotiation potentially leading to an Other Transaction

award.

- **Bibliography** (no page limitation).

- **Resource Sharing Plan** (no page limitation)**:** Individuals are required to comply with the instructions for the Resource Sharing Plans as provided in the SF424 (R&R) Application Guide.
- **Data Management and Sharing Plan** (no page limitation)**:** All applications, regardless of the amount of direct costs requested for any one year, must address a Data Management and Sharing Plan.

- **Plan for Enhancing Diverse Perspectives (PEDP)** (2 pages): All applicants must include a summary of strategies to advance the scientific and technical merit of the proposed project through expanded inclusivity. Broadly, diverse perspectives can refer to the people who do the research and the places where the research is done, as well as who participates in the research as part of the study population. The PEDP should provide a holistic and integrated view of how enhancing diverse perspectives is viewed and supported throughout the application and can incorporate elements with relevance to any review criteria as appropriate. The PEDP will be considered a part of the scientific and technical merit of the proposed project and assessed as part of the scientific evaluation in making funding decisions consistent with applicable law.

  The PEDP will vary depending on the scientific aims, expertise required, the environment and performance site(s), as well as how the project aims are structured. Where possible, applicant(s) should align their description with the required elements within the project plan section. The PEDP should include a timeline and milestones for relevant components. Examples of items that advance inclusivity in research and may be part of the PEDP can include, but are not limited to:

  - Discussion of engagement with different types of institutions and organizations (e.g., research-intensive, undergraduate-focused, minority-serving, community-based).
  - Description of any planned partnerships that may enhance geographic and regional diversity.
  - Plan to develop transdisciplinary collaboration(s) that require unique expertise and/or solicit diverse perspectives to address research question(s).
  - Outreach and planned engagement activities to enhance recruitment of individuals from diverse groups as participants including those from under-represented backgrounds.
  - Plan to ensure equitable dissemination of data, tools, and products to all end users.

  The PEDP must include the following:

  - Description of defined activities and actionable strategies for the inclusion of diverse perspectives in the project.
  - Description of how the PEDP will bring unique advantages or capabilities to the project.
  - Milestones or other metrics for the evaluation of PEDP activity progress and success.
  - Proposed monitoring activities to identify and measure PEDP progress benchmarks.
  - Anticipated timeline of proposed PEDP activities.

  While applicants may discuss prior activities, the PEDP should emphasize efforts and contributions that directly relate to the proposed project. Additional information and FAQs about the PEDP are available on the program website at https://commonfund.nih.gov/venture/sysbio .

- **Additional letters of support are not allowed and will not be considered during review process**. Please do not include letters of support in the application beyond the required institutional letter of support.

8.4 Budget details

The Common Fund may allocate up to $4,800,000 for the first-year total costs (direct + F&A) for the four functions defined above. The level of funding for awards made under this solicitation and how funds may be split between the functions has not been predetermined. The funding split will depend on (1) the objectives for the functions proposed by the applicants and how well they fit with the goals of SysBio, (2) the quality of the applications received, (3) availability of funds and (4) programmatic priorities.

The NIH may elect to negotiate any or all elements of the proposed budget.

Institutions with an established Facilities and Administrative (F&A) rate should use their federally approved rate to calculate indirect costs.

Indirect costs on cloud computation, cloud storage, and cloud hosting are capped at 10%. This supersedes the institutionally established indirect costs rate.

F&A costs on foreign -component will be reimbursed at a rate of eight (8) percent of modified total direct costs, exclusive of tuition and related fees, direct expenditures for equipment, and subawards in excess of $25,000.

Procurement of hardware, cloud storage, cloud computing, and the development of software capabilities to support the SysBio portal and the SysBio cloud-based workspace are allowable costs.

In ASSIST Core tab, applicants should enter the total dollar number in the field of **Total Requested Funds.** For budget details, applicants shall download the form from https://commonfund.nih.gov/OTforms and then complete SF424 budget forms on their own computers instead of in internet browsers. The prime applicant is responsible for including all third parties' budget and budget justification. In order to successfully upload budget forms as an attachment into ASSIST, the applicant should flatten the fillable PDF. There are a number of methods to flatten a PDF, the easiest of which is to print it as a PDF.

The detailed budget request should be provided for each year of the three year work period. For each year, it should provide the overall expected cost for each of the following categories: personnel, equipment, travel, funds for third parties (i.e., sub-applicants), if applicable, other direct costs, and total cost (with indirect costs included). The **key** team members must attend SysBio or AMP virtual meetings and actively participate in consortium-wide working group and committee activities. Costs associated with these activities must be appropriately reflected in the proposed budget.

Budget justification must be provided for all budget items.

Budgets must adhere to latest NIH salary limitation notice. NOT-OD-24-057: Guidance on Salary Limitation for Grants and Cooperative Agreements FY 2024 (nih.gov)

Sub-applicants are required to provide details of cost breakdown. Prime applicant should follow their internal policies and procedures to calculate sub-applicant's budget.

8.5 Milestones and Deliverables

The expected initial project duration is 3 years. Given the dynamic nature of SysBio, **applicants must provide detailed description of the goals, milestones and deliverables for the first year.** Provided details should include the goal of the milestone, its deliverables, completion criteria, due dates, how success is defined for a given milestone (e.g., Go/No-Go criteria), and payment/funding schedule. **Each year 1 milestone must also have an explicit total cost associated with its completion.** An *example template* is provided below for reference. **Applicants must also provide the goals, milestones and deliverables for years 2-3.** Details for the latter may not be as extensive, however, enough details should be provided such that the overall goals and aims of the project over the three-year period can be properly assessed in the review. For years 2-3, budget by milestone is optional and not required, but a detailed budget request is still required.

Applicants should plan such that key team members attend the mandatory virtual SysBio PI meetings. Similarly, the key team members are expected to participate in and often lead the technical working groups and committees, which needs to be considered in planning the project and personnel involvement.

Example table of milestones and deliverables:

Note 1: Applicants must ensure that the total budget request (cf. Sections 8.4) is consistent with the sum of item budget estimates in Milestones and Deliverables table for the project.

Note 2: Provided costs for the task should include all the costs for personnel, equipment, facilities, other resources, travel, and other associated costs.

Note 3: Total cost (direct and indirect) for the tasks should be provided.

Milestone	**Tasks/ Subtasks**	**Due Date (Months after award)**	**Milestone Definition**	**Estimated total (direct and indirect) cost for the task**
1	1.1	3	Milestone Name/Description • Bulleted list of tasks completed • Bulleted list of deliverables (including data sharing) • Completion criteria for the task • Potential risk factors and decision points	$375,000
1	1.2	3	Milestone Name/Description a. Bulleted list of tasks completed b. Bulleted list of deliverables (including data sharing) c. Completion criteria for the task d. Potential risk factors and decision points	$500,000

2	2.1	6	Milestone Name/Description 1. Bulleted list of tasks completed 2. Bulleted list of deliverables (including data sharing) 3. Completion criteria for the task 4. Potential risk factors and decision points	$500,000

8.6 Systems Registration

Applicants must submit the full application via the NIH eRA Commons ASSIST system by 5:00 PM local time on the due date (see Key Dates in Section 10). Use OTA-24-008 in the Funding Opportunity Announcement field. Here are instructions for submitting via the NIH eRA ASSIST system. Technical assistance is available from the eRA Service Desk.

To submit a full application via ASSIST, the applicant organization must be registered in eRA Commons (See Submission Instructions). You must be registered in eRA Commons, which may take six (6) weeks or more to complete, so applicants should therefore begin the registration process as soon as possible.

On the eRA Commons home page, select the "Register Organization" link for more details.

To complete registration, if you have not done so already, you may need to register for the following:

• System for Award Management (SAM) – Applicants must complete and maintain an active registration, which requires renewal at least annually. The renewal process may require as much time as the initial registration. SAM registration includes the assignment of a Commercial and Government Entity (CAGE) Code for domestic organizations which have not already been assigned a CAGE Code.

• Unique Entity Identifier (UEI) - A UEI is issued as part of the SAM.gov registration process. SAM registrations prior to fall 2021 were updated to include a UEI. The same UEI must be used for all registrations, as well as on the other transactions application.

• eRA Commons - Once the unique organization identifier (UEI after April 2022) is established, organizations can register with eRA Commons in tandem with completing their full SAM and Grants.gov registrations; all registrations must be in place by time of submission of the full application. eRA Commons requires organizations to identify at least one Signing Official (SO) and at least one Program Director/Principal Investigator (PD/PI) account in order to submit an application.

If you encounter a system issue beyond your control that threatens your ability to complete the submission process on-time, you must follow the Dealing with System Issues guidance.

9. Objective Review

The intent of the objective review for the SysBio initiative is to determine whether the proposed activities meet the goals and vision of this project.

Applications to Other Transactions Research Opportunity Announcements, such as this one, are not reviewed by the standard NIH peer review process, but use custom processes referred to as Objective Review. Responsive, full applications submitted in response to the ROA will be reviewed by subject matter experts via an objective review process. Objective review will involve the submission of written

critiques by subject matter experts against the Review Criteria described below, and interactive individual discussions between those experts and NIH program staff. The subject matter experts will include NIH staff, other federal staff, and may include individuals external to federal government. The review will facilitate further dialogue between select applicants, subject matter experts and NIH program staff so that applications are improved by the review process. Applications may be accepted into the final plan in whole, in part, or not at all. The outcome of each review could result in a modified work plan for each application based on reviewers' comments and recommendations. The modified workplan, as shaped by the review process, will serve as a blueprint for the final negotiated terms and milestones for the resulting awards.

NIH will NOT provide feedback on applications, except as a part of follow-up on an as-needed basis.

NIH will not accept an appeal of the objective review or funding decision outcomes.

Review of Full Applications

Full applications will undergo objective review by subject matter experts including NIH federal employees, NIH contractors, federal employees of other agencies, and outside experts, as needed.

The Overall Impact will be assessed by the four Scored Review Criteria and Additional Review Criteria outlined below:

Scored Review Criteria

The following individual review criteria and their scores will contribute to the final cumulative score.

- Reasonableness and merit of the proposed plans and approaches
  - To what extent are the planned activities likely to advance the goals of the SysBio program and successfully address the four key functions listed in Section 1?
  - Are the milestones and deliverables, and the timeline for fulfilling the planned activities achievable within the three year project time frame?
  - Do the milestones and deliverables have meaningful/quantifiable success criteria?
  - Does the applicant provide an adequate plan for identifying and mitigating technical and management risks?
  - Is the Termination and Transition plan implementable and is it likely to result in an orderly shutdown of SysBio or an orderly transition of support, development, and operations of SysBio to a new source?
  - Is the PEDP well developed?
  - Are the plan for and/or documentation of ability to meet the necessary FISMA-moderate (NIST SP 800-53) equivalent information security compliance provided?
- Appropriateness of the key personnel
  - Is the expertise, demonstrated capabilities, and past performance of the PI(s), PM/PDs, and key personnel appropriate for the proposed activities and successful execution of the proposed complex program? Is the necessary expertise illustrated, documented, and shown adequately with relevant examples from past work?
  - Are the leadership plan and the multiple PI (if applicable) plans appropriate? Is the organizational and reporting structure appropriate? What expertise, if any, is missing from the team?
  - Is there adequate Project Management and administrative support to ensure effective execution and monitoring of activities necessary to complete the project milestones?

- Appropriateness of the equipment and facilities, and other resources
  - Are the proposed facilities, computing infrastructure, backup plans, physical security of any data, communication networks, relevant other equipment, and project management tools adequate to support the successful execution of the proposed work?
  - Are the plans for providing uninterrupted access to the portal and to the cloud-based workspace adequate?
  - Are the plans for replacement of personnel or recruitment of additional personnel adequately addressed?

- Appropriateness of the proposed budget
  - Is the proposed budget reasonable and commensurate with the proposed work?
  - Are there any areas where less funding is needed or where more funding would improve the overall impact?

As needed, the program may follow up with top-scoring applicants by allowing them an opportunity to respond to the weaknesses identified by the objective review, and any additional concerns identified by NIH program staff. Interviews may be conducted if appropriate. A funding decision will be made based on the results of the review and any subsequent responses from the applicants. **NIH will NOT provide feedback on applications, except as a part of follow-up on an as-needed basis**.

Post-review Funding Plan

NIH intends to fund one award for SysBio but may fund two or more entities (potentially across different applications) as part of a reorganized collaboration, teaming arrangement, or other means acceptable to the government. However, the actual number of awards will depend on the availability of funds and on how the objectives proposed by the applicants fit the goals of SysBio. If multiple awards are made, the level of funding for individual awards made under this solicitation and how funds may be split between functions has not been predetermined and will depend on (1) the objectives for the centers proposed by the applicants and how well they fit with the goals of SysBio, (2) the quality of the applications received, (3) availability of funds and (4) programmatic priorities. The OT mechanism allows for significant flexibility to make budget adjustments as needed to meet NIH's programmatic priorities. Award levels may increase or decrease over time based on funding availability, establishment or termination of sub-awards, recipient performance, and other program priorities.

Following the review of applications, NIH may assemble teams from all or parts of applications to establish SysBio. Individual components from distinct applications may be selectively funded to achieve the goals set forth herein. Additionally, if, over the duration of the project, some of the components either gain relevance or lose relevance to programmatic goals, the funding for such components may be increased, decreased, or be discontinued.

At any relevant point in the process, including the objective review, NIH reserves the right to:

1) Invite all, some, one, or none of the Principal Investigators (PIs) submitting applications in response to this solicitation to present their application in a Web-based videoconference or a teleconference.
2) Share applications between and among any proposer(s) as necessary for configuring teams, economizing work, and prioritizing activities.
3) Select for negotiation all, some, one, or none of the applications received in response to this solicitation.

4) Accept applications in their entirety or to select only portions of the application for award.

Appeals of the objective review will not be accepted for applications submitted in response to this ROA.

10. Application Timeline

Key Events	**Receipt Dates**	**Action needed by Applicants**
Research Opportunity Announcement (ROA) posted	March 13, 2024	Submit inquiries to sysbio@od.nih.gov and anthony.kirilusha@nih.gov
Informational Webinar	March 18, 2024	Webinar information and its date will be posted on the Frequently Asked Questions website
Submission Deadline for Letters of Intent (LOI)	April 3, 2024	e-mail a single collated PDF to sysbio@od.nih.gov and to anthony.kirilusha@nih.gov
Submission Deadline for Full Applications from invited applicants	May 15, 2024	Submit to ASSIST and e-mail a single collated PDF to the sysbio@od.nih.gov and to anthony.kirilusha@nih.gov; **late applications will NOT be accepted**
Award Negotiations expected to begin	June 12, 2024	Respond to written inquiries; attend videoconferences or teleconferences as requested
Earliest Start Date	August 1, 2024	

11. Special Award Terms and Information

NIH Discretion

The OT award mechanism allows significant ongoing involvement from NIH, including the OT Program Officer, SysBio Initiative Working Group members, OT Agreements Officer, and Division of Other Transaction Management (DOTM) Staff. The OT mechanism provides NIH the flexibility to alter the course of the project in real-time to meet the overarching goals. This may mean an awarded activity could be expanded, modified, partnered, not supported, or discontinued based on program needs, emerging methods or approaches, performance, or availability of funds.

Performance during the award period will be reviewed on an ongoing basis and course corrections will be made, as necessary. As a result, the NIH reserves the right to:

1. Fund projects in increments and/or with options for continued work depending on agreed upon "go/no go" milestones or successful completion of specific project deliverables. The "go/no go" milestones may be both time-based and performance based.
2. Fund projects of two or more entities (potentially across different applications) as part of a reorganized collaboration, teaming arrangement, or other means acceptable to the government.
3. Request additional documentation (certifications, etc.), and
4. Remove participants from award consideration should the parties fail to reach a finalized agreement by addressing the concerns identified in the objective review, and any additional concerns identified by NIH program staff, or the proposer fails to provide requested additional information in a timely manner.

Applications selected for award negotiation may result in the issuance of an OT award based on the nature of the work proposed, the required degree of interaction between parties, and other factors. The NIH reserves the right and sole discretion to engage in negotiation with the selectees submitting a full application under this solicitation.

Award Governance

The NIH will actively engage with awardee(s) to establish a vision and capabilities for the SysBio initiative and to oversee the effort of the awardees to achieve the vision.

NIH Roles and Responsibilities:

- Other Transactions Agreements Officer (OTAO): NIH representative responsible for legally committing the government to an OT award and to the agreement through which terms and conditions are established, and for the administrative and financial aspects of the award. The OTAO is the focal point for receiving and acting on requests for NIH prior approval and is the only NIH official authorized to change the funding, duration, or other terms and conditions of award.
- Other Transactions Agreements Specialist (OTAS): A designee of the OTAO for administrative and financial aspects of the award.
- Other Transactions Program Official (OTPO): Individual within NIH who provides day-to-day programmatic oversight of individual awards, working closely with the OTAO. The OTPO ensures the successful implementation of the SysBio initiative by integrating input from OSC leadership, SysBio Initiative Working Group, SysBio co-chairs, Project Scientists, and other collaborators. The OTPO evaluates and reviews strategic planning activities and award performance, recommends approval

and acceptance of deliverables to the OTAO, and, if warranted by progress or evolving program priorities, recommends budget adjustments to OSC leadership. Additionally, the OTPO may propose creation, adjustment, or removal of milestones and deliverables.

OT Agreement Governance

Other Transactions (OT) are a special type of legal instruments other than contracts, grants or cooperative agreements. Generally, these awarding instruments are not subject to the Federal Acquisition Regulation (FAR), nor to grant regulations unless otherwise noted for certain provisions in the terms and conditions of award. They are, however, subject to the OT authorities that govern the initiative and/or programs as well as applicable legislative mandates. The NIH and its components, including OSC, have been authorized by Congress to use them. They provide considerable flexibility to the government to establish policies for the awards, so the policies and terms for individual OT awards may vary between awards. Each award is therefore issued with a specific Agreement, which is negotiated with the recipient and details terms and conditions for that specific award. Program and administrative policies and the terms and conditions of individual awards are intended to supplement, rather than substitute for, governing statutory and regulatory requirements. Awards or a specified subset of awards also may be subject to additional requirements, such as those included in executive orders and appropriations acts (including the other transaction legislation cited in the Agreement), as well as all terms and conditions cited in the Agreement and its attachments, conditions on activities and expenditure of funds in other statutory or regulatory requirements, including any revisions in effect as of the beginning date of the next funding segment. The terms and conditions of the resulting OT awards are intended to be compliant with governing statutes.

For the awards funded under this ROA, the NIH will engage in negotiations, and all agreed upon terms and conditions will be incorporated into the Agreement. Either a bilateral agreement or a Notice of Award (NoA) will be used as the official Agreement. The signature of the Signing Official in the application certifies that the organization complies, or intends to comply, with all applicable terms and conditions, policies, and certifications and assurances referenced (and, in some cases, included) in the application instructions.

Reporting and Project Meetings

The terms and conditions of award will address this criterion as appropriate based upon the final negotiated terms and agreed upon budget.

The recipient and key project team members will be required to:

- Participate in an initial virtual kick off meeting with NIH staff and SysBio collaborators.
- Participate in site visits or reverse site visits as deemed necessary by the OTPO.
- Participate in monthly virtual progress meetings with NIH staff to ensure program continues to achieve objectives and to discuss progress and strategies. The meeting frequency may be adjusted at the discretion of the NIH program staff to maximize the probability of successfully meeting milestones. At a minimum, virtual progress meetings with NIH staff will be held quarterly.
- Submit a written budget and milestone report quarterly (or more frequently as stated in the OT agreement).
- Actively participate in consortium-wide working group and committee activities.
- i-Edison: Agreement terms and conditions will contain a requirement for patent reports and notifications to be submitted electronically through the i-Edison Federal patent reporting system at https://www.nist.gov/iedison.
- Work with the designated NIH Infosec officer to establish and maintain FISMA compliance.

Costs associated with these activities must be appropriately reflected in the proposed budget.

Management Systems and Procedures

Recipient organizations are expected to have systems, policies, and procedures in place by which they manage funds and activities. Recipients may use their existing systems to manage OT award funds and activities as long as they are consistently applied regardless of the source of funds and across their business functions. To ensure that an organization is committed to compliance, recipient organizations are expected to have in use clearly delineated roles and responsibilities for their organization's staff, both programmatic and administrative; written policies and procedures; training; management controls and other internal controls; performance assessment; administrative simplifications; and information sharing.

Financial Management System Standards

Recipients must have in place accounting and internal control systems that provide for appropriate monitoring of other transaction accounts to ensure that obligations and expenditures are congruent with programmatic needs and are reasonable, allocable, and allowable. A list of unallowable costs will be included in the terms and conditions of the award. In addition, the systems must be able to identify unobligated balances, accelerated expenditures, inappropriate cost transfers, and other inappropriate obligation and expenditure of funds, and recipients must notify NIH when problems are identified. A recipient's failure to establish adequate control systems constitutes a material violation of the terms of the award.

Property Management System Standards

Recipients may use their own property management policies and procedures for property purchased, constructed, or fabricated as a direct cost using NIH OT award funds. The terms and conditions of award will address this criterion as appropriate based upon the final negotiated and agreed upon budget. Procurement System Standards and Requirements Recipients may acquire a variety of goods or services in connection with an OT award-supported project, ranging from those that are routinely purchased goods or services to those that involve substantive programmatic work. Recipients must acquire goods and services under OT awards in compliance with the organizations established policies and procedures. The terms and Conditions of award will address this criterion as appropriate based on the final negotiated and agreed upon budget.

Organizational Conflicts of Interest (OCIs)

Applicants are required to identify and disclose all facts relevant to potential OCIs involving subrecipients, consultants, etc. Under this section, the proposer is responsible for providing this disclosure with each Detailed Plan. The disclosure must include the PI/Collaborators', and as applicable, proposed member's OCI mitigation plan. The OCI mitigation plan must include a description of the actions the proposer has taken, or intends to take, to prevent the existence of conflicting roles that might bias the proposer's judgment and to prevent the proposer from having an unfair competitive advantage.

The government will evaluate OCI mitigation plans to avoid, neutralize, or mitigate potential OCI issues before award issuance and to determine whether it is in the government's interest to grant a waiver. The government will only evaluate OCI mitigation plans for applications that are determined selectable. The government may require applicants to provide additional information to assist the government in evaluating the proposer's OCI mitigation plan. If the government determines that a proposer failed to fully disclose an OCI or failed to reasonably provide additional information requested by the government to assist in evaluating the proposer's OCI mitigation plan, the government may reject the Detailed Plan and withdraw it from consideration for award.

Monitoring

Recipients are responsible for managing the day-to-day operations of OT award-supported activities using their established controls and policies. However, to fulfill their role in regard to the stewardship of federal funds, the program team will monitor their OT awards to identify potential problems and areas where technical assistance might be necessary. This active monitoring is accomplished through review of reports and correspondence, audit reports, site visits and other information, which may be requested of the recipient. The names and contact information of the individuals responsible for monitoring the programmatic and business management aspects of awards will be provided to the recipient at the time of award.

Monitoring of a project or activity will continue for as long as NIH retains a financial interest in the project or activity as a result of property accountability, audit, and other requirements that may continue for a period of time after the OT award is administratively closed out and NIH is no longer providing active OT award support.

Audit

NIH OT recipients for the Program are subject to the audit requirements of OMB 2 CFR 200, Subpart F-Audit Requirements, as implemented by DHHS 45 CFR Subpart F. In general, 45 CFR 75, Subpart F-Audit Requirements requires a state government, local government, or non-profit organization (including institutions of higher education).

For-profit organizations have two options regarding the type of audit that will satisfy the audit requirements. The recipient either may have (1) a financial-related audit (as defined in, and in accordance with, the Government Auditing Standards (commonly known as the “Yellow Book”), GPO stock 020-000-00-265-4, of a particular award in accordance with Government Auditing Standards, in those cases where the recipient receives awards under only one DHHS program, or (2) an audit that meets the requirements of 45 CFR 75, Subpart F-Audit Requirements.

Noncompliance or Enforcement Actions: Suspension, Termination, and Withholding of Support. If a recipient has failed to materially comply with the terms and conditions of award, NIH may take one or more enforcement actions, which include disallowing costs, withholding of further awards, or wholly or partly suspending the OT award, pending corrective action. NIH may also terminate the OT award.

Public Policy Requirements and Objectives

NIH intends to uphold high ethical, health, and safety standards in both the conduct of the research it funds and the expenditure of public funds by its recipients. The signature of the Signing Official on the application certifies that the organization complies, or intends to comply, with all applicable policies, certifications, and assurances.