The Human BioMolecular Atlas Program (HuBMAP) Integration, Visualization & Engagement (HIVE) Collaboratory (OT2)

Research Opportunity Announcement

Overview Information

Participating Organization(s)	National Institutes of Health (NIH)
Components of Participating Organizations	This Research Opportunity Announcement (ROA) is developed as a Common Fund Initiative through the NIH Office of the Director, Office of Strategic Coordination (OD-OSC). All NIH Institutes and Centers participate in Common Fund initiatives. The FOA will be administered by OD-OSC on behalf of the NIH.
Research Opportunity Announcement Title	The Human BioMolecular Atlas Program (HuBMAP) Integration, Visualization & Engagement (HIVE) Collaboratory (OT2)
Activity Code	**OT Other Transaction (OT2)** This Research Opportunity will use the Other Transactions Authority governed by 42 U.S. Code § 282 (n)(1)(b). Other Transactions (OT) are not grants, cooperative agreements, or contracts. They are used by the NIH to provide considerable flexibility in establishing policies for the awards; policies and terms for individual OT awards may vary between awards, each negotiated with a specific agreement, which may be expanded, modified, partnered, not supported, or later discontinued based on program needs, changing research landscape and or availability of funds. The OT2 will allow aspects of different proposals to be selected and funded to work collaboratively to achieve the goals of the HuBMAP program.
Research Opportunity Announcement (ROA) Number	OTA-21-012
Related Notices	RFA-RM-21-026, Tissue Mapping Centers for the Human BioMolecular Atlas Program (U54 Clinical Trial Not Allowed) RFA-RM-21-027, Demonstration Projects for the Human BioMolecular Atlas Program (U01 Clinical Trial Not Allowed)
Catalogue of Federal Domestic Assistance (CFDA) Number(s)	N/A
Research Opportunity Purpose	The purpose of this Research Opportunity Announcement (ROA) is to solicit applications for the HuBMAP Integration, Visualization & Engagement (HIVE) Collaboratory that will: 1) manage the data generated by the HuBMAP Consortium, 2)

	coordinate internal and external Consortium activities, 3) develop novel tools for visualizing, searching, and modelling data and 4) build an atlas of tissue maps. The HIVE will be composed of projects funded in three component areas all of which are expected to work closely together to act as the unified backbone for the HuBMAP Project. The HIVE is expected to work closely with the other funded projects as part of the HuBMAP Consortium to catalyze development of a framework for mapping the human body and exemplarily maps with high spatial resolution. An application may propose only work in one component area. However, a coordinated set of separate applications, each describing a separate component but with a common vision, can be proposed. NIH encourages investigators or teams who have not been supported to date by HuBMAP to apply.

Objective Review	NIH will convene appropriate review groups to evaluate proposals. See the Objective Review section of this opportunity for further details.
Eligibility	See the Eligibility section of this opportunity.
Funds Available and Anticipated Number of Awards	The budget for this effort is planned for approximately $40 million over a 4-year period. NIH anticipates making 5-8 awards. However, NIH Common Fund procedures and OT mechanisms allow for significant flexibilities to make adjustments necessary to pursue catalytic and transformative initiatives. Award levels may increase or decrease over time based on programmatic needs, funding availability, and recipient performance. Application budgets should reflect the actual needs of the proposed project. Awards resulting from this opportunity may be up to $4,000,000 total costs per year. OT applicants will be required to provide a well-justified budget that is appropriate for the scope of the proposed work.
Award Project Duration	Initial project periods are expected to be four years or less in duration. Budget periods may be extended with additional award segments from the initially funded budget period by one month to 12 months.
Submission Instructions	All HIVE proposals must be submitted via the NIH eRA ASSIST System by 5:00 p.m. local time on the due date (see Key Dates below). See Proposal Submission Instructions for further information.
Authority	Other Transaction awards will be made pursuant to current authorizing legislation, including Section 402(n) of the Public Health Service Act, by 42 U.S. Code § 282 (n)(1)(b), as amended.

Key Dates

Posted Date	July 2021
Letter of Intent Due Date	October 1, 2021 A Letter of Intent (LOI) is required. See Letter of Intent section.
Invitation to Submit Full Proposal	October 15, 2021. NIH will select specific LOI submitters to submit a full application. See Letter of Intent section.
Earliest Submission Date	October 22, 2021
Proposal Due Date	December 3, 2021. Full proposals must be submitted via ASSIST. See How to Apply section.
Applicant Interview	March 7-8, 2022. See section Objective Review Process.
Earliest Start Date	July 1, 2022
Kickoff Meeting	A HIVE kickoff meeting will be held in September 2022 in Bethesda, MD.

Agency Contacts

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

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List of Sections

The HuBMAP Program

The vision for the Human BioMolecular Atlas Program (HuBMAP) is to catalyze development of a framework for mapping of the human body at high resolution to transform our understanding of tissue organization and function. This will be achieved by:

- Accelerating the development of the next generation of tools and techniques for constructing high resolution spatial tissue maps that quantify multiple types of biomolecules either sequentially or simultaneously.
- Generating foundational 3D tissue maps using validated high-content, high-throughput imaging, and omics assays.
- Establishing an open data platform that will develop novel approaches to integrating, visualizing, and modelling imaging and omics data to build multi-dimensional maps, and making data rapidly findable, accessible, interoperable, and reusable by the global research community.
- Coordinating and collaborating with other funding agencies, programs, and the biomedical research community to build the framework and tools for mapping the human body.
- Supporting pilot projects that demonstrate the value of the resources developed by the program to study individual variation and tissue changes across the lifespan and the health-disease continuum.

This program is funded through the NIH Common Fund as a short-term, goal-driven strategic investment, with deliverables intended to catalyze research across multiple biomedical research disciplines. The NIH Common Fund supports cross-cutting programs that are expected to have exceptionally high impact. All Common Fund initiatives invite investigators to develop bold, innovative, and often risky approaches to address problems that may seem intractable or to seize new opportunities that offer the potential for rapid progress.

The HuBMAP Consortium will scale-up the range of tissues, technologies, data management and its community engagement activities throughout the duration of the program.
The five research initiatives that compose the program are:

- **Transformative Technology Development (TTD)**- This set of initiatives, issued in FY2018 and FY2020, has focused on establishing proof-of-principle with initial validation of transformative new tools, techniques, and methods for mapping the human body at high resolution.

- **Rapid Technology Integration (RTI)** - This initiative, issued in FY2019, has focused on improving the quality and throughput of map generation at key steps of the production pipeline including sample collection, tissue mapping, and data integration and analysis.
- **Tissue Mapping Centers** (TMCs) – This set of initiatives, issued in FY2018, FY2020, and FY2022, seeks to build, benchmark, standardize, validate, and generate extensive data from high-content, high-throughput imaging, and omics technologies to produce 3D human tissue maps at high resolution. Centers are expected to integrate and optimize all parts of the data generation pipeline, from tissue collection and preservation through to data integration, analysis, and interpretation.
- **The HuBMAP Integration, Visualization and Integration (HIVE) Collaboratory** - This set of initiatives issued in FY2018 and FY2022 support a multi-component Collaboratory that is responsible for: 1) managing the data generated by the Consortium, 2) coordinating internal and external Consortium activities, 3) developing novel tools for visualizing, searching and modelling data and 4) building an atlas of tissue maps.
- **Demonstration Projects** - The goal of this initiative, issued in FY2022, is to demonstrate how HuBMAP resources, in combination with new or other datasets or biospecimens as needed, can be used to build better statistical and analytic tools and models of cellular organization and communication in tissues.

Background

Understanding how tissue organization influences a cell's molecular state, interactions, and history is critical for enhancing our understanding of variation in organ function across the lifespan and health-disease continuum. Despite vastly improved imaging and omics technologies as well as many important foundational discoveries, our understanding of how tissues are organized is restricted to a very limited number of microscopic structures. Better insights into the principles governing organization-function relationship will potentially lead to better understanding of the significance of inter-individual variability, changes across the lifespan, tissue engineering, and the emergence of disease at the biomolecular level. However, integrating imaging and omics analysis to comprehensively profile biomolecular distribution and morphology of tissues in a high throughput manner and placing this information into 3D tissue maps amenable to modelling has yet to be fully realized.

In a June 2016 meeting organized by the NIH, experts from the research community identified the following scientific priorities necessary to develop these tissue maps: 1) sourcing high quality tissue from multiple human normal organ sites, 2) processing and preserving tissue for multiple imaging and omics assays, 3) quality control, validation and variation in data generation, 4) data coordination across multiple acquisition techniques, 5) annotation, curation and archiving of the data, 6) browsing, visualizing and searching the data, 7) building statistical and analytic techniques and models for nonlinear analysis of highly multidimensional data and 8) community engagement.

The HuBMAP program was designed to tackle these priorities in four stages: a setup phase in 2018, a scale-up phase from 2019 to 2021, a production phase from 2022 to 2025 including a transition phase in 2025. The Consortium has made significant progress during the setup and scale-up phases and further information can be found on the Consortium's website. This research opportunity is designed to support the production phase of the program.

Vision for the HIVE (this opportunity)

The primary role of the HIVE is to catalyze the creation and use of cell-resolution molecular maps of human tissues as references for the research community. Building a complete atlas of all human tissues is a very long-term goal that is expected to last well beyond the lifetime of the HuBMAP program. In this context, the HIVE's role is to layout a framework for building such an atlas, demonstrating the construction of exemplary high-quality maps as part of the HuBMAP program and gaining and retaining the trust of the global scientific community in ensuring data sharing and interoperability, portability of analysis methods and common reference outputs.

During the production phase of HuBMAP, the vision for the HIVE is to: 1) build and expand HuBMAP-based reference maps as new data is produced and adapt as the technology improves; and 2) undertake data integration to create more comprehensive, well-annotated maps, 3) actively accept single-cell and related data from the community in addition to managing the HuBMAP data; 4) play a crucial role in coordinating HuBMAP efforts with the worldwide ecosystem of single cell resources to strengthen the utility of HuBMAP as a resource; and 5) develop novel tools to enhance the community's access, capability to assess quality, to query data and help the resource developed by HuBMAP to become the single cell reference for normal human tissue. This vision will be achieved in close collaboration with the HuBMAP Consortium, other programs, and the worldwide research community working closely together to develop an atlas of human tissue maps created from data generated from many different modalities, groups, and tissue donors. Throughout the production phase, users of the HIVE will be able to access, search, query, visualize, and model a growing body of data to better understand the relationship between tissue organization and function, how this relationship may change over the lifespan, across the health-disease continuum, or differences between individuals or populations. These efforts will need algorithmic and ontology based solutions that are focused on biomedical use-cases.

To realize the goal of becoming the "go-to" resource for human tissue reference maps in the rapidly changing biological and biomedical research landscape, it will be key for the HIVE to manage the increased volumes of data, as well as new assays and datatypes, technologies, and software for analysis and visualization. Additionally, a rapidly evolving landscape of related programs and investigator-initiated projects will challenge the HIVE in building a cohesive community and framework. To address these challenges, this research opportunity uses Other Transaction Authority (OTA) which enables the nimble addition or subtraction of specific needed expertise, tools, technologies, and partnerships to realize this vision and proactively adapt to the changing landscape. Use of OTA also facilitates development of close working relationships with non-traditional participants in NIH research and national and international partners pursuing similar goals, to shape a collaborative relationship in a time-critical and sustainable manner.

NIH especially encourages groups and investigators who have not been supported by the HuBMAP program to date to apply. The flexibility provided by the Other Transaction Authority as well as specific requirements that ask each applicant to address features of the current HuBMAP data portal (see section Existing Data Portal) that will be retained, built-upon, expanded and/or phased out will help establish a new, vibrant and effective group of HIVE awardees to meet the goals of the production phase of the HuBMAP program.

Role of the HIVE in the HuBMAP Consortium

All HuBMAP-funded teams are part of the HuBMAP Consortium. All teams are expected to frequently interact with each other, share data, protocols, and tools within the Consortium and, as rapidly as possible, with the broader scientific community. All HuBMAP OT awardees are required to agree to the HuBMAP OT Award Policy Guide and established Consortium policies. HuBMAP is actively managed, and the Consortium will continually be adjusted by adding or subtracting research elements to achieve the overall HuBMAP goal. All awardees will be expected to collaborate and cooperate with NIH staff, one another, and potentially other contributors to HuBMAP.

All HIVE principal investigators, or their designates, and other significant personnel will be required to attend semi-annual HuBMAP investigator meetings, regular teleconferences with Consortium members, and meetings with NIH Staff for the duration of the funding cycle. To this end, all applicants are expected to budget and commit resources to HIVE and Consortium activities.

Scope of an Application

A responsive application to this ROA must address a single component out of the three components that comprise the HIVE (Infrastructure, Tools, or Mapping). The following sections must be included for a complete application and are described below in more detail:

- A research strategy that addresses the activities described below for one of the three components that comprise the HIVE and includes detailed milestones and deliverables,
- A plan to address the scientific, engineering, and sociological needs of that component,
- Biosketches for key personnel,
- A resource sharing plan,
- A plan for enhancing diverse perspectives (PEDP), and
- A plan for coordination, collaboration, and engagement activities (CCE).

In addition, successful proposals will recognize and address the following throughout the application:

- Joint Responsibilities for the entire HIVE and be responsive to these needs.
- How future proposed work builds on existing data and solutions generated by the Consortium and HIVE during the setup and scale-up phases.

An application can be submitted as part of a coordinated set of separate applications, where there is a common vision shared by several teams applying. Further details of the process to follow is included below.

HIVE Component Activities

(Please Note – An earlier version of this Research Opportunity Announcement mistakenly contained information about the PEDP in this section, which has been removed.

Given the complexity of the challenges and diversity of expertise needed, NIH has determined that the HIVE will be composed of projects focused on one of three distinct components. Each application to this ROA will address ***only one*** component, though a coordinated set of applications to more than one component is acceptable and encouraged when pre-existing collaborations and synergies exist.

The three Components compromising the HIVE will require distinct experience and expertise but will function seamlessly together. Primary responsibilities of each component are as follows, however, note that for a seamlessly working HIVE there will be several overlapping, secondary responsibilities.

- **Infrastructure Component (IC)** – the IC will be responsible for building and optimizing the data ingestion, storage, query, and archiving roles and support the internal and external facing informatics tools and Application Programming Interface(s) for the Consortium; use-case driven development that integrates algorithmic and ontology-based methods would be important.
- **Mapping Component (MC**) - the MC will be responsible for building and optimizing the framework for integrated maps and for integrating HuBMAP Tissue Mapping Center-generated tissue maps together in the context of the human body and providing maps to biologists and computational scientists; use-case driven development that integrates algorithmic and ontology-based methods would be important.
- **Tools Component (TC)** – the TC will be responsible for building and optimizing search, analysis, and visualization tools for data generated by HuBMAP and enable adoption and usage of relevant data from the larger community as well as serving data to biologists and computational scientists; use-case driven development that integrates algorithmic and ontology-based methods would be important.

The major scientific and technical activities and goals for each of the components of the HIVE activities are described below. It is likely that multiple projects may be awarded under each component and that awards will be in different geographical areas. It is also expected that interfacing between components will be refined during negotiation of awards or even after awards are made. Thus, it is important for each applicant to demonstrate an understanding of the organization and responsibilities of the HIVE and HuBMAP's overall goals, as well as propose methods for promoting integration of the Components to form an integrated Collaboratory. The HuBMAP Tissue Mapping Centers are expected to bring their own analytical expertise for their assays, and it will be expected that the HIVE will work closely with the TMCs to create uniformly processed datasets.

Infrastructure Component (IC)

The goal for this component is to establish, optimize and scale a reliable, accessible infrastructure for archiving and analysis of data generated by HuBMAP and the wider research community. Applicants should propose a complete solution for continuation of the current data management infrastructure and describe how it will scale-up operations quickly to support an increasing amount of data from TMCs with the consortium as well as community-contributed datasets.

Scientific and Technical Activities

The scientific and technical activities identified below are examples and not intended to be a complete or exhaustive list and the applicants are free to propose others. Applicants for the IC should carefully

consider the vision and goals of the HIVE and the requirements to establish a comprehensive infrastructure for HuBMAP.

The IC is primarily responsible for establishing, maintaining, and/or enhancing the following tasks:

- the infrastructure for storage, computational needs, the pipelines for ingesting, archiving, and exposing the data generated by the TMCs in a controlled, monitored fashion. This should support tracking donors, organs, biospecimen including their spatial location within the organ.
- data ingest infrastructure from non-HuBMAP sources (donor, organ, and biospecimen and their spatial location as and where available).
- infrastructure for HuBMAP web (data) portal and tracking usage of the portal.
- scalable, modular data infrastructure so that it will support multiple analytical pipelines and tools for accessing and visualizing data (both hybrid and public clouds are important elements for building out the infrastructure and should be considered).
- frameworks that minimize resource utilization e.g., electricity consumption as the data available in the portal scales-up the compute needs.
- flexible access to the data by other HIVE components, HuBMAP scientists and the community using APIs.
- capabilities to run different workflows & pipelines run efficiently, at scale. Automating and containerizing these as needed for running these based on various triggers.
- the infrastructure to test, deploy and support the tools and services developed by the other Components and workspaces to HuBMAP consortium members as needed.
- security of the portal and other infrastructure to comply relevant laws and policies for keeping identifiable human data including genomic data protected.
- the scope of data curation responsibilities for the component including addressing the special challenges when ingesting non-HuBMAP data into the HuBMAP resource.
- reporting to the HuBMAP Steering Committee and NIH Program staff about data releases from HuBMAP awardees and usage statistics of the various HuBMAP resources.
- effective dashboards to track progress and usage ensuring FAIR-ness of data and other HuBMAP resources.
- user-authentication based access to controlled access human HuBMAP data; and depositing these in other relevant repositories like NCBI's dbGaP.

Mapping Component (MC)

The purpose of this component is to develop the framework for spatially mapping the data in the context of the human body, organ(s), and regions, as well as implementing novel methods to build tissue level maps that can be stitched together using multi-modal data. The MC component is expected to be able to also define appropriate formats for querying, integrating, and sharing such maps. The maps should be able to support spatial queries including cell identity and naming using expression signatures as well as identification of features representing cell-cell interactions. This will require identifying biologically relevant data by accounting for technical variation. Often tissue location is known only at a rough or crude level leading to approximate placement within a common coordinate framework. In turn, the concept of a common coordinate can be understood at different levels e.g., physical location in 3-D space with a common origin or building up 3-D maps from 2-D slices based on approaches of data integration. The challenges in creating useful maps at scale remain a completely open problem with no

ready answers or the mathematical language to frame it and is in real need of creative solutions. Maps that cut across data modalities and approaches should be proposed. The MC should propose strategies for acquiring new datasets from across the community so that the HuBMAP data portal can grow to become a normal human reference and faithfully represent entire organs over time. It is important to propose a method on how you will evaluate the value of a new datatype (or dataset) that would enhance the value of the normal reference to the community as technologies mature. Prioritizing open-source development will engage the community and increase the trustworthiness of the HuBMAP portal.

Scientific and Technical Activities

The scientific and technical activities identified below are examples and is not intended to be a complete or exhaustive list and the applicants are free to propose others. The applicants should carefully consider the vision and goals of the HIVE and the requirements to establish a comprehensive mapping for HuBMAP.

The MC is primarily responsible for establishing, maintaining, and/or enhancing the following tasks:

- approaches towards creating a common coordinate framework for the organs involved in the HuBMAP program.
- pipelines that construct integrative maps from HuBMAP and non-HuBMAP data using single and multi-modal data.
- integrate and deploy maps created by the Tissue Mapping Centers or others in the larger community.
- biological use-case driven approach to maps construction, storage, and sharing for computational modeling and machine learning methods.
- suitable metadata & APIs for supporting biologically driven use-cases.
- statistical and spatial analysis and quality assessment of the data.
- support for spatial analysis that allows comparisons of healthy vs disease states of a tissue.
- engagement with specific biomedical sub-communities of relevance to MC goals.
- construction of maps at multiple levels of resolution that enables construction of organ-level maps that scale in resolution from single cells to micron-level to size/placement of tissue slices within organs.
- construction of appropriate user-interfaces to browse, search, overlay maps to address specific use-cases.
- identification of data layers and types of maps needed by the research community through a needs assessment or similar; these maps may include reference maps for well-defined tissue microenvironments, genetic variant maps, pseudo-space maps organized with reference to the vasculature, nerves, or other potential tissue landmarks, or changes in biomolecular distribution associated with functional or developmental transitions.
- usage and modifications to (as needed) ontologies to present and utilize these maps effectively.
- the identification, suitable processing, and incorporation of non-HuBMAP datasets that will enhance maps available in the HuBMAP portal.
- the scope of data curation responsibilities for the component including addressing the special challenges when ingesting non-HuBMAP data into the HuBMAP resource.
- computational and algorithmic efficiency needs seriously by creating a framework and reporting standards.

Tools Component (TC)

The major focus of the Tools Component is to create and/or use community standard methods for data analysis, processing, interpretation, and visualization of HuBMAP data. Standardization and uniform processing of all datatypes should be the goal of the Tools Component. The HuBMAP Tissue Mapping Centers are expected to bring their own analytical expertise for their assays, and it will be expected that the HIVE will work closely with the TMCs to create uniformly processed datasets. Another primary focus of this Component is supporting the user community. This particular focus includes ensuring the trustworthiness, quality, and biomedical utility and biological significance of the web (data) portal. The solutions proposed and adopted by this Component must be state of the art while considering computational and algorithmic efficiency. A third key focus is undertaking data analysis by integrating across multiple data modalities. The TC should propose strategies for acquiring new datasets from across the community so that the HuBMAP data portal can grow to become a normal reference. It is important to propose a method on how you will evaluate the value of a new datatype (or dataset) that would enhance the value of the normal reference to the community as technologies mature. Prioritizing open-source development will engage the community and increase the trustworthiness of the HuBMAP portal.

Scientific and Technical Activities

The scientific and technical activities identified below are examples and is not intended to be a complete or exhaustive list and the applicants are free to propose others. The applicants should carefully consider the vision and goals of the HIVE and the requirements to establish a comprehensive mapping for HuBMAP.

The TC is primarily responsible for establishing, maintaining, and/or enhancing the following tasks:

- standardizing data analysis using reproducible workflows across HuBMAP while remaining state of the art at the algorithmic level.
- analytical strategies for validating biological significance of the discoveries.
- enable query framework that accounts for technical variation to better understand and identify biologically relevant data.
- suitable access for biologists and computational scientists can effectively utilize the HuBMAP reference.
- methods to undertake integrative data analysis across multiple modalities of single cell data.
- tools for handling and processing imaging, spatial proteomic or metabolomic data covering activities like image segmentation etc.
- machine learning models to address questions in single cell biology while enabling the larger community to build such models.
- visualization of data, the capability for spatial querying of maps are core activities that the Tools component should support.
- access to APIs (that are open, standardized, secure and documented) so the community can build their own pipelines and visualizations by bringing together data from HuBMAP and other single cell focused efforts to address biomedical questions.
- utility of hybrid or public clouds efficiently to perform computations and running workflows and other pipelines.
- strategies for identifying non-HuBMAP data to add to the HuBMAP portal is a critical and continuing activity for the TC.

- the scope of data curation responsibilities for the component including addressing the special challenges when ingesting non-HuBMAP data into the HuBMAP resource.

Scientific, Technical, and Sociological Challenges

Each component of the HIVE will face many significant scientific, engineering/technical, and sociological challenges that the HIVE needs meet to realize the vision of HuBMAP. Some of these will overlap and it is expected that applicants will demonstrate required flexibility.

There are many open **scientific challenges** that need to be addressed to achieve the scientific vision of HuBMAP becoming the primary source of normal human reference maps. Some of these include:

- how to effectively utilize multiple and seemingly disparate molecular readouts to understand tissue organization, structure, cell-cell communication, and other biological principles?
- how to effectively build out the human spatial reference maps for different tissues while maintaining appropriate orientation and location information based on approaches like defining and developing a common coordinate framework?
- how to effectively curate HuBMAP data, flexibly implement metadata structures while pushing them to the research community to provide sufficiently deep annotations, deepen the structure and content of existing ontologies that are fundamental to HuBMAP needs, and implement experimental design frameworks that are useful in automated processing and useful in ML/AI frameworks?
- how to work with the Tissue Mapping Centers (TMCs; see RFA-RM-21-026) to undertake experimental design so that data integration between multiple molecular readout assays can be effectively undertaken?
- how to evolve and grow existing tissue reference maps as the data grows?
- how to support normal vs disease-related queries when sample sizes are small?
- how to visualize multi-modal data and maps that support biological queries from a diverse background?
- how to effectively integrate sparse 3D data with 2D data?
- how to communicate the state of the art regarding analytical choices adopted?
- how to effectively address the long-standing and novel challenges with imaging data?

Engineering and technical challenges complement the scientific challenges described above and include the following:

- how to implement multiple pathways for users to submit, query, interact with, and visualize data and metadata using web interfaces and API-based (Application Programming Interface-based) connections.
- how to make HuBMAP data, metadata, software, and other digital objects open, findable, accessible, interoperable, and reusable (FAIR) with special emphasis on enabling analysis by individuals with limited software engineering expertise?
- how to continuously update and adapt accessibility as data quantities and diversity increases?
- how to ensure confidentiality, data integrity, provenance, standards, trust, and accountability among the HuBMAP members and within the community?
- how to address all relevant human privacy concerns and proper stewardship of human genomic, phenotypic, and other sensitive information?

- how to ensure cost-effectiveness (both short and long-term) of the solutions adopted?
- how to best incorporate user-feedback into the development cycle?
- how to remain state-of-the-art in this new and constantly evolving scientific area e.g., adapting to continuously developing metadata standards and ever evolving data formats or working within a federated ecosystem of resources or the choice of frameworks for building pipelines?

The biomedical community has found using the some of the following features to be important in solving these challenges, while avoiding over-engineering mistakes such as solving generalized problems, or using too much abstraction in the software engineering approach:

- open and modular approach using iterative techniques significant end-user input.
- optimize, adapt, re-use, and connecting to as many existing standards as possible.
- incentivizing the community by developing and providing solutions that fit within the community's workflows; use-case and 'minimum viable product' based design.
- learning from other communities, in this case, the geospatial mapping, geographic information systems, and astronomy communities tackled similar mapping challenges.

Many of the scientific and technical challenges are complemented by **sociological challenges**:

- Each of the HIVE projects will be heavily dependent on the others to meet their individual and overall goals. Being jointly and independently liable for the outputs of the HIVE, means that strong project management and managers within the HIVE are critical to ensure good communication and alignment of expectations and effort across the consortium
- HIVE projects will be expected to work in close collaboration with other members of the Consortium in many activities including contributing and encouraging adherence to SOPs, data and metadata standards, ontologies, metrics for data generation, participating in cross-site studies, engaging in cross-training, and guiding development of data analysis and visualization tools that can be used by the broader scientific community. Each of the other groups in the Consortium however have specific areas of expertise, goals for their project, and limitations on time and resources for working with the HIVE; therefore, it is critical the HIVE groups are flexible in their approach, build consensus through working groups and the Steering Committee and recognize when and how to proceed when there may not be a complete answer.
- The formation of a strong partnership amongst all HIVE projects and NIH staff cognizant of the entire HuBMAP effort is a key aspect to the success of this initiative. NIH staff will work closely with awardees to assess progress, trouble-shoot, suggest new and alternative directions, and develop agreed-on goals and milestones for each funding period. NIH staff also utilizes External Program Consultants to provide advice directly to NIH.
- For HuBMAP resources and maps to have a significant impact, the HIVE groups need to work closely with the wider international community, getting feedback on needs or use cases, running pilots, and building partnerships to harmonize resources to ensure generated datasets, tools and maps are widely used.
- The larger goal of mapping the entire human body is outside the time and resources available through the HuBMAP program. There are many efforts funded by the NIH and others working on different aspects of this larger goal, each generating their own resources. Our goal is to effectively communicate within and outside of HuBMAP so that these resources are interoperable and not siloed; therefore, a key challenge for the HIVE is how to build and demonstrate an inter-consortia infrastructure that demonstrates this expected level of integration.

Plan for Enhancing Diverse Perspectives (PEDP)

This ROA requires a Plan for Enhancing Diverse Perspectives (PEDP) as part of the application. Applicants are strongly encouraged to read the ROA instructions carfully and view the available PEDP guidance material. The HuBMAP program understands that diverse teams working together and capitalizing on innovative ideas and distinct perspectives outperform homogeneous teams. There are many benefits that flow from a diverse scientific workforce, including: fostering scientific innovation, enhancing global competitiveness, contributing to robust learning environments, improving the quality of the research, advancing the likelihood that underserved populations participate in, and benefit from research, and enhancing public trust.

To support the best science, the HuBMAP Initiative encourages inclusivity in research. Examples of structures that promote diverse perspectives include but are not limited to:

- Transdisciplinary research projects and collaborations among single cell biologists and technologists and researchers from fields such as pathology, anatomy, computational biology, physics, engineering, mathematics, computer, and data sciences, as well as bioethics.
- Engagement from different types of institutions and organizations (e.g., research-intensive, undergraduate-focused, minority-serving, community-based).
- Individual applications and partnerships that enhance geographic and regional heterogeneity.
- Investigators and teams composed of researchers at different career stages.
- Participation of individuals from diverse backgrounds, including groups traditionally underrepresented in the biomedical, behavioral, and clinical research workforce (see NOT-OD-20-031), such as underrepresented racial and ethnic groups, those with disabilities, those from disadvantaged backgrounds, and women.
- Project-based opportunities to enhance the research environment to benefit early- and mid-career investigators.

Applicants should consider how to promote diversity, equity and inclusion (see NIH's Interest in Diversity, information about IDeA states, and the NIH UNITE initiative), and include Component-specific details in the required Plan for Enhancing Diverse Perspectives (PEDP). See below for instructions.

Plan for Coordination, Collaboration and Engagement (CCE) Activities

This ROA requires a Plan for Coordination, Collaboration and Engagement (CCE) Activities for all applications. These activities are crucial for building a cohesive vision, as well as a strong community that will be more than the sum of its parts. The activities identified below are examples for collaborative activities and are not intended to be a complete or exhaustive list. Applicants should carefully consider the vision and goals of the HuBMAP and HIVE and should propose appropriate activities for the Consortium during the production phase. Activities may include:

- organizing HuBMAP workshops and quarterly meetings
- organizing and publicizing technical webinars and working groups meetings
- facilitating collaborative projects, both within HuBMAP and with other consortia

- managing communication channels within the consortium including internal website, shared calendar, email lists, weekly newsletter, etc. that will enable the HuBMAP consortium to work effectively and productively
- managing communication with the wider research community including social media, press releases, external website content, and organizing workshops
- enhance the utility, trustworthiness, and awareness of HuBMAP activities and resources
- curating documents and materials developed by the Consortium
- providing technical training on how to implement and use HuBMAP resources

All components of the HIVE are expected to include CCE activities in their goals and milestones. Based on review of the CCE plans and the needs of the Consortium, funded components of the HIVE should be cognizant that they will be asked to take a lead on different Consortium-wide coordination and collaboration activities that may or may not have been part of their specific CCE plan. See below for instructions.

Joint Responsibilities for all HIVE Components

The three HIVE Components are expected to work together to act as the primary vehicle for internal and external researchers with different levels of interest and capability to access HuBMAP data, by providing a consistent and integrated framework for submitting, checking, publishing, querying, visualizing, and analyzing data.

Joint responsibilities include:

- ensuring FAIR-ness of HuBMAP resources
- ensuring HuBMAP resources are well-curated and documented
- Gaining buy-in from the consortium for best –fit solutions and rapidly developing and implementing them
- ensuring that a federated ecosystem of single-cell resources is supported around the community
- including human centered design and user experience thinking
- enhancing the usability, utility, and usage of HuBMAP resources
- ensuring on-time delivery of milestones so as to minimize adverse impact on other Components of the HIVE and other HuBMAP awardees
- engaging the community to identify and meet the overall goals of the program.

Existing Assays, Datatypes and Solutions

HuBMAP's portfolio of assays generating data is large and diverse. Most assays are high resolution where one can reliably and reproducibly assign specific, identifiable biomolecules to individual cells or extracellular compartments of a tissue. We expect in the production phase that the majority of data within HuBMAP will use one of the following technologies: single-cell RNA or multi-omics sequencing, multiplexed immunofluorescence, RNA-FISH, or Imaging Mass-Spectrometry. Other proven methods adopted by the Tissue Mapping Centers may also makes an important contribution.

In addition, the HuBMAP project generates histological images to verify the quality of the tissue and organ-level imaging like traditional histological staining, autofluorescence, micro-CT images, or OCT (Optical Coherence Tomography) images which are intended to be used to align, integrate and register data in a common coordinate framework. The HuBMAP Tissue Mapping Centers are expected to bring their own analytical expertise for their assays and it will be expected that the HIVE will work closely with the TMCs to create uniformly processed datasets and ensure that technical variability of computational pipelines is minimized, and multiple maps can be integrated into a whole will be the HIVE's responsibility. The HIVE works with the TMCs in assessing and conveying to the community the QA/QC features of the datasets available at the HuBMAP portal.

Existing Data Portal

Several processes, standards, and solutions have been adopted and deployed by the HuBMAP Consortium including the data portal by the HIVE during the scale-up phase of HuBMAP. The current portal and all the tools deployed on it is being developed using modern software design principles. Use of containerization, workflows and API-driven UI development has been emphasized. Other principles include open-source development, modular design, and re-use of existing and popular libraries has been emphasized. These allow for ease of maintenance, flexibility in developing new directions and changes to technology software stacks. Many of these details are available on the HuBMAP data portal.

NIH is also specifically encouraging applications that tackling several important areas that remain to be solved supporting the growth and scientific utility of the HuBMAP data portal. The NIH particularly encourages applications from multidisciplinary teams that would bring any synergistic experience and strengthen the work of the HIVE during the production phase. Prospective applicants are strongly encouraged to contact NIH staff with questions regarding the existing solutions including data ingest, standards, data portal, website, and other solutions created by the awardees in HuBMAP and HIVE during the scale-up phase.

Coordinated Applications

If proposing a coordinated set of separate applications, each describing a separate component, they need to each describe a common vision. Such applications can replicate the same plan to address CCE though specific activities directly relevant to the mission of the component should be separated out. Coordinated applications that establish an overarching structure to harmonize multiple functions and multiple Components are encouraged, although this is not a requirement. Coordinated applications can have the same PD/PI or the same group of multi-PIs (with same or different contact PIs). Coordinated applicants should be cognizant however that only a subset of proposed Components may be funded. Each proposed component will be reviewed separately based on objective review criteria detailed below. It is important to note different Components need different degrees of innovative solutions, different expertise, and will be managed separately with different budget envelopes.

Technical Assistance Conference Call(s)

All applicants are strongly encouraged to contact NIH Staff to discuss the alignment of their proposed work with the goals of this FOA and the HuBMAP Program. A Technical Assistance teleconference will be held for potential applicants from 2-3pm Eastern Time on Friday August 27, 2021. NIH staff will be available to answer questions related to this FOA. Dial in information for the call is posted on the HuBMAP website and slides will be made available on the website for those unable to attend. A list of frequently asked questions (FAQs) related to the program are also posted on the FAQ web page. The information session is open to all prospective applicants, but participation is not a prerequisite to apply.

How to Apply

Eligibility

Successful applicants may or may not have received NIH funding in the past. All entities public and private, small or large, for-profit or not-for-profit, are eligible to apply.

Organizations

Non-domestic (non-U.S.) Entities (Foreign Applicants) **are not** eligible to apply.
Non-domestic (non-U.S.) components of U.S. Organizations **are not** eligible to apply.
Foreign components **are** allowed.

The following entities are eligible to apply under this FOA:

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)

For-Profit Organizations

- Small Businesses

- For-Profit Organizations (Other than Small Businesses)

Governments

- State Governments
- County Governments
- City or Township Governments
- Special District Governments
- Indian/Native American Tribal Governments (Federally Recognized)
- 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)
- Faith-based or Community-based Organizations
- Regional Organizations

Financial and Risk Assessment

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

Cost Sharing

Cost Sharing is not required; however, applicants 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).

Letter of Intent

Applicants are ***required*** to submit a Letter of Intent (LOI) that includes the following information (please follow NIH recommendations on Font and Margin requirement found here, and not to exceed five (5) pages):

- Cover Page to contain the following:
  - Number and title of this research opportunity.
  - Clearly identify the Component the applicant will be requesting funding for.
  - Descriptive title of proposed activity. For a LOI covering multiple, coordinated component applications, please submit separate information for each component, use the same title for all components and denote "[M of N]" (e.g., 1 of 3) in the title. Please also clearly indicate for each component any overlap in personnel.

- Table of Principal Investigator(s), Key Personnel, and Co-Investigators, and their respective Roles and Institutional Affiliations.
- International subawards. YES/NO. If YES, please provide details of foreign PIs and institutions involved.

- Overview and strategy (3 pages maximum). Common descriptions can be used for coordinated applications.
    - Provide an overview of the proposed effort and describe how these will contribute to achieving the goals of the HuBMAP and the HIVE.
    - Briefly address your approach to any potential changes in the current data portal.
    - Describe your approach to PEDP.
    - Describe the research strategy you will pursue to realize the goals of the Component and the HIVE.
    - List deliverables and milestones for the first year of funding and give an overview of major goals and milestones beyond the first year.
    - Give examples of projects you have been instrumental in developing that is relevant to the Component you are applying while describing how you overcame specific challenges in past work. Clearly describe how the challenges you faced in prior work overlap with the Component you are applying to.
    - Describe your experience in working in large complex programs, complex software engineering and sociological situations.
    - Describe the scientific, software engineering, and sociological principles that you will follow in establishing interactions and effective working relationship to develop a seamless HIVE between your Component and the other Components.
    - Describe any collaborative linkages being developed between the project and other NIH funded projects.
    - Describe planned Coordination, Collaboration and Engagement activities
- Personnel qualifications: (1 page maximum). Please indicate personnel involved in coordinated applications.
    - Description of relevant expertise for all key personnel, not to exceed 100 words per person
    - Describe your experience in milestone driven projects.
    - Describe your experience in contributing towards enabling overall goals of a larger effort.
    - Describe your software development philosophy and approaches that you have used in past projects that would be useful in this effort.
    - Estimated budget for the first year.
- Provide up to 3 letters of support, as appropriate. Include any letters of support for the proposed project by appropriate institutional officials. Letters should address the commitment of the parent organization, or any of its partners, to the project and its goals including the PEDP efforts. Do not provide letters of support from individuals who will not be involved in the project's research activities.

The LOI must be emailed to:

Tyler Best, Ph.D.
Email: HUBMAP@mail.nih.gov

by 11:59 PM Eastern Time on or before the due date by the institution's Authorized Organization Representative/Signing Official. The contact Principal Investigator and other relevant institutional officials must be cc'd.

Letters of Intent will be evaluated by NIH Program Staff based on the scientific and technical merit of the proposed project, including: (1) the relevance of the proposed research to the HIVE and the HuBMAP, (2) the expertise, commitment and track-record of the project team, (3) whether the vision and benchmarks, deliverables, timeline, and budget are congruent with the tasks of that component and (4) whether the proposed work will realistically deliver the required capabilities. Collaborative applicants should be cognizant however that only a subset of proposed Components may be invited to submit a full application. Teams which submit Letters of Intent by October 1, 2021 will be notified by October 15, 2021 if they are invited to submit a full application.

Proposal Submission Instructions

To submit a proposal via ASSIST, the proposer must be registered in eRA Commons (see Submission Instructions). Organizations already registered in eRA Commons do not need to register. Once the organization is registered, the individual(s) with the roles of Authorized Organizational Representative (AOR) and Principal Investigator must be affiliated with the organization and have eRA Commons credentials to complete the submission process.
Complete proposals must be submitted via ASSIST by the Authorized Organizational Representative. Use OTA-21-012in the field requesting Research Opportunity Announcement. Here are instructions for submitting via the NIH eRA ASSIST system. Technical help is available at the eRA Service Desk.

Institutions

Participating organizations must complete and maintain the following registrations to be eligible to receive an award. There should NOT be any cost associated with ANY of these registrations. All registrations must be completed prior to award issuance. Registration can take 6 weeks or more, so proposers should begin the registration process as soon as possible.

- **Dun and Bradstreet Universal Numbering System (DUNS)** – All registrations require that proposers be issued a DUNS number. After obtaining a DUNS number, proposers can begin both SAM and eRA Commons registrations. The same DUNS number must be used for all registrations, as well as on the grant application.
- **System for Award Management (SAM) (formerly CCR)** – Proposers 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.
- **eRA Commons** - Proposers must have an active DUNS number and SAM registration in order to complete the eRA Commons registration. Organizations can register with the eRA Commons as they are working through their SAM registration. eRA Commons requires organizations to identify at least one Authorized Organizational Representative and at least one Program Director/Principal Investigator account in order to receive an award. Unaffiliated individuals will be registered as “independent scholars” and will also act as the Authorized Organizational Representative, with the same authority in eRA Commons that the Authorized Organizational Representative(s) has in Grants.gov.

Principal Investigators

All Principal Investigators(s) should already have an eRA Commons account. If not, Principal Investigators should work with their organizational officials to either create a new account or to affiliate their existing account with the proposer organization in eRA Commons. If the Principal Investigator is also the organizational Authorized Organizational Representative, they must have two distinct eRA Commons accounts, one for each role. Obtaining an eRA Commons account can take up to 2 weeks.

Full Proposal Format

The proposal should clearly and fully demonstrate the proposer's capabilities, knowledge, and experience and the budget proposed. Proposals will be accepted from organizations and individuals listed in the Eligibility section of this Announcement and that submit a proposal. Plans must be submitted by the due date listed in the Application Timeline, in text-recognizable PDF (Adobe) format. Applications should follow NIH recommendations on Font and Margin requirement found here. The file size must be no greater than 20 MB.

Budget

The Budget section must provide a realistic, fully justified annual budget and cost proposal for performing the work specified in the FOA over a period of 4 years. Applicants must complete a SF424 budget. **Do not complete the budget form in the ASSIST module**, instead download and complete the relevant form(s) found here: https://commonfund.nih.gov/OTforms. The completed SF424 budget PDF form(s) will then need to be included in the application as an "other attachment" in ASSIST. **Budget information and any related administrative documentation does not count toward the total proposal page limit**.

The Budget should provide the overall expected cost for each of the following categories:

- **Personnel**: The PD/PI of an individual Component must devote a minimum of 2 person-months of effort. For a multi-PI application, the effort for each PI must exceed 1.2 person-months of effort per component. For collaborative applications with the same PD/PI on multiple components, the PD/PI effort must exceed 1.2 person-months of effort per Component.
- **Equipment**: If pieces of specialized equipment or computers are requested, the application must provide a clear justification for the purchase in Budget Justification.
- **Travel**: Applicants should budget for attending in-person annual meetings that could be held in different parts of the country. The number of personnel needed for travel must be justified. Additionally, applicants need to budget for travel to other consortium sites for information exchange and international activities. HIVE Components are encouraged to plan to send personnel to the Tissue Mapping Centers for extended visits to enable effective communication, development of tools and solutions that would enable the Component to create the most effective solutions for realizing the overall goals of the HuBMAP.

- **Resource Sharing Plan -** Applicants are encouraged to identify costs associated with their Resource Sharing Plan, such as costs associated with training on using the shared resources.
- **PEDP Implementation Costs** - Applicants may include allowable costs associated with PEDP implementation
- **CCE Implementation Costs** - Applicants should budget for holding meetings, productivity platforms, and other activities as part of their CCE plan. If workshops and other events are proposed they should be specifically requested as separate items.
- **Subawards/subcontracts/consultants** – including set aside funds to bring in new partners for short-term needs
- **Other direct costs**
- **Total cost** (with indirect costs included)
- **Proposed Cost Share contribution**

Research Plan

The proposal should clearly and fully articulate the proposer's capabilities, knowledge, and experience and the budget proposed.
Proposals will be accepted from organizations and individuals listed in the Eligibility section of this Announcement and must be submitted by the due date listed in the Proposal Timeline. Applications should follow NIH recommendations on Font and Margin requirement found here. The file size must be no greater than 20 MB.

Page Limitations

- Research Plan (20 pages max)
    - Vision and Overview (3 pages max)
    - Scientific, Technical and Management Strategy (12 pages max)
    - Key Personnel Experience and Staffing Plan (3 pages max)
    - Previous Experience (2 pages max)
- Other Attachments
    - Biosketches of Key Personnel
    - Resource Sharing Plan (5 pages max)
    - PEDP Plan (1 page max)
    - Plan for Coordination, Collaboration and Engagement (2 pages max)

On the Research Plan attachment, please use the sub-sections defined below.

Vision and Overview

This section should provide an overview of the component and the vision for how the component will work as part of the HIVE and the HuBMAP Consortium. **Do not** consider this to be a traditional Specific Aims page for hypothesis-driven research. The vision for a coordinated set of applications should be the same for each Component application. Briefly state the goals of the component and how the deliverables address the aims and goals of this ROA. Provide a summary of major tasks to be accomplished with milestones and benchmarks, a timeline, and deliverables. In addition, the following elements should be specifically addressed in the vision and overview section:

- The applicant's vision for how the proposed work fits in within the overall scope of the HIVE and the HuBMAP program as described in this ROA including the long-term vision for the HIVE beyond the duration of HUBMAP;
- Role of diverse perspectives in this vision;
- How the applicant proposes to work with NIH staff and other components of the HIVE to create an integrated Collaboratory;
- Qualifications, past performance, and experience of the key personnel, particularly working on actively managed, milestone-driven projects;
- Flexibility to adapt to the changing needs of this complex project including existing solutions/approaches, and HuBMAP's role within the broader ecosystem of single cell efforts.
- Approach towards Coordination, Collaboration and Engagement;
- Approach towards data curation, data quality responsibilities for the component including addressing the special challenges when ingesting non-HuBMAP data into the HuBMAP resource.
- Specify a framework for how the interactions and handover between the different components should best be handled and how your proposal would fit into such a framework;
- Details of any cost-sharing, institutional commitment or existing infrastructure or collaborations that the component is building off.

Scientific, Technical and Management Strategy

Do not consider this to be a traditional Research Strategy. The objective of this ROA is to identify projects and teams who can develop the data infrastructure and collaborative community needed by the HuBMAP Consortium and the broader research community as described above. This strategic plan should reflect the challenges and activities outlined above in the Scope of an Application throughout.

All applications should address the following.

- *Impact and Significance:* Identify the HIVE Component being addressed in this application. Briefly describe the key features of this application and highlight any conceptual, technical, and/or methodological innovations that increase the significance of the proposed project. Compare your approach to existing state-of-the-art approaches. Applicants should clearly articulate high priority use cases.
- *Implementation Plan:* Describe in detail the specific tasks of relevance and importance to realizing the goals and vision for the Component, the HIVE, and HuBMAP (as appropriate). The plan should demonstrate deep understanding of the technical, scientific, and sociological challenges and present a credible plan to achieve the goals. Some of the key challenges and specific expectations are outlined above in Section I and careful consideration should be given to address these challenges.
- *Building on existing solutions:* How this proposal builds on existing solutions adopted by the HIVE during the scale-up phase should be addressed in the proposal. This could include strategies for retaining and/or deprecation should be proposed including timelines and working with NIH and other awardees.
- *Validation Plan:* Describe relevant use cases and tools that is being proposed including plans to adjust (if needed) based on feedback from NIH staff, the HuBMAP consortium, or the larger community. It is essential to consider the features available in the existing data portal and describe what new features and use-cases are necessary for advancing the goals described in this ROA. Describe how the tasks identified fit into these use cases.
- *Risk Analysis*: Provide a description of potential pitfalls and limitations, and approaches to mitigate them.

- *Tasks, Milestones, Timeline:* For each major task in the first year of the project, describe the expected outcomes and deliverables as well as associated budget and personnel. Include milestones for each task that can be used to evaluate interim and final progress towards the deliverables. Milestones should include quantifiable criteria for success (i.e., go/no-go), identify the customer/user (feedback provider), any interdependencies on other milestones, and should aggressively address major risks in the first year of the project. The criteria for success and milestones should be based on quantitative estimates, if possible. The timeline must include milestones, deliverables, and release of specific infrastructure or other tools. A Gantt chart or similar approach is strongly encouraged. Specific milestones are only required for the first year of the project, while broad outline of theoretical tasks for years 2-4 are required.
- *Flexibility:* Multiple molecular and cellular imaging, sequencing, and mass spectrometry-based mapping assays are currently being utilized by HuBMAP Tissue Mapping Centers. Applications must describe plans for addressing this diversity of assays and plans to accommodate new assay types. Applications need to outline a plan on how feedback will be obtained to refine and adapt objectives and approaches based on expanding data modalities and quantities.

Additional Infrastructure Component (IC) Instructions

There are two additional topics to be included in IC applications:

- The first is that the IC is primarily responsible for supporting the process for requesting data access and maintaining a user authentication system to allow secure access to the data and computing services of the HIVE by individual researchers and groups of users with different access privileges. The user authentication system developed for the HIVE should also be interoperable with established NIH authentication systems, such as the eRA Commons, for approved users of NIH data resources. Also, current NIH processes that authorize access to controlled access data through the NIH Data Access Committees should be supported. The IC in collaboration with the other components is also expected to develop and implement streamlined technical and administrative processes to review and authorize controlled-access data requests, while considering the data use limitations of the studies hosted by the HIVE. The IC is also the entity that will ensure that relevant data is submitted to dbGAP or other such designated resources by the NIH. The IC is expected to implement (as relevant and identified by the NIH or the HuBMAP Steering Committee) relevant policies for data and resource access within and outside the HuBMAP. The Infrastructure Component is expected to propose specific goals and milestones for these tasks and to clearly articulate deliverables on a timeline.
- The second unique requirement comes from the fact that the HIVE will store and permit controlled access to genomic data. This is one of the primary roles of the IC. Genomic and other data must be handled consistent with the NIH Genomic Data Sharing Policy (NOT-OD-14-124) and the NIH Notice for Use of Cloud Computing Services for Storage and Analysis of Controlled-Access Data Subject to the NIH Genomic Data Sharing (GDS) Policy (NOT-OD-15-086). The GDS Policy allows investigators to perform genomic analyses on a cloud platform and should be implemented to protect the privacy and confidentiality of research participants and prevent unauthorized access to data. The IC should conduct regular audits of its data security and protection processes, which should be validated by third party independent assessments. The Precision Medicine Initiative's Data Security Principles Implementation Guide provides an example for auditing and data security protection processes.

Key Personnel Experience and Staffing Plan

Proposers should include a detailed leadership and staffing plan detailing the necessary project administration, organization, and staff to ensure communication, coordination, compliance with ROA expectations, and necessary staffing adjustments. Proposers must demonstrate that the staffing plan has the necessary time commitment and expertise to realize the milestones of the project. The staffing plan must also summarize relevant, key experience of key personnel and current commitment levels on other projects; highlight project managers who will be committing the majority of their time to this project. Describe past collaborations between the key personnel, if any. Responsibility for interfacing with the HuBMAP Tissue Mapping Centers and other Components of the HIVE must explicitly be assigned to one or more individual(s). If the proposal is to be carried out in more than one department or institution, identify what parts of the project will take place at each organization and which senior/key individuals will be responsible for each portion. Identify relevant approaches to managing the complex structure of the HIVE and its inter-dependent milestones and achieving overall partnership to achieve the HIVE goals. Highlight any tools that will be used for communication, coordination or project management. It is essential to describe how solutions proposed will fit the needs of a HIVE made up of unfamiliar personnel in other Components.

As a separate "Other Attachment" please provide biosketches describing key staff who will be assigned to manage performance and supervise the work for each task and subtask (as appropriate). These biosketches will be reviewed to evaluate whether the individuals possess the required experience to perform the specific tasks. **Biosketches should be no more than three (3) pages in length and shall not count toward the page limits**. At a minimum, 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); and a personal statement that briefly describes the individual's role in the project and why they are well-suited for this role. The format used for an NIH grant application is acceptable.

Previous Experience

Proposers should provide a description of any prior and contemporary work that is of significance to the proposal. For each example, please include total funding awarded, dates, deliverables, contact information for a sponsor able to serve as a reference, and a brief description of the project itself, including how the project was analogous to the needs identified in this ROA. Applicants will need to demonstrate prior work AND competency working on milestone-driven, data coordination projects. Applicants are encouraged to clearly identify their unique contributions to existing resources and solutions that are widely used, community engagement strategies used to improve resources, and the inclusion of diverse perspectives.

Other Attachments

Resource Stewardship Plan

In an "Other Attachment" entitled "Resource Stewardship Plan" all applications, are required to summarize a plan for responsible management and sharing of resources. Applicants should indicate their willingness to abide by NIH and Consortium policies regarding privacy, confidentiality and sharing

of information consistent with achieving the goals of the program. A primary goal of the HuBMAP is to lay the foundation for a widely accessible tissue maps and this will require data and resources to be shared quickly and openly once validated. Restrictive licensing and sharing practices for HuBMAP-generated data, tools, and resources could substantially diminish their value and public benefit, and applicants are expected to follow existing or other future HuBMAP policies. Accordingly, awardees should manage data, resources, protocols, tools, and software in a way that achieves this goal without compromising privacy or confidentiality of researchers or research participants. Sharing practices that would prevent or block access to or use of HuBMAP program data, tools, and resources for research purposes or the misuse of data for purposes other than for which it is approved will be considered as breeching the goals of the HuBMAP. Prior to funding, NIH Program Staff may negotiate modifications to the Sharing Plan with the applicant The HIVE components are expected to participate in the NIH Common Fund Data Ecosystem (CFDE) program. This may include participating in working groups, testing interoperability of schemas and data, or creating translators or other means to address incompatibility.

Plan for Data Privacy and Confidentiality: Data security encompasses confidentiality, data integrity, and availability. All three elements are important for the HuBMAP and HIVE and maintaining confidentiality of controlled access data is a particularly high priority. Describe your plans to achieve these goals as pertinent, applicable, and of significance for your Component. Highlight any standards or widely accepted frameworks that you will adopt or be compliant with. Infrastructure Component applicants are expected to provide a detailed explanation of its role and identify individuals with specific responsibilities.

Plan for Public Access*:* The NIH Common Fund intends to maximize the availability of publications and the sharing of underlying data for HuBMAP Projects. Applicants should describe their proposed process for making resulting publications and to the extent possible, the underlying primary data immediately and broadly available to the public or provide a justification if such sharing is not possible. Underlying primary data is expected to be made as widely and freely available as possible while safeguarding the privacy of participants and protecting confidential and proprietary data. Applicants are encouraged to use existing, open licensing approaches and preprint repositories, and may include anticipated charges for Publication or data sharing and resources that may be needed to support a proposed Resource Sharing Plan in the budget plan of their application.

Plan for Data Sharing: Implementation of FAIR (Findable, Accessible, Interoperable, Reusable) Principles is essential for the success of HuBMAP. Consistent with achieving these principles, the NIH expects that information such as collected data, technical protocols, and any other metadata collected under this ROA is to be rapidly made available to the community and in a recognized and reusable format. The HIVE will serve as the central access point for information regarding data, tools, and reagents being developed by the HuBMAP Consortium. If applicable, applicants must abide by the NIH Genomic Data Sharing Policy and should indicate their agreement to abide by it in the data sharing plan.

Plan for Protocol, Tool, and Reagent Sharing*:* As one of the primary goals of this program is to advance research through development, establishment, broad dissemination and use of community resources across the research community, NIH intends that protocols, tools, and reagents generated by the HuBMAP Consortium be broadly available and distributed at minimal cost, and without undue intellectual property constraints, so that they can be as widely used as possible, thus enabling downstream investigations of understudied proteins by the larger scientific community. For all applications and where otherwise applicable, the applicant should discuss plans for sharing and

distribution of non-data resources that will be generated by the proposed project, including models, protocols, biomaterials, and reagents. The HIVE will work with all HuBMAP Consortium investigators to collect, curate, and disseminate information regarding tools and reagents being developed by the HuBMAP Consortium to be disseminated through the HIVE and other sources as appropriate.

Plan for Sharing Software: Applicants are asked to propose a plan to manage and disseminate the improvements or customizations of their tools and resources by others. This proposal may include a plan to incorporate the enhancements into the "official" core software, may involve the creation of an infrastructure for plug-ins, or may describe some other solution. There is no prescribed single license for software produced in this project; however, reviewers will be asked to evaluate the software sharing and dissemination plan based on its likely impact. Any software dissemination plans represent a commitment by the institution (and its subcontractors as applicable) to support and abide by the plan. A software sharing plan guided by the following principles is thought to promote the largest impact:

- The software should be freely available to biomedical researchers and educators in the non-profit sector, such as institutions of education, research institutions, and government laboratories.
- The terms should also permit the dissemination and commercialization of enhanced or customized versions of the software, or incorporation of the software or pieces of it into other software packages.
- To preserve utility to the community, the software should be transferable such that another individual or team can continue development in the event that the original investigators are unwilling or unable to do so.
- The terms of software availability should include the ability of researchers outside HuBMAP and its collaborating projects to modify the source code and to share modifications with other colleagues as well as with HuBMAP. An applicant should take responsibility for creating the original and subsequent "official" versions of a piece of software.

Intellectual Property*:* Intellectual property rights asserted by proposers must be aligned with the open source regime used to distribute software made under the award. Exceptions to open source technology will be considered only in compelling cases. Awardees will own the software and data developed under this award, subject to the Government's royalty-free, nonexclusive, irrevocable right to use, disclose, reproduce, prepare derivative works, distribute copies to the public, and perform publicly and display publicly, in any manner and for any purpose, and to have or permit others to do so. In addition, inventions, technical solutions and methods developed under this solicitation will remain the property of the awardees, who may freely use them for their own commercial purposes, subject to a nonexclusive, nontransferable, irrevocable, paid-up license to the Government to practice, or have practiced for or on its behalf, the inventions, technical solutions and methods throughout the world. Applicants should also be familiar with the NIH statements regarding intellectual property of resources developed with Federal funds (NIH Research Tools Policy and other related NIH sharing policies).

Plan for Enhancing Diverse Perspectives (PEDP) Attachment

In an "Other Attachment" entitled "Plan for Enhancing Diverse Perspectives," all proposals must include a summary of strategies to be used to advance the scientific and technical merit of the proposed project through expanded inclusivity. This PEDP attachment may be no more than 1-page in length and should act like an Executive Summary. This attachment 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 (significance, investigator(s), innovation, approach, and environment) as appropriate. Where possible, applicant(s) should align their description with these required elements within the research strategy section. The PEDP strategies will vary depending on the scientific aims, expertise required, the environment and performance site(s), as well as how the project aims are structured. As described above timelines, milestones and evaluation of these strategies should be described in the research strategy and will be considered as part of the review. 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 enhance recruiting of women and individuals from groups traditionally under-represented in the biomedical, behavioral, and clinical research workforce.
- Proposed monitoring activities to identify and measure PEDP progress benchmarks; indication of willingness to participate in NIH evaluations of PEDPs.
- Plan to utilize the project infrastructure (i.e., research and structure) to support career-enhancing research opportunities for diverse junior, early- and mid-career researchers.
- Description of any training and/or mentoring opportunities available to encourage participation of students, postdoctoral researchers, and co-investigators from diverse backgrounds.
- Plan to develop transdisciplinary collaboration(s) that require unique expertise and/or solicit diverse perspectives to address research question(s).
- Publication plan that enumerates planned manuscripts and proposed lead authorship.
- Outreach and planned engagement activities to enhance recruitment of individuals from diverse groups as research participants including those from under-represented backgrounds.

For further information on the Plan for Enhancing Diverse Perspectives (PEDP), please see resources on the HuBMAP website: https://commonfund.nih.gov/HuBMAP/generalfaqs (see section HuBMAP: Plan for Enhancing Diverse Perspectives (PEDP)).

Plan for Coordination, Collaboration and Engagement

In an "Other Attachment" entitled "Plan for Coordination, Collaboration and Engagement" all proposals must summarize their strategies to advance the cohesion of the consortium and improve communication with the wider research community. The CCE should provide a vision detailing key team-building activities opportunities for feedback and a communications strategy that will integrate the very diverse HuBMAP community and strengthen bridges with other consortia and the wider research community. A CCE plan should not exceed 2 pages, including a timeline detailing key deliverables.
The plan should describe an innovative approach to solving the multi-layered and complex collaboration and outreach needs of the HuBMAP program. Identifying key personnel with an interest and prior experience in encouraging team science approach and a separate budget is necessary as outlined above. Three important constituencies are (1) within HIVE (2) within HuBMAP and (3) within the larger ecosystem of single cell efforts both within other Consortia and individual labs. Within HIVE approaches should identify ways by which multiple groups that constitute the HIVE can work towards an overall goal as well as managing the HIVE's identity and presence. Within HuBMAP approaches should identify

elements like training, scientific presentations, joint publications, all-hands and other types of relevant meetings, and effective solutions for enabling collaborations between computational groups across HuBMAP and experimental and HIVE interactions that can support experimental design. Finally, a vision and strategy about the role of HuBMAP within the larger ecosystem is needed to identify specific strategies and approaches the larger community engagement. Important metrics here include strategies for increasing the user-base both the depth and breadth aspects of the community.

Letters of Support

Provide letters of support, as appropriate. Include any letters of support for the proposed project by appropriate institutional officials. Letters should address the commitment of the parent organization, or any of its partners, to the project and its goals. The parent institution is expected to recognize the project as a formal organizational component and provide documented evidence of space dedicated to the needs of the project, protected time to devote to project activities, staff recruitment, dedicated equipment, or other financial support for the proposed project. Support for the PEDP plans should be reflected in these letters at the appropriate level. The parent institution should provide assurance of its commitment to continuing support of the project in the event of a change in leadership and a well-defined plan for this eventuality should be in place. Both the institution and pertinent departments must show a strong commitment to supporting the project.

If collaborative linkages are being developed between the project and other local NIH funded centers in related areas a letter of agreement from the collaborating PD(s)/PI(s) should be included. Do not provide letters of support from individuals who will not be involved in the project's research activities.

Objective Review Process

Applications will be evaluated by an appropriate review group convened by the Office of the Director, NIH and may include relevant NIH staff and outside experts.

The objective review of the Research Strategy will consider:

- Scientific and technical merit of the proposed project as determined by objective review.
- Availability of funds.
- Relevance of the proposed project to program priorities.
- Evidence that the applicant and investigators are committed to policies as established by the Consortium Steering Committee including with regard to confidentiality, publications, sharing of information and resources, and collaboration.
- Evidence of previous productive, cooperative, collaborative technology development taking into consideration the needs of end users.
- Evidence that the project will contribute to the diversity of technical and intellectual approaches and to the overall goals of the HuBMAP program including the PEDP.

As part of objective review process, all applications:

- Using the criteria described below, those candidates identified as the most outstanding will be invited to participate in an interview on March 7-8, 2022. Interviews will be conducted by a panel of distinguished experts. The interviews will be conducted either in-person or via

videocast. NIH will not support travel for these interviews. The same review criteria described below will be used during the interviews.
- Will receive a review summary upon request.

Funding decisions will be based on the outcome of the objective review process. The level of funding for awards made under this solicitation has not been predetermined but will depend on (1) the objectives proposed by the applicants and how well they fit with the goals of the HuBMAP Program, (2) quality of the proposals received, and (3) availability of funds.

Agreements for all awards will be negotiated with eligible entities whose applications are determined to be the most advantageous and provide the best value to the NIH.
NIH reserves the right to:

- Share proposals between and among any proposer(s) as necessary for configuring teams, economizing work, and prioritizing activities;
- Select for negotiation all, some, one, or none of the proposals received in response to this solicitation;
- Accept proposals in their entirety or select only portions of plans for award.

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

Review Criteria

Only the criteria described below will be considered in the review process. For this announcement, reviewers will consider each of the criterion below and assign each an impact score of 1-9 (1=high score, 9 = low score). An application does not need to be strong in all categories to be judged likely to have major scientific impact. Note that innovation is not a scored criterion. The criteria below are listed in the order of relative importance for evaluation purposes.

Criterion: Merit of Scientific, Technical and Management Strategy

- Vision:
    - Will this Component make a significant contribution to the overall goals and objectives of the Human BioMolecular Atlas Program?
    - Will the proposed work of the Component lead to be a better understanding of the relationship between tissue organization and function?
    - Does the Component have an optimal balance in proposing state-of-art, cutting-edge technologies and approaches that are also proven, validated and reliable to meet the vision for the HIVE?
    - Does the application address relevant scientific, engineering, technological, and sociological challenges?
    - Is there a reasonable likelihood that the approaches specified in this component will work with a different group of applicants for other components?
- Approach:
    - Does the application in its use of technical approaches etc. demonstrate adequate and appropriate flexibility required for the needs of the other components and HIVE overall?
    - Are the proposed project use-cases scientifically important, relevant, feasible and congruent with the goals outlined for the Component?

    - Are anticipated risks associated with the approach adequately addressed? Are the proposed mitigation plans acceptable?
    - Does the preliminary data presented of relevance and adequate in addressing the specific needs and challenges for the HIVE?
    - Does the proposal adequately address challenges posed by the existence of a data portal and the potential changes in HIVE program?
    - Are the proposed milestones and timelines relevant and feasible?
    - Are the data curation goals clear, adequate, and fit for purpose?
    -
- Management:
    - Is the management plan and other activities adequate and sound for creating a partnership between the HIVE components and avoids assuming that the existing groups will continue in the production phase?
    - Will the proposed work be managed effectively, achieve its goals and be flexible to evolving needs as an Other Transaction award?
- Plan for Enhancing Diverse Perspectives:
    - To what extent do the efforts described in the Plan for Enhancing Diverse Perspectives further the significance, approach, and innovation of the application? Have the applicants proposed metrics and goals that could iteratively improve the PEDP outcomes?
- Plan for Coordination, Collaboration and Engagement:
    - Are the plans for coordination, collaboration, and engagement adequate and effective for meeting the overall HuBMAP needs?
    - To what degree do the proposed plans address the multi-faceted outreach needs of the HuBMAP program?
- Resource Stewardship Plan:
    - Reviewers will comment on whether the Resource Stewardship Plan respects privacy and confidentiality while making resources available quickly and in a useable manner by the wider research community.

Criterion: Personnel Qualifications

- Does the performance and duties of the Component Director demonstrate strong qualifications to lead the Component and match their role in the HIVE?
- Does the Component Director and key personnel have the appropriate experience in managing complex, distributed projects involving diverse teams of scientists?
- Does the Component Director and key personnel have a strong track-record of managing, integrating, or analyzing multiplexed, multi-scale imaging and omics data as part of a consortium?
- Is there a clear leadership plan that will enhance the likelihood of success?
- Is the necessary expertise and time committed to the degree required for the research project to be successful as an Other Transaction?
- Are the personnel adequate for the diversity of assays and data involved?
- Are there qualified project manager(s) to meet the needs of the component?
- To what extent will the efforts described in the Plan for Enhancing Diverse Perspectives strengthen and enhance the expertise required for the project?
- Are the personnel qualified and committing sufficient time for meeting the coordination, collaboration and engagement needs of the Consortium?

Criterion: Institutional Commitment

- Is there evidence of a long-term commitment by the applicant's organization (if any) to the applicant and the research in the form of a letter of support?
- Is there evidence of long-term commitment by the applicant's organization to the PEDP proposed?

Award Terms and Information

All Other Transaction awards under HuBMAP include the NIH Other Transaction Award Policy Guide for the HuBMAP Program as part of the Notice of Award. For these terms of award, see the NIH Other Transaction Award Policy Guide for the HuBMAP Program Part II: Terms and Conditions of HuBMAP Other Transaction Awards.
The following special terms of award are in addition to, and not in lieu of, other HHS, and NIH Other Transactions administration policies.

Other Transaction Terms and Conditions of Award

The administrative and funding instrument used for this program will be the Other Transaction, OT2 mechanism, in which active oversight and management by the NIH is expected during the performance of the activities. Under an OT, the NIH purpose is to support and stimulate the recipients' activities by involvement in and otherwise working jointly with the award recipients. OTs offer considerable flexibility to renegotiate or terminate agreements when necessary to promote the overall objectives of the program. The award and post-award negotiations will reinforce program objectives and, if necessary, adjust conditions by which progress is assessed.

Definitions

- **NIH Working Group (NIH WG):** Consists of NIH programmatic staff from multiple Institutes and Centers of the NIH as well as the Office of the Director. This group will be primarily responsible for the stewardship of the HuBMAP Program and will participate as non-voting members in the Consortium committees. The HuBMAP WG is led by the HuBMAP Program Manager and co-chaired by the Directors of NIBIB, NHLBI, and NIDDK. It reports to the Directors of the Office of Strategic Coordination/Common Fund and the Division of Program Coordination, Planning, and Strategic Initiatives for final funding decisions.
- **HuBMAP Program Manager*:*** The HuBMAP Program Manager is an NIH extramural scientist who is responsible for overall coordination of the Consortium and chairs the NIH WG. They will have substantial involvement in assessing progress and making recommendations about future funding. The HuBMAP Program Manager will have substantial scientific programmatic involvement in the direction of all the HuBMAP awards and may consult other NIH and non-NIH experts in making determinations. They will participate as a non-voting member of all Consortium committees and will review and approve Consortium policies.
- **Steering Committee (SC):** The purpose of the SC is to recommend direction for the HuBMAP Consortium consistent with the program goals, develop Consortium policies and projects to build synergy and improve communication and collaboration between the projects, and to

provide a forum for discussing progress, challenges and opportunities for the Consortium. The SC will include PDs/PIs of each of the awards and NIH WG members. The SC will be chaired by two PD/PIs that are nominated by the SC and approved by the NIH WG. An Executive Committee (EC) composed of the co-chairs and the NIH Program Team Leads will meet to set the agenda for SC meetings. The SC will establish subcommittees to oversee the development and implementation of Consortium policies including data release, publications, and standards. It is expected that most of the decisions on the activities of the HUBMAP Steering Committee will be reached by consensus. If a vote is needed, each project PD/PI (or Contact PI in the case of multi-PI projects) will have one vote. NIH staff will be non-voting members of the SC, but will review and approve policies developed by the Steering Committee. When a vote is required, at least 60% of the votes will be required for approval. Steering Committee recommendations will go to the HuBMAP Program Manager and the NIH Working Group for approval.

- **External Program Consultants (EPCs*):*** As part of the HuBMAP program, NIH staff will engage 5-10 external program consultants (EPCs) not funded as part of the program but with relevant scientific and consortium experience to provide input and advice to the NIH WG. This could include reviewing and evaluating the progress of the entire HuBMAP Program or individual awardees as well as recommending changes in priorities for the HuBMAP Program based on scientific advances within and outside of the Consortium. The EPCs will be senior, scientific experts who are not directly involved in the activities of the HuBMAP Program and who agreement to a confidentiality policy. NIH is solely responsible for appointing the EPCs. The EPCs will meet at least twice a year, once in conjunction with the annual investigators meeting. The EPCs may also meet by phone or web at other times of the year, as needed. Annually, the EPCs will provide individual assessments to the NIH of the progress of the Consortium and will present recommendations regarding any changes in the HuBMAP Program as necessary. The assessments and recommendations will be provided through the NIH WG to the Director of the Office of Strategic Coordination, NIH
- **HuBMAP Consortium*:*** The HuBMAP Consortium will be made up HuBMAP awardees, the NIH WG and other scientists and groups the SC agrees to include within the Consortium. The Consortium structure is meant to efficiently and effectively guide all the funded projects to meet the overall goals of the HuBMAP Program.

Project Director/Principal Investigator (PD/PI) Rights and Responsibilities

The Principal Investigator (PI) will coordinate project activities scientifically and administratively. The PI will have primary responsibility for defining the details for the projects and for meeting the goals and milestones developed. The PI will agree to accept the close coordination, cooperation, and participation of the NIH staff (HIVE Project Scientist(s), HIVE Project Manager and Agreement Officer) in those aspects of scientific and technical management of the project as described below.

The Program Director/Principal Investigator (PD/PI) will assume responsibility and accountability to the applicant organization officials and to the NIH for the performance and proper conduct of the research supported under this Research Opportunity Announcement in accordance with the terms and conditions of award, as well as all pertinent laws, regulations and policies (NIH Other Transaction Award Policy Guide for the HuBMAP Program). Furthermore, the Awardee(s)/PD(s)/PI(s) will:

- Work with the HIVE Project Manager to define the research objectives and approaches; plan research; conduct analyses; and publish results, interpretations, and conclusions of studies conducted under the award;
- Adhere to the project benchmarks negotiated at the time of the award, and modified as necessary, by the HIVE Project Manager and Agreement Officer to ensure progress;

- Provide, on request, updated goals and milestones for software engineering and other tasks involved in implementation, including costs as requested;
- Serve on the HuBMAP Steering Committee meetings and relevant Consortium working groups on the phone or in person;
- Assist in developing HuBMAP policies, including data release, privacy, data protection, IP, publications, and other issues that will affect the success of the HuBMAP program;
- Adhere to HuBMAP policies, including those related to data release, IP, publications, and other policies that might be established, as agreed upon by the HuBMAP Steering Committee; for individual awards these policies may be superseded by negotiated terms and conditions of award;
- Ensure that all the goals of the Component are met in a manner that assists other Components of the HIVE to succeed in their goals;
- Serve on the HIVE Implementation Committee and adhere to its decisions and policies, software, and engineering solutions;
- Work in a cooperative and interactive manner with NIH staff, the other HIVE Components and with the other participants in the HUBMAP Consortium to make HuBMAP data rapidly available in an open, findable, accessible, interoperable, and re-useable manner;
- Adhere to the goals and function according to the process and requirements described in this Research Opportunity Announcement and the NIH Other Transaction Award Policy Guide for the HuBMAP Program.

NIH Responsibilities

HIVE Program Officer

The HIVE Program Officer is an NIH extramural scientist who would have substantial involvement in assessing progress and making recommendations about future funding for the HIVE. The HIVE Program Officer may consult other NIH and non-NIH experts in making determinations.
The HIVE Program Officer will:

- Have substantial scientific programmatic involvement in the direction of the Component including in areas such as quality control, research coordination and performance monitoring;
- Coordinate, facilitate and otherwise actively manage the relationships with the HIVE Components; they may also coordinate across individual projects to combine, add to, or subtract from research being done in order to increase quality, accelerate the progress of research, realize economies, or discontinue duplicative or low-priority approaches;
- With the Agreement Officer, and appropriate supplemental personnel, the Program Officer will establish, monitor, and administer each OT award on an ongoing, adaptive basis;
- Approve progress reports, and negotiate goals and milestones;
- Participate in HuBMAP Steering Committee and Executive Committee meetings as a non-voting member;
- Review all activities with input from multiple sources to ensure objectives are being met;
- Attend working meetings of HuBMAP organized activities that involve more than one awardee, as needed, to provide input;
- Assist in developing policies relating to data, experiments, priorities, that effect the entire HuBMAP program;
- Coordinate across individual projects in the HuBMAP program to combine, add to, or subtract from research being done in order to increase quality, accelerate the progress of research, realize economies, or discontinue duplicative or low-priority approaches;

- Recommend any budget changes including termination of an award to the HuBMAP Agreements Officer.

HIVE Project Scientist(s)

HIVE Project Scientist(s) are NIH extramural program scientists who will have substantial scientific involvement during the conduct of this activity, through technical assistance, advice, and coordination. To carry out their duties, Project Scientists may consult with non-NIH experts in the field.
HIVE Project Scientists will:

- Assist in developing and adapting reasonable milestones for the project with the goal of ensuring overall HIVE goals are met;
- Assist in exploring new technologies and approaches for implementing solutions;
- Assist in developing SOPs and policies for all aspects of the HIVE;
- Assist in integrating with all awardees of the HuBMAP program and other relevant non-HuBMAP activities as relevant;
- Assist in avoiding unwarranted duplication of effort;
- Assist in defining appropriate handover and other dependencies between the Components of the HIVE;
- Review and comment to progress of each Component as well as other Components of the HIVE;
- Participate in HIVE Implementation Committee meetings, the HuBMAP Steering Committee meetings and associated working groups and EPC meetings;
- Coordinate across individual Components of the HIVE to combine, add to, or subtract from research being done in order to increase quality, accelerate the progress of research, realize economies, or discontinue duplicative or low-priority approaches;
- Participate in HuBMAP Steering Committee meetings as non-voting members;
- Assist in developing HuBMAP policies on data release, IP, publications, and other issues that will affect the success of HuBMAP program.

Areas of Joint Responsibility

Close interaction among the Component PD/PIs will be required, as well as significant interactions with other funded projects as part of HuBMAP and NIH staff during each phase of the program. The awardees, the HIVE Project Manager and Project Scientists, and other designated NIH Staff will participate in the annual in-person investigator meeting and scheduled conference calls and share information on data resources, methodologies, analytical tools, as well as data and preliminary results. PDs/PIs, key co-investigators, and pre- and post-doctoral trainees, especially those who are members of under-represented minority groups or those from different but related disciplines, are eligible to attend these meetings. EPCs will attend the annual in person meetings. Other government staff may attend the annual investigators meetings.
The SC will serve as the main scientific body of the Consortium, with the following roles:

- The SC will be responsible for coordinating the activities of the projects and is the committee through which the NIH WG formally interacts with the investigators. SC membership will include the PI(s) of each Project, (limited to one vote for a Project with multiple PIs) and NIH staff (non-voting members). The SC Chair(s) will be appointed by the HuBMAP Program Manager and drawn from the individual project PIs. The SC may add additional, non-voting, members, as needed.
- The SC may choose to open Consortium membership to collaborators not funded through the HuBMAP Program, provided that such members agree to abide by policies enacted by the SC. The SC may generate additional conditions that apply to non-awardee members of the Consortium.

- The SC may set up subcommittees as needed to address particular issues. These subcommittees will include representatives from the HuBMAP projects, NIH staff and possibly other experts. The SC will have the overall responsibility of assessing and prioritizing the progress of the various subcommittees.

It is anticipated that multiple subcommittees may need to be formed, for example, to address topics such as:

- Data and Reagent Deposition and Sharing
- Quality Control and Validation
- Publications and Outreach

Termination / Extension

NIH may terminate or extend an award for convenience. For example, to advance the goals of the HUBMAP program, NIH may extend or terminate due to a change in programmatic needs or changes in the availability of funds for the project.

Records will be kept to document performance. In the case of failure to achieve benchmarks, the HUBMAP Program Manager and the Agreement Officer will make serious efforts to assist in improving the performance of a project to meet or adjust benchmarks in order to achieve programmatic goals and protect the investment. NIH generally will suspend (rather than immediately terminate) an OT award and allow the recipient an opportunity to take appropriate corrective action before NIH makes a termination decision. However, NIH may decide to terminate the award if the recipient does not take appropriate corrective action during the period of suspension. NIH may immediately terminate an award when necessary, such as to protect the public health and welfare from the effects of a serious deficiency. If the NIH decides to terminate an award, the termination of the award will be considered a unilateral change and the recipient will not have the right to appeal. Unilateral changes will be based on HIVE Project Manager, HuBMAP Program Manager and external evaluators' assessments and are subject to approval by the Director of the Division of Program, Coordination, Planning, and Strategic Initiatives. Although a decision is made to terminate an award, the recipient must continue to comply with the Record Retention and Access requirements contained in the NIH Other Transaction Award Policy Guide for the HUBMAP Program.

In addition, if NIH determines that 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 Other Transaction award, pending corrective action. NIH may also terminate the award for cause.

An Other Transaction award meeting or exceeding its milestones and playing a central role in meeting programmatic needs may also be extended in time with prior NIH approval. NIH staff will work with awardees to determine additional benchmarks and goals for an extension.

An Other Transaction award also may be terminated, partially or totally, by the recipient. If the recipient decides to terminate a portion of an Other Transaction award, NIH may determine that the remaining portion of the award will not accomplish the purposes for which the Other Transaction award was originally awarded. In any such case, NIH will advise the recipient of the possibility of termination of the entire Other Transaction award and allow the recipient to withdraw its termination request. If the recipient does not withdraw its request for partial termination, NIH may initiate procedures to terminate the entire award for cause.