Personalized Regenerative Immunocompetent Nanotechnology Tissue (PRINT)
Health Science Futures (HSF) Office
Innovative Solutions Opening (ISO) ARPA-H-SOL-24-101
09 April 2024

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PART I: PROGRAM OVERVIEW INFORMATION

- **Federal Agency Name: Advanced Research Projects Agency for Health (ARPA-H), Health Science Futures Office (HSF)**
- **Program Title: Personalized Regenerative Immunocompetent Nanotechnology Tissue (PRINT)**
- **Announcement Type – Initial Announcement**
- **Innovative Solutions Opening Number –** ARPA-H-SOL-24-101
- **Assistance Listing Number –** 93.384
- **Dates (tentative)**
  - Posting Date: **April 9, 2024**
  - Proposers' Day: **May 7, 2024**
  - Solution Summary Due Date and Time: **May 28, 2024, 9:00 AM ET**
  - Proposal Due Date and Time: **July 8, 2024, 5:00 PM ET**

Concise description of the funding opportunity – The **PRINT** program aims to transform organ biofabrication by leveraging recent advances in 3D bioprinting, cell manufacturing, biomaterials, modeling, and tissue engineering. The platform will use patient-matched organ biofabrication to restore normal human organ function for the kidney, heart, or liver. While over 45,000 transplants are performed in the US annually, there are still more than 120,000 patients remaining on wait lists who experience 10% mortality while waiting for donated organs. Current efforts at biofabrication have been limited by their ability to produce a sufficient number of cells and print and maintain complex tissues ready for transplantation. Additionally, no existing approach has been able to deliver a fully patient immunocompetent solution. The **PRINT** program will assemble the necessary tools to facilitate production from a human cell source to a patient matched biofabricated organ to restore at least 40% normal organ function as demonstrated in a large animal model. These tools include: 1) robust methods for cell source differentiation and/or expansion of immunocompetent organ specific cell types, 2) bioreactors and cell biobanks to reach organ level cell number, 3) a library of bioinks capable of recapitulating each unique microenvironment and cellular niche, 4) software to both model complex tissue organization as well as control advanced printing systems, 5) hardware for rapid high resolution precision bioprinting controllers and nozzles, and 6) perfusion chamber enabling effective tissue maturation and transportation to the patient bedside prior to transplantation, among others, as necessary. Successful delivery of this approach will have significant health impact for the future of organ transplantation and pave the way for the necessary next steps in scaling tissue and organ engineering.

- **Anticipated individual awards –** Multiple awards are anticipated.
- **Potential award instruments –** Cooperative Agreements or Other Transaction Agreements (OTA).
- **Agency Contact –** All inquiries shall be sent to **PRINT**@ARPA-H.gov

ACQUISITION STRATEGY

ARPA-H is soliciting proposals to transform organ biofabrication by leveraging recent advances in 3D bioprinting, cell manufacturing, biomaterials, modeling, and tissue engineering. The platform will use patient-matched organ biofabrication to restore normal human organ function for the kidney, heart, or liver. Ultimately, ARPA-H intends to negotiate multiple Cooperative Agreements or Other Transaction (OT) Agreements with proposers whose proposals are most advantageous to the Government.

Proposals are expected to use innovative approaches that include novel technology, enabling revolutionary advances in medicine and healthcare. Specifically excluded are proposals that represent an evolutionary or incremental advance in the current state of the art, including clinical trials of an otherwise developed product. Additionally, proposals directed towards policy changes, traditional education and training, or center coordination, formation, or development, and construction of physical infrastructure are outside the scope of the ARPA-H mission.

PART II: FULL TEXT OF ANNOUNCEMENT

1. Funding Opportunity Description

This publication constitutes a merit-based process in accordance with 2 Code of Federal Regulations (CFR) § 200.205 and is in accordance with 42 U.S. Code § 290c. Any resultant award negotiations will follow all pertinent laws and regulations.

The mission of ARPA-H is to accelerate better health outcomes for everyone by advancing innovative research that addresses society's most challenging health problems. Awardees will develop groundbreaking new ways to tackle health-related challenges through high-potential, high-impact biomedical and health research. ARPA-H is soliciting proposals to develop toolkits and enabling technologies to bioprint organs on demand to replace patients' organs, restoring normal function. The focus areas include immune competent kidney, heart, and liver bioprinting for transplantation without the need for anti-immune rejection drugs. This solicitation requests an end-to-end solution to show safety and efficacy of these bioprinted organs in animal models. It is important to note that proposals will not be considered if 1) the proposal merely offers incremental improvements in the existing state of the art, such as a simple tissue graft with limited cellular complexity, vascularization, and thickness resulting in minimal improvement in overall organ function, 2) the proposal does not address the objectives of the program, or 3) the proposal is directed towards policy changes, traditional education and training, or center coordination and construction of physical infrastructure, as these areas are outside the scope of the ARPA-H mission.

1.1. PROGRAM OVERVIEW

The **PRINT** program aims to create a process to enable biofabrication of the kidney, heart, and liver using advanced cell manufacturing and 3D bioprinting. To fundamentally transform the human organ supply chain and regenerative medicine approaches, **PRINT** will develop effective cell differentiation and expansion methods for all necessary organ cell types, which can then be transitioned to Good Manufacturing Practice (GMP) manufacturing grade. Organ level tissue complexity will be recapitulated using tissue modeling software, bioinks and supporting materials, precision bioprinting hardware, and bioreactors to provide active perfusion and sustain viability prior to transplantation. The combined effort of all teams will develop a biofabrication process that will enable the production of bioprinted organs to work to address the US and global organ shortage.

Current approaches for biofabrication using 3D bioprinting are costly, time-consuming, and have not yielded tissues thick or complex enough to restore organ function. Due to the technical complexities, most developers have used 3D bioprinting for either simple tissue grafts or, most commonly, for uniformity of precision medicine applications such as drug development or screening. Multiphysics tissue modeling software has been used to optimize spatial configurations of tissues, vascular geometry, and simulate fluid dynamics. However, optimized printing parameters remain to be matched with existing bioprinting hardware and software capabilities. Similarly, even with a number of natural and synthetic bioinks and materials, vascularization of tissue at or exceeding 1cm thickness continues to remain a barrier for production of complex tissues. Additionally, lack of cell availability and production capacity have posed a challenge in having sufficient material, limiting the potential for many more advanced tissue engineering applications. Of the currently available cell types, none are universally immunocompetent. While some processes exist for organ biofabrication, none address the mentioned issues and require significant additional integration and improvement.

PRINT program will address these limitations by:

1. Selecting patient cell sources and developing effective protocols to differentiate/expand all necessary organ specific cell types while maintaining immunocompetence.
2. Developing large scale Good Laboratory Practice (GLP)/GMP manufacturing processes, cell biobank, and effective storage and cell transport conditions.
3. Developing a library of natural and synthetic bioinks for structural integrity while exhibiting native tissue biomechanics, effective vascularization at the time of print, self-assembly of tissue units, and unique native tissue environments.
4. Building high speed and precision bioprinting software and hardware.
5. Developing a bioreactor system that will enable active perfusions at the time and point, post print maturation, and maintain viability up to transplantation.
6. Down-selecting to the most promising teams for functional and structural evaluation in a large animal model.

The utilization of these advanced technologies will revolutionize biofabrication, resulting in a substantial decrease in the US and global organ shortage, provide equity to those in need, and more importantly, save lives. Discoveries and approaches produced from **PRINT** will also impact all_regenerative medicine research and development as the principles required for biofabrication apply to understanding the foundation for tissue engineering and relates to human disease models and applications.

1.2. TECHNICAL APPROACH AND STRUCTURE

1.2.1. Technical Areas (TAs)

The **PRINT** program will transform the field of bioprinting, in part by developing a set of enabling technologies, to address a huge unmet healthcare need and meet the demands for the organ transplant waiting list. The process includes three (3) technical areas (TA): Generation of all necessary organ cell types from best cell source(s) (TA1), large scale manufacturing of organ cell types informed by TA1 data (TA2), and organ biofabrication and Investigational New Drug (IND) enabling *in vivo* testing for safety, immunogenicity, and efficacy (TA3). The final bioprinted organ products from this program will either be full size functioning organs, partial organs, or ectopic organ substitutes. Additionally, the program structure allows for non-standard organ design as long as normal organ function is achieved.

- **Technical Area 1 (TA1): Generation of all necessary organ cell types (Phase I)**: Identify best in case cell source, either autologous or allogeneic (without any immunogenicity from tissue biopsy) induced Pluripotent Stem Cells (iPSCs). Criteria for selecting a cell source should be cost effective, multipotent, and immunocompetent. Assessment may include the verification of morphology using microscopy, multipotency, Fluorescence-activated cell sorting (FACS), or Quantitative polymerase chain reaction (qPCR), but is not limited to these techniques. The ultimate goal for this technical area will be to demonstrate cell type specific organ function *in vitro*.

- **Technical Area 2 (TA2): Large scale manufacturing of organ cell types (Phase I & II):** Based on the data from TA1, produce enough (in billions) of all necessary cell types to generate organs for *in vivo* safety, immunogenicity, and efficacy testing. As a part of Quality Assurance (QA)/ Quality Control (QC) testing, perform toxicity, tumorigenicity, and mutagenicity assays. Define storage conditions with high percentage viability and transportability using 4′,6-diamidino-2-phenylindole (DAPI) staining or any alternative more sensitive method. The final goal for this TA in Phase I will be GLP manufacturing of organ cell biobank. In Phase II, leveraging the knowledge from Phase I, performers will scale up manufacturing to GMP for IND enabling studies in large animals.

- **Technical Area 3 (TA3): Organ Biofabrication and *in vivo* testing (Phase I and II):** This TA aligns with Phase I to develop biofabrication technologies. Some examples include, but are not limited to, (1) technologies to improve current bioreactors for cost-saving and better performance of the organ, (2) bioink formulations that support anisotropic tissue printing, (3) bioprinting methods to improve printing speed, (4) multi-physics modeling to inform 3D organ design (shape and size of the organ to match the patient), and (5) perfusion system to mature the organ *in vitro* before transplantation. The main goal of this TA is to **PRINT** suturable, functional organs that will be transplanted and tested in humanized small animals.

Performers must submit proposals that address all TAs (TA1 – 3) for one (1) of the target organs (i.e., kidney, heart, or liver). As teams advance product candidates through proof-of-concept studies, challenges, and pre-clinical studies, there are opportunities within all TAs to iterate and improve on the organ functional design, resolution, and modeling approaches. The iterations will be validated and guided by animal data for safety, immunogenicity, and efficacy.

To ensure the applicability of tools developed to the broader community and for the success of **PRINT** candidates, proposers must have demonstrated team capabilities across all TAs. Proposals that fail to address the required technical areas will be deemed non-conforming and may be rejected without further review. Teams must also include data access plans and commercialization plans including Food and Drug Administration (FDA) meeting milestones, technology transfer milestones to contract manufacturing organization (CMO) partners, preclinical proof of concept objectives, and market analysis and partnership models for commercialization. The proposed candidates for TA1–3 should meet the specifications listed in **section 1.3**.

TA1: Generate all necessary organ cell types.

Since the discovery of Pluripotent stem cells (PSCs) in 2006, PSCs have emerged as a promising alternative to overcome the ethical and immunogenic challenges of embryonic stem cells. PSC reprogramming technology still faces some challenges, especially with respect to cell proliferation and differentiation. But the real promise of PSCs lies in their ability to develop autologous, or patient-specific, stem cell–based therapies with long-term engraftment without the need for immunosuppression, providing safer treatments for patients. Another approach to circumvent immune rejection is to use allogeneic PSC-derived transplants creating universal, or immunocloaked, cells lines. These cell lines require gene editing to avoid T-cell invasion or must be knocked in to avoid NK-cell invasion. The 3D bioprinting field has also been

contributing to these strategies, taking advantage of these discoveries to bioprint organs for transplantation. Advances in iPSC-derived differentiated cells have already been used in several clinical trials (e.g., retinal cells, dopaminergic neurons, platelets), showing their true potential to treat damaged tissue and organs.

TA1 aims to produce all cell types necessary to bioprint 3D organs to restore function without any adverse events including immune rejection. To achieve that, within each selected performer team, TA1 performers will collaborate with TA2 performers to establish repeatable differentiation protocols for their choice of cell source. The cell source can be autologous or immune competent allogeneic. Similarly, performers from TA1 and TA2 will also carefully develop QA/QC criteria to test the safety, immunogenicity, and efficacy of the differentiated cells *in vitro* by utilizing existing FDA compliant methods or develop novel methods validated by FDA. Performers working on autologous cell sources will be required to address the potential risks associated with genetic/hereditary conditions of patients.

This program announcement outlines the broad scope of the TA1 objectives. Proposals should consider each of the following, and include strategies and information to achieve each milestone during Methods Development Phase 1 (1-12 months) I:

- Identification of the best cell Source(s).
- A detailed plan to develop organ specific cell differentiation protocol.
- Development of QA/QC safety assays validated by FDA.
- Demonstration of organ specific function *in vitro.*
- Independent validation of final differentiation protocol and *in vitro* function by FDA certified contract research organization or TA2 team.
- Description of potential risks and associated mitigation strategies for cost, schedule, and performance for TA1 objectives.
- A detailed schedule or timeline for each milestone and the overall deliverables.

To achieve the goals of the program, performers may propose a variety of technical, functional biochemical and immunological characterization approaches. These approaches can be separate or combined. These may include but are not limited to:

- Multipotency assays.
- Microscopy.
- Fluorescence-activated cell sorting (FACS).
- Quantitative polymerase chain reaction (qPCR).
- Single cell sequencing.
- Organ specific biomarkers staining.
- Enzyme Assays.
- Other biophysical techniques to test mechanistic and electrical ion channel function.
- Biosensor technology.
- Epitope binning technology.
- Other immunological functional assays.

TA2: Large scale manufacturing of organ cell types.

Modern bioprocessing technology and protocols have developed to the point of producing functional, clinically relevant numbers of pluripotent stem cells for use as cell and tissue source material. However, optimization of differentiation and final manufacturing protocols require larger resources and can be cost prohibitive, with characterization of phenotype being labor intensive. In addition, in-process heterogeneity, and the evolving regulatory requirements for assessment of cell-derived therapeutics has made development difficult. It has been especially hard to develop scalable and robust processes that are strictly standardized

and economically viable. Clinical outcomes are dependent on the biological function of the product, with quality hindered by obstacles such as a lack of reproducibility and robustness for scale-up and scale-out. Addressing these limitations and obstacles in the development of cell-based therapeutics includes the incorporation of technologies and methods capable of continuous monitoring and assessment of phenotype throughout the bioprocess, in conjunction with process control, standardization, and automation of protocols as they are developed.

As highlighted in the TA1 overview, TA1 aims to bridge the knowledge gap in identifying the best-in-class cell source and differentiation protocol for 3D bioprinting organs and will accurately map the standard operating procedures and QA/QC methods and criteria to scale up manufacturing of differentiated organ cell types in TA2. These protocols will be reproducible and validated by third party FDA compliant CRO.

TA2 aims to advance the integration of process systems, and novel analytics, technologies, and computational methods throughout development and optimization. TA2 also aims to address the challenges and potential strategies to overcome obstacles faced in controlling pluripotent and differentiated phenotype in the context of restoring normal functionality, i.e., efficacy, immunogenicity, and safety throughout biomanufacturing. Therefore, the proposers should outline plans to document compliance with guidelines that govern Good Laboratory Practice (GLP), as defined by 21 CFR (58), and current Good Manufacturing Practice (cGMP), as defined by 21 CFR (211), manufacturing supporting the TA3 IND enabling studies that will be performed under the program.

This program announcement outlines the broad scope of the TA2 objectives. Proposals will consider each of the following, and include strategies and information to achieve each goal during Methods Development Phase 1 (1-36 months) and Implementation Phase II (37-60 months):

- GLP manufacturing of organ specific differentiated cell types for *in vivo* efficacy, immunogenicity, and safety testing (Phase I).
- GMP manufacturing of organ specific differentiated cell types for *in vivo* efficacy, immunogenicity, and safety testing (Phase II).
- QA/QC safety assays for toxicity, tumorigenicity, and mutagenicity (both Phases).
- Detailed plan to create and store Master Biobank for organ cell types (both Phases).
- Description of potential risks and associated mitigation strategies for cost, schedule, and performance for TA1 objectives (both Phases).
- A detailed schedule or timeline for each milestone and the overall deliverables (both Phases).

To achieve the goals of the program, performers may propose a variety of technical approaches to manufacture large quantities of organ specific cell types for *in vivo* testing. These approaches can be separate or combined. These may include but are not limited to:

- Multipotency assays.
- Microscopy.
- Fluorescence-activated cell sorting (FACS).
- Quantitative polymerase chain reaction (qPCR).
- Single cell sequencing.
- Organ specific biomarkers staining.
- Enzyme Assays.
- Other biophysical techniques to test mechanistic and electrical ion channel function.
- Biosensor technology.
- Epitope binning technology.
- Other immunological functional assays.

TA3: Organ Biofabrication and *in vivo* safety and efficacy testing in animal models.

Even though 3D bioprinting is advancing at a commendable rate with researchers trying to develop new printing modalities as well as improve existing modalities, a multitude of challenges still exist. Current bioinks are both bioprintable and accurately represent the tissue architecture needed to restore organ function post-printing. But hybrid bioinks should be designed to amalgamate both mechanical and functional aspects of the printed organ. Moreover, the bioprinting process itself needs to be more amenable to cell viability and cell health. Additionally, vascularization of bioprinted constructs for proper nutrient exchange, as well as integration of printed vasculature with host vasculature post organ implantation, is another major obstacle. While the cell distribution within bioinks is typically homogeneous, incorporating appropriate cellular patterning within the bioprinted constructs is an essential first step towards the eventual formation of anisotropically organized tissue matrix essential to its biomechanical form and function. For example, cardiac muscle tissue consists of cardiomyocytes with striated myofibrils that withstand the expansive and contractile forces associated with cardiac cycle. Over the last two decades, tissue engineering (TE) technologies have been developed to create tissues for clinical and diagnostic applications. In these technologies, achieving the appropriate cellular patterning, as a precursor to achieving the desired extra-cellular matrix (ECM) organization, is essential to replicate the functionality of the engineered tissues and their relevance to practical applications. Bioprinting not only involves the computer aided deposition or curing of cell-laden biomaterials (bioinks) in a layer-wise fashion but is also able to mimic the macro-geometry of the native tissues. These techniques are critical for precise placement of different cell-types, materials, and growth factors for fabrication of complex tissues such as heart, kidney, and liver.

Overall, 3D bioprinting is a rapidly evolving field of research with immense challenges but has tremendous potential to revolutionize modern medicine and healthcare. The **PRINT** program is aimed at bioprinting organs for fulfilling organ shortage demands as well as improving cell patterning for better tissue fabrication on demand. **PRINT** also aims to alleviate current hurdles and should improve bioink formulation, 3D printing methods and software (to print anisotropic, vascularized tissue with improved mechanical properties), and bioreactors (to increase tissue viability). Additionally, the selected platform should be scalable and allow for low-cost manufacturing that ensures accessibility of personalized organs on demand to all Americans.

To achieve the goals of the program, performers may propose various technical approaches to assess printing efficacy *in vitro* and *in vivo*. These approaches can be separate or combined. These may include but are not limited to:

- Ultrasound, Magnetic resonance imaging (MRI) or other methods imaging techniques.
- Microscopy (confocal and intravital).
- Computer vision and image analysis/processing.
- Quantitative polymerase chain reaction (qPCR).
- Fluorescence-activated cell sorting (FACS).
- Single cell -omics analysis of cell specific molecular markers/profiles (transcriptomics, proteomics).
- Structural and hydrodynamic stress testing.
- Cell and tissue viability assays.
- Assays for cell and tissue functions based on organ type (cell products, filtration, mechanical performance, biochemical, blood-based biomarkers, sensor-based biomarkers, standard vitals).
- Toxicity assays.
- Mutagenesis assays.
- Genomic stability assays
- Immunogenicity assays.
- Tumorigenicity assays.
- Postmortem tissue analysis.

- Bioreactor byproducts, metabolites, glucose, temperature, oxygenation, or other metrics that may be measured to assess bioreactor cell growth conditions.

Efforts within TA3 should include co-Investigators with expertise in biomaterials, bioengineering/tissue engineering, and expertise in surgical organ transplantation.

This program announcement outlines the broad scope of the TA3 objectives. Performers must also provide the following information in the proposal:

- Intended *in vitro* assays and *in vivo* models to examine potential human efficacy.
- Justification for the number of animals to be used and other models employed *in vitro* and *in vivo.*
  - The approval process of the Institutional Animal Care and Use Committee (IACUC) protocol and the Office of Laboratory Animal Welfare (OLAW) submission will likely take a minimum of three (3) months. Performers should have the protocol ready for approval in anticipation of the **PRINT** program award and should include a milestone for IACUC and OLAW approval in synchronization with the program timeline.
- Strategic plan for collaborations with other TA experts to facilitate the development of IND-ready products.
- Description of potential risks and associated mitigation strategies for cost, schedule, and performance for TA3 objectives. (both Phases).
- A detailed schedule or timeline for each milestone and the overall goal.

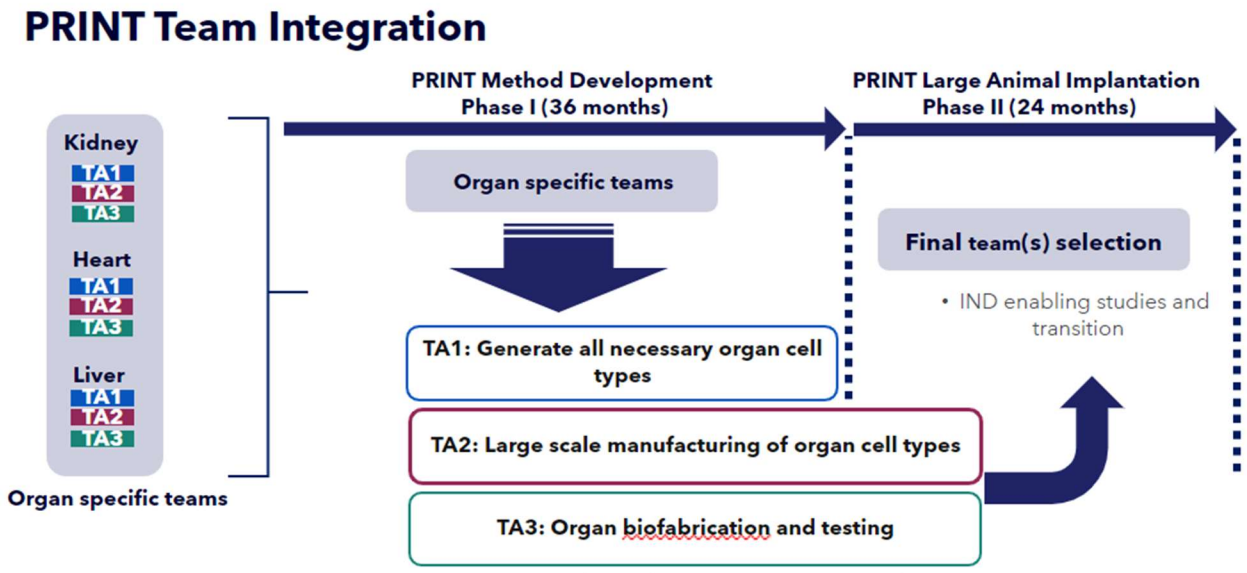
The progress made by TA3 will be evaluated by program-wide goals before the 36-month **PRINT** Phase 1 period ends. The main goal aims to demonstrate that the candidate organ shows safety and efficacy in small animal models to restore normal function of the organ (Kidney, Heart, or Liver). The USG labs and resources will oversee and evaluate the candidates, and the results will play a significant role in making Go/No-Go decisions for **PRINT** Phase II and determining the advancement of candidate organs for further evaluation in large animal models.

TA1, TA2, and TA3 metrics and timelines are outlined in **Table *1*** and **Table *2***. Monthly technical and financial status reports will be required and discussed with the ARPA-H Program Manager Team at monthly meetings. ARPA-H may request performer data as deemed necessary throughout the program to validate progress toward achieving the program goals. ARPA-H reserves the right to Independent Verification & Validation (IV&V) of all standard operating procedures and QA/QC assays developed by performers by extramural and intramural USG labs for analysis and comparison.

1.2.2. Program Structure

The **PRINT** program is structured as a 5-year effort with 2 Phases: (1–36-month Phase I) and (37-60-month Phase II) as shown in **Figure 1**. **PRINT** methods development Phase I includes realistic and measurable goals for performers to ensure development of all necessary technologies for the success of the program. Phase I will include check points for successful transitions and will conclude with defined deliverables. During **PRINT** large animal implementation Phase II, performers must utilize the resources provided by USG stakeholders, Project Accelerator Transition Innovation Office (PATIO), and the Expert/Entrepreneur in Residence (XIR/EIR) network to transition successful programs and projects to advanced developers capable of moving the organ 3D bioprinting technology to the market.

Figure 1. Program Structure and General Overview



1.2.3. Equity Requirements

ARPA-H has indicated it is committed to equitable healthcare access irrespective of race, ethnicity, gender/gender identity, sexual orientation, disability, geography, employment, insurance, and socioeconomic status. Access to donated organs for many Americans waiting for organ transplantation is inequitable across the U.S. The transplantation system in U.S. produces glaringly worse results for certain groups of patients, especially those marginalized by perceived race, ethnicity, sex, religion, socioeconomic status, disability status, and their geographic location of residence. Further, lack of educational marketing tools for organ transplantation prevents the full benefit of these public health tools from being realized across the U.S.

PRINT enables a cost-effective organ transplantation supply chain through efficient biofabrication, eliminates lifelong side effects and comorbidities associated with anti-rejection drugs, and eliminates the need for dialysis for kidney failure patients. **PRINT** will also leverage existing and create new reimbursement mechanisms. Banked cells will be universally immunocompetent and/or racially and ethnically diversified to be accessible to everyone due to affordability across the U.S. The **PRINT** program will implement models for both on-site biofabrication capabilities (purchase or lease) at major transplant centers and hospitals as well as on-demand service center organ biofabrication sites located to provide access to this technology in both rural and urban areas within 60 miles.

1.2.4. Data Sharing Plan

For both Phases of the **PRINT** program, the proposers will develop a data sharing platform across all team members and performing organizations. The proposers are required to validate and standardize data sets' format, content, and data management platforms across all teams. Proposers must agree to openly share any non-proprietary data acquired during the period of performance. The specific repository where data will be deposited will be chosen in agreement with the ARPA-H program manager. The proposers will need to present explicit solutions to address the significant data storage and computing challenges presented by the program, with the understanding that the plans and repository may change later in the program.

1.2.5. PRINT Checkpoints

The **PRINT** program will be accomplished over three (3) overlapping technical areas TA1, TA2, TA3, and two (2) sequential phases. **PRINT** Phase I consists of research and development in TA1, TA2, and TA3, and spans 36 months. Phase II spans 24 months and integrates the GMP cell manufacturing from TA2 and supporting printing processes from TA3 (software, bioreactor, and bioink formulation) culminating in the implantation of a biofabricated organs for large animal experimentation. See **Table *1*** and **Table *2*** for each requirement associated with each TA.

In year 1, TA1 teams will select a cell source and develop protocol(s) to produce organ specific cell types while TA3 teams will work concurrently developing the print method.

Year 1 Expectations:

- Y1 Q2: Cell source identified.
- Y1 Q4: Cell protocol(s) finalized and validated for organ type specific cells.
- Y1 Q4: Printing software finalized and validated.
- Y1 Q4: Bioreactor (used during bioprinting) constructed.
- Y1 Q4: Bioink library generated.

In year 2, TA1 cell protocols will be further optimized for GLP manufacturing as part of TA2 and a master biobank will be created. The printing method and hardware will be developed as well as *in vitro* bioprinted organ efficacy assessed as part of TA3.

Year 2 Expectations:

- Y2 Q4: GLP manufacturing established and validated.
- Y2 Q4: Master biobank from GLP process created for all cell types.
- Y2 Q3: Printing Method finalized and validated.
- Y2 Q4: Bioprinted organ functionally validated *in vitro.*

In year 3 in **PRINT** Phase I, teams will be advanced based on performance against **PRINT** Phase I metrics as described in the metrics (**Table *1*** and **Table *2***). Progression to Phase II will also be dependent on funding availability. Additionally, any performer that does not meet the equity requirements may also be identified and not selected to move forward. **PRINT** Phase II will not have specific TA1 requirements; however, there may be funds available in Phase II for additional support to TA2 and TA3 if necessary.

Year 3 Expectations:

- Y3 Q4: Safety, immunogenicity, and efficacy testing in humanized mice.

In year 4, GMP manufacturing will be established, a master cell bank will be generated, and large animal studies will be initiated.

Year 4 Expectations:

- Y4 Q4: GMP manufacturing established and validated.
- Y4 Q4: Master cell biobank from GMP process created for all cell types.
- Y4 Q1: Safety and efficacy study in humanized pigs initiated.

In year 5, all IND enabling studies are completed and the biofabrication platform is ready for future IND filing and first in-human Phase I clinical trials.

Year 5 Expectations:

- Y5 Q4: Finalized humanized large animal (pig) animal safety, immunogenicity, and efficacy testing studies.

1.3. PROGRAM METRICS

To evaluate the effectiveness of a proposed solution in achieving the stated program objectives, the following program metrics will serve as the basis for determination of satisfactory success to warrant continued funding. Although the program metrics are specified below, proposers should note that the Government has identified these goals with the intention of bounding the scope of effort while affording maximum flexibility, creativity, and innovation of proposed solutions to the goals. Proposals should cite the quantitative and qualitative success criteria that the effort will achieve at each phase's program milestone, as well as the measurement of intermediary metrics. *If the metrics stated below (***Table *1*** *and* **Table *2****) are not meaningful for a particular case, proposing teams are expected to provide their own metrics and describe the quantitative improvement that those metrics represent over the state-of-the-art.*

1.3.1. TA1, TA2, and TA3 Metrics and Objectives

The overall **PRINT** structure based on the timeline is shown in **Figure 1**. The overall program metrics and deliverables are listed in **Table *1*** and **Table *2***. In addition to frequent performance reviews throughout the phases, performers must provide an end-of-phase final report that summarizes all efforts and data for each completed **PRINT** Phase.

Table 1 TA1, TA2 and TA3 Summary of Overall Program Goals for PRINT

Cell Sources Identified	Select either autologous or allogenic cell sources which are immunocompetent
Develop Differentiation Protocol	Demonstrate organ specific differentiation with phenotype (morphology + molecular markers), functional assays, and provide product quality assurance (QA) *in vitro*.
GLP Manufacturing and Master Biobank	Develop cell master bank based on TA1 and GLP/GMP manufacturing for small and large animal studies. Demonstrate organ specific differentiation with phenotype (morphology + molecular markers), functional assays, and provide product QA and quality control (QC) for cell characterization and safety *in vitro*.
Bioink Formulations	Library of bioink formulations to support microenvironments, specialized cell development, and customizable material properties.
Printing Method	Improved software and hardware, vascularized tissue with active perfusion, and organ specific biomechanics.
***In vitro* bioprinted organ efficacy assay**	Demonstrate bioprinted 3D organ function *in vitro*.
***In vivo* safety and efficacy testing in small and large animals**	Demonstrate bioprinted 3D organ system safety, immune compatibility, and function to sustain life in small and large animal models.
GMP Manufacturing and Master Biobank	Develop cell master bank and GMP manufacturing for large animal studies as well as QA and QC.
Equity Requirements	Performers account for health inequalities with respect to cost and accessibility of care, protection regardless of socioeconomic status of ethnicity. Develop solutions with equity in mind at the start.
Overall goals	Pre-IND enabling studies, organ biofabrication process, GMP manufacturing with biobank.

Table 2 TA1, TA2 and TA3 Overall Program Goals for PRINT

PRINT Technical Areas				
Technical Area	**Milestone Title**	**Milestone Description**	**Start Y1Q1**	**End Y5Q4**
Phase I: PRINT Method Development				
TA1	**Milestone Title**	**Generate all necessary organ cell types**	**Y1Q1**	**Y1Q4**
M1.1	Identify the best cell Source(s).	Identify best in case cell source for mass production and differentiation (from biopsy, iPSCs, etc.). Criteria: cost (Target: ≤$5,000/ billion cells), availability, expandability (ability to manufacture ~10 billion cells/ organ), multipotency, and >85% viability after storage.	Y1Q1	Y1Q2
M1.2	Develop differentiation Protocol	Verify cell specific morphology and multipotency of the expanded cells using techniques such as FACS sorting, qPCR etc. Achieve high purity (>90%) of defined cell types after differentiation (verified by techniques such as immunostaining, FACS sorting, and qPCR etc.) Demonstrate the absence of tumorigenicity of expanded and differentiated cells in vitro (such as gene expression of immortalized cells, anchorage-independent cell growth detection, genomic instability tests).	Y1Q1	Y1Q3
M1.3	Cell type generation by organ	Generate all necessary cell types for the function of the target organ. (Total: ~10 billion cells/organ) • For kidney teams: Demonstrate normal (≤ ±20% difference from patient derived cells) kidney-relevant functions of the differentiated cells (i.e., reabsorption capacity of albumin, glucose, and ions (epithelial cells), contractility and phagocytic activity when stimulated (mesangial cells), barrier function (podocytes)) • For heart team: Demonstrate normal (≤ ±20% difference from patient derived cells or immortalized cell lines) heart-relevant functions of the differentiated cells (i.e., electrophysiological and beating motion measurement (cardiomyocytes), contractility measurement (cardiac fibroblasts)) • For liver teams: Demonstrate normal (≤ ±20% difference from patient derived cells or immortalized cell lines) liver-relevant functions of the differentiated cells (i.e., CYP450 enzyme activities (hepatocytes), response to wound healing assay (hepatic stellate cells), phagocytic activity (Kupffer cells))	Y1Q2	Y1Q3
Deliverable	Finalized protocols for cell differentiation for all necessary cell types, high expansion, and storage conditions to create a biobank for bioprinting.			
TA2	**Milestone Title**	**Large scale manufacturing of organ cell types**	**Y1Q4**	**Y4Q4**
Phase I: PRINT Method Development				
M2.1	GLP manufacturing and Master Biobank	GLP manufacturing of 1 billion cells per organ (expansion and differentiation of selected cell source) to	Y1Q4	Y3Q4

		generate all 3 organs and for small animal testing (TA3) (cost: ≤$15,000/ billion cells)		
M2.2	QA/QC	Demonstrate cell specific characteristics in vitro (quantitative metrics same as TA1, M1.2 and 1.3) Identify transportability and storage conditions with ≥85% viability after storage	Y2Q3	Y3Q4
Deliverables	GLP manufactured cell biobank			
Phase II: PRINT Implementation				
M2.3	GMP Manufacturing	Scale-up GMP manufacturing of biobank cells (10 billion cells per organ) for in vivo safety and efficacy studies in large animals (cost: ≤$50,000/ billion cells) Pre-IND documentation for CMC.	Y4Q1	Y4Q4
M2.4	QA/QC	Demonstrate milestones from M2.2	Y4Q1	Y4Q4
Deliverables	GMP manufactured cell biobanks. Pre-IND enabling studies and documentation			
TA3	**Milestone Title**	**Organ biofabrication of organs and in vivo testing**	**Y1Q1**	**Y5Q4**
Phase I: PRINT Method Development				
M3.1	Printing software	Multi-physics modeling to inform 3D organ design (i.e., vascular branching, cell density, tissue layers at ≤50 µm resolution)	Y1Q1	Y1Q4
M3.2	Bioreactor	Perfusion system that can sustain organ maturation and monitor organ function via non-invasive imaging and biochemical measurements (Maturation time <30 days).	Y1Q1	Y1Q4
M3.3	Bioink Formulation	Develop organ-specific bioinks that are immuno-competent and support organ regeneration and function (>99% cell viability and non-immunogenic).	Y1Q1	Y1Q4
M3.4	Printing Method	Hardware to achieve ~50µm resolution and various organ sizes for both mouse and pig, Enable printing of anisotropic and vascularized tissue with organ specific biomechanics. (≤±20% difference from normal organ)	Y1Q3	Y2Q2
M3.5	In vitro bioprinted organ efficacy assay	• For kidney team: Demonstrate kidney function in a perfusion model (i.e., Renal blood flow: 100-350 ml/min*100 g, Glomerular filtration rate: 15-80 ml/min*100 g) • For heart team: Demonstrate heart function in a perfusion model (i.e. heart rate 60-120 BPM, cardiac output 3-6 L/min, ejection fraction 50-70% etc.) • For liver teams: Demonstrate liver function in a perfusion model (i.e. oxygen consumption: 1-5 ml O2/min/100g, ALT: <2000 U/L, AST: <2000 U/L)	Y2Q1	Y2Q4
M3.6	In vivo safety and efficacy testing in small animal	Demonstrate safety and immune compatibility (no teratomas, rejection, toxicity, mutagenicity) in small animal model.	Y2Q4	Y3Q4

		Demonstrate successful implantation of bioprinted organ in >10 small animals. Demonstrate viability and longevity of the bioprinted organ in small animal model (3–6-month survival). Demonstrate normal organ structure and host response postmortem.		
Deliverable	Finalized print modeling software; Finalized bioreactor for active perfusion. Finalized library of bioinks; Finalized print system. Functional organ in vitro and safety profile *in vivo*. Organ function and demonstrated in humanized mice and initiate INTERACT meeting with FDA.			
Phase II: PRINT Implementation				
M3.10	IND enabling studies large animals	Demonstrate successful implantation of bioprinted organ in >5 large animals. Demonstrate viability and longevity of the bioprinted organ in large animal model (3–6-month survival). Demonstrate safety (no teratomas, rejection, toxicity) in large animal model at 6-month post transplantation. For kidney teams: Achieve normal kidney function *in vivo* based on parameters such as glomerular filtration rate from 100-200ml/min/70kg, total renal blood flow 3-5ml/min/g, serum creatinine <2mg/dL. For heart team: Achieve normal heart function *in vivo* based on parameters such as heart rate (60-120 BPM), cardiac output (3-6 L/min), ejection fraction (50-70%). For liver teams: Achieve normal liver function *in vivo* based on parameters such as ALT 30-60 U/L, AST 30-85 U/L, ALP 40-180U/L, serum creatinine <2mg/dL, Bilirubin ≤1 mg/dL. Postmortem IHC and molecular markers of organ structure. Finalize QA/QC and IND documentation and transition.	Y4Q1	Y5Q4
Deliverable	Achieve normal organ function in a humanized pig model and survival of 3-6 months post transplantation; Pre-IND filing for bioprinted kidney transplantation			

1.3.2. Overall Program Objectives

The overall objectives of the **PRINT** program are listed below and should be referenced within the context of individual proposed efforts for **PRINT**. Additionally, the target product profile (TPP) (**Table *3***) should be utilized as a guideline throughout the process of discovery and development, in preparation for future IND filing and Phase I human clinical studies:

- Effective protocols using a patient cell source to differentiate/expand all necessary organ specific cell types while maintaining immunocompetence.
- Large scale GLP/GMP manufacturing processes, cell biobank, and effective storage and cell transport systems.
- Library of natural and synthetic bioinks.
- Multi-physics modeling to inform 3D organ design (vascularization, fluid dynamics, structural integrity) and optimized for bioprinter capabilities.
- Bioprinting method(s) (droplet-based, laser-assisted, stereolithography and digital light processing, and extrusion-based bioprinting) and hardware
- Printing software to enable precision control of print hardware and that has been synchronized with multi-nozzle, multi-materials, and robotic (arms, stages) bioprinter capabilities to accurately match design specifications.
- Bioreactor system to facilitate active perfusion at the time of print and enable post-print maturation prior to transplantation.
- Candidates showing strong proof-of-concept demonstrations and challenge performance are to be selected for evaluation in large animal IND-enabling studies.
- Surgical techniques (sealants/glue, suturing) compatible with biofabricated organ tissues.
- Product fit to TPP (example TPP below – further TPPs in generation with PATIO team and ARPANET-H's Customer Experience Hub for broad acceptability and accessibility).

Table 3 Examples of organ specific TPP.

Kidney Product Properties	**Attributes (Ideal)**
Indication for use	Kidney failure due to disease and/or injuries
Target population	Patients in need of kidney transplant
Safety/Immunocompetency	Safe and immunocompetent product without need for immunosuppressive drugs
In Vivo Efficacy	Kidney functional restoration based on parameters such as glomerular filtration rate from100-200ml/min/70kg, total renal blood flow 3-5ml/min/g, serum creatinine <2mg/dL.
Structural Integrity	Enable anastomosis and mechanical properties match to normal kidney
Hemodynamic Stability	Volumetric flows and pressure load capacity same a normal kidney
Intervention	Kidney transplantation
Administration route	Surgical implantation
Adverse events (AEs)	Mild, transient AE may be observed post implantation
Shelf life (cell master bank)	>5 years at -80 ºC for Master Cell Bank, viability >75%
Storage temperature	37 ºC viability for 48 hours
Product cost	<$200,000
Equity	Health inequalities should be considered with respect to cost, accessibility to care, and protection regardless of socioeconomic status, ethnicity, or geographical location. Develop solutions with equity in mind at the start.

Liver Product Properties	**Attributes (Ideal)**
Indication for use	Liver failure due to disease and/or injuries
Target population	Patients in need of liver transplant

Safety/Immunocompetency	Safe and immunocompetent product without need for immunosuppressive drugs.
In Vivo Efficacy	Liver functional restoration based on parameters such as ALT 30-60 U/L, AST 30-85 U/L, ALP 40-180U/L, serum creatinine <2mg/dL, Bilirubin ≤1 mg/dL.
Structural Integrity	Enable anastomosis and mechanical properties match to normal liver
Hemodynamic Stability	Volumetric flows and pressure load capacity same a normal liver
Intervention	Liver transplantation
Administration route	Surgical implantation
Adverse events (AEs)	Mild, transient AE may be observed post implantation
Shelf life (cell master bank)	>5 years at -80 ºC for Master Cell Bank, viability >75%
Storage temperature	37 ºC viability for 48 hours
Product cost	<$400,000
Equity	Health inequalities should be considered with respect to cost, accessibility to care, and protection regardless of socioeconomic status, ethnicity, or geographical location. Develop solutions with equity in mind at the start.

Heart Product Properties	**Attributes (Ideal)**
Indication for use	Heart failure due to disease and/or injuries
Target population	Patients in need of heart transplant
Safety/Immunocompetency	Safe and immunocompetent product without need for immunosuppressive drugs
In Vivo Efficacy	Heart functional restoration based on parameters such as heart rate (60-120 BPM), cardiac output (3-6 L/min), ejection fraction (50-70%)
Structural Integrity	Enable anastomosis and mechanical properties match to normal heart
Hemodynamic Stability	Volumetric flows and pressure load capacity same a normal heart
Intervention	Heart transplantation
Administration route	Surgical implantation
Adverse events (AEs)	Mild, transient AE may be observed post implantation
Shelf life (cell master bank)	>5 years at -80 ºC for Master Cell Bank, viability >75%
Storage temperature	37 ºC viability for 48 hours
Product cost	<$350,000
Equity	Health inequalities should be considered with respect to cost, accessibility to care, and protection regardless of socioeconomic status, ethnicity, or geographical location. Develop solutions with equity in mind at the start.

1.4. GENERAL REQUIREMENTS

1.4.1. Proposing Teams

To ensure the applicability of tools developed to the broader community and for the success of **PRINT** candidates, proposers must have demonstrated team capabilities across all TAs. Proposals that fail to address the required technical areas will be deemed non-conforming and may be rejected without further review. Teams must also include data access plans and commercialization plans including Food and Drug Administration (FDA) meeting milestones, technology transfer milestones to contract manufacturing organization (CMO) partners, preclinical proof of concept objectives, and market analysis and partnership models for commercialization. The proposed candidates for TA1–3 should meet the specifications listed in **section 1.3**. The proposers are also solely responsible for creating team structures, and collaboration plans for specific content, communications, networking, and team formation. The proposers must submit a plan that addresses all program phases, as applicable. The proposers may only submit one proposal as the prime proposer.

Proposers may only submit one (1) proposal as the prime proposer and a sub-proposer on one (1) other, or sub-proposer on two (2) proposals. Proposers may not participate in research and development activities for more than two (2) proposals. Proposers can provide an agent/device at cost for more than two (2) teams, as long as there are no development efforts for any teams past two (2).

ARPA-H will hold a Proposers' Day (see Other Information) where interested parties may network to form proposer teams or share information among other interested proposers.

2. Award Information

2.1. GENERAL AWARD INFORMATION

Multiple awards are anticipated. The resources made available under this ISO, and number of awards made will depend on the quality of the proposals[1] received and the availability of funds. ARPA-H reserves the right to make multiple awards, a single award, or no awards.

The Government reserves the right to select for negotiation all, some, one, or none of the proposals received in response to this ISO and to make awards without negotiations with proposers. The Government also reserves the right to conduct negotiations if it is later determined to be necessary. Additionally, ARPA-H reserves the right to accept proposals in their entirety or to select only portions of proposals for negotiation and award. The Government reserves the right to fund proposals in phases, including as optional phases, as applicable.

Proposals identified for negotiation are expected to result in Cooperative Agreements or Other Transactions (OTs). Selection of award instrument will be based upon consideration of the nature of the work proposed and other factors. The Government may request additional necessary documentation, tailored to the individual proposals once it makes the award instrument determination. The Government reserves the right to remove proposals from award consideration should the parties fail to reach agreement on award terms, conditions, and/or cost/price within a reasonable time, and/or if the proposer fails to timely provide requested additional information.

Proposers looking for innovative, commercial-like contractual arrangements are encouraged to consider requesting OTs.

[1] In this document, proposal refers both to the solution summary and the full proposal unless otherwise indicated.

In all cases, the Government's applicable OT Agreement and Grants Officer(s) shall have sole discretion to select award instrument type, regardless of instrument type proposed, and to negotiate all terms and conditions with selectees.

3. Eligibility Information

3.1. ELIGIBLE APPLICANTS

All responsible sources capable of satisfying the Government's needs may submit a proposal. Proposers may only submit one (1) proposal as the prime proposer and a sub-proposer on one (1) other, or sub-proposer on two (2) proposals. Proposers may not participate in research and development activities for more than two (2) proposals. Proposers can provide an agent/device at cost for more than two (2) teams, as long as there are no development efforts for any teams past two (2).

3.1.1. Federal Entities and Federally Sponsored Entities

Federal entities and federally sponsored entities (e.g., Government/National laboratories, Federally Funded Research and Development Centers (FFRDC), University Affiliated Research Center (UARC), military educational institutions, etc.) are not eligible for award under this announcement. However, ARPA-H is committed to working with its federal partners. Federal partners interested in working with ARPA-H on this program should contact **PRINT**@arpa-h.gov to discuss supporting this effort.

3.1.2. Other Applicants

ARPA-H will prioritize awards in accordance with 42 U.S.C. § 290c(n). Without limiting the foregoing ARPA-H will prioritize awards to domestic entities (organization and/or individuals) that will conduct funded work in the US. However, non-US entities may participate to the extent that such participants comply with nondisclosure agreements, security regulations, export control laws, and other governing statutes and regulations applicable under the circumstances. Non-US entities are encouraged to collaborate with domestic US entities. In no case will awards be made to entities organized under the laws of a covered foreign country (as defined in section 119C of the National Security Act of 1947 (50 U.S.C. § 3059)) or entities suspended or debarred from business with the Government.

3.2. ORGANIZATIONAL CONFLICTS OF INTEREST (OCI)

Proposers are required to submit an OCI mitigation plan that identifies and discloses all facts relevant to potential OCIs involving the proposer's organization and any proposed team member (including proposed subproposers). Although the Federal Acquisition Regulation (FAR) does not apply to OTs or Cooperative Agreements, ARPA-H requires OCIs be addressed in the same manner prescribed in FAR subpart 9.5. Regardless of whether the proposer has identified potential OCIs under this section, the proposer is responsible for providing a disclosure with its proposal. The disclosure must include the proposers, and as applicable, proposed team members' OCI mitigation plans. The OCI mitigation plan(s) must include a description of the actions the proposer has taken, or intends to take, to prevent the existence of conflicting roles that might bias the proposer's judgment and to prevent the proposer from having unfair competitive advantage. The OCI mitigation plan will specifically discuss the disclosed OCI in the context of each of the OCI limitations outlined in FAR 9.505-1 through FAR 9.505-4. The disclosure and mitigation plan(s) do not count toward the page limit and may be included in Volume II.

3.2.1 Agency Supplemental OCI Policy

In addition, ARPA-H restricts performers from concurrently providing professional support services, including Advisory and Assistance Services or Science, Engineering, and Technical Assistance support services, and being a technical performer. Therefore, as part of the FAR 9.5 disclosure requirement above, a proposer must affirm whether the proposer or any proposed team member (proposed sub awardee, etc.) is providing professional support services to any ARPA-H office(s) under: (a) a current award or subaward; or (b) a past award or subaward that ended within one calendar year prior to the proposal's submission date.

If any professional support services are being or were provided to any ARPA-H office(s), the proposal must include:

- The name of the ARPA-H office receiving the support.
- The prime contract numbers.
- Identification of proposed team member (proposed sub proposer) providing the support.
- An OCI mitigation plan in accordance with FAR 9.5.

3.3 Government Procedures

The Government will evaluate OCI mitigation plans to avoid, neutralize, or mitigate potential OCI issues before award and to determine whether it is in the Government's interest to grant a waiver. The Government will only evaluate OCI mitigation plans for proposals determined selectable under the ISO evaluation criteria.

The Government may require proposers to provide additional information to assist the Government in evaluating the OCI mitigation plan.

If the Government determines a proposer failed to fully disclose an OCI; or failed to provide the affirmation of ARPA-H support as described above; or failed to reasonably provide additional information requested by the Government to assist in evaluating the proposer's OCI mitigation plan, the Government may reject the proposal and withdraw it from consideration for award.

An OCI based on a performer currently providing professional support services, as described above, cannot be mitigated.

4. Application and Submission Information

4.1. ADDRESS TO REQUEST APPLICATION PACKAGE

This announcement and any references to external websites herein constitute the total solicitation. If proposers cannot access the referenced material posted in the announcement found at https://www.sam.gov/, please contact the administrative contact listed herein.

4.2. CONTENT AND FORM OF APPLICATION SUBMISSION

NOTE: Non-conforming submissions that do not follow ISO instructions may be rejected without further review at any stage of the process.

All submissions must be written in English with type not smaller than 12-point font (Arial or Times New Roman) and 1-inch margins. Smaller font may be used for figures, tables, and charts. Documents submitted

must be clearly labeled with the ARPA-H ISO number, proposer organization, and proposal title/proposal short title.

4.2.1. Solution Summary Format

Proposers to the ISO must first submit a Solution Summary in order to be invited to submit a full proposal. Based on evaluation of the Solution Summary, ARPA-H may request a full proposal from ISO respondents. The cover sheet should be clearly marked "SOLUTION SUMMARY," and the total length should not exceed five (5) pages in length. The maximum page count excludes the cover page and the Rough Order of Magnitude. The Government will not review pages beyond 5; and any Solution Summary submitted that exceeds five (5) pages will only be reviewed at ARPA-H's discretion. An official transmittal letter is not required.

A. Cover Page

The cover page should follow the same format as the full proposal described in paragraph A in Section 4.2.2. The cover page does not count towards the page limit.

B. Concept Summary

Describe the proposed concept with minimal jargon and explain how it addresses the topic area(s) of the ISO.

C. Innovation and Impact

Clearly identify the health outcome(s) sought and/or the problem(s) to be solved with the proposed technology concept. Describe how the proposed effort represents an innovative and potentially revolutionary solution to the technical challenges posed by the ISO. Explain the concept's potential to be disruptive compared to existing or emerging technologies. Describe how the concept will have a positive impact on at least one of ARPA-H's mission areas.

To the extent possible, provide quantitative metrics in a table that compares the proposed technology concept to current and emerging technologies and includes:

- State of the art / emerging technology "baseline"
- Target for proposed technology in its final, commercializable form
- Target for proposed technology at the end of the proposed ARPA-H program

D. Proposed Work

Describe the final deliverable(s) for the program, one (1) or two (2) key interim milestones, and the technical elements and approaches used to achieve program objectives in a logical sequence. Discuss alternative approaches considered, if any, and why the proposed approach is most appropriate for the program objectives. Describe the background, theory, simulation, modeling, experimental data, or other sound engineering and scientific practices or principles that support the proposed approach. Provide specific examples of supporting data, relevant prior work by the proposers, and/or appropriate citations to scientific and technical literature. The list of citations does not count towards the page limit. Identify commercialization challenges to be overcome for the proposed technology to be successful in the health market.

Describe why the proposed effort is a significant technical challenge and the key technical risks to the program. At a minimum, the Solution Summary should address:

- Does the approach require one or more entirely new technical developments to succeed?
- How will technical risk be mitigated?

E. Team Organization and Capabilities

Indicate the roles and responsibilities of the organizations and key personnel that comprise the Program Team. Provide the name, position, and institution of each key team member and describe in 1-2 sentences the skills and experience they bring to the team.

F. Rough Order of Magnitude (ROM)

Please include a ROM estimate of timeline and federal funds requested, as well as the total program cost including cost sharing, if applicable. The ROM should also include a breakdown of the work by direct labor, labor rates, subcontracts, materials, equipment, other direct costs (e.g., travel), indirect costs, profit, cost sharing, and any other relevant costs. Cost sharing is neither required nor forbidden and is not considered a factor in evaluation. The below table may be used for this breakdown:

Cost Category	**Amount**
Direct Labor	
Indirect Costs	
Sub-proposers	
Materials	
Equipment	
Travel	
Other Direct Costs	
Profit	
Total	
Cost Sharing *(if applicable)*	

However, proposers should ensure the ROM encompasses all applicable costs and should modify the above to best reflect the proposer's expected costs. The ROM does not count toward the page limit.

4.2.2. Full Proposal Format

Proposals must be in the format given below. The typical proposal should express a consolidated effort in support of one or more related technical concepts or ideas. Disjointed or unrelated efforts should not be included in a single proposal. Proposals shall consist of two volumes: 1) **Volume I, Technical and Management Proposal (composed of 2 parts),** and 2) **Volume II, Cost Proposal**. The Cover Page shall be no more than one (1) page in length. The page limitation includes all figures, tables, and charts. All pages shall be formatted for printing on 8-1/2 by 11- inch paper. Margins must be 1-inch on all sides, font size should be no less than 12 pt (Arial or Times New Roman), and page numbers should be included at the bottom of each page. Copies of all documents submitted must be clearly labeled with the ARPA-H ISO number, proposer organization, and proposal title/proposal short title (in the header of each page). Please use the following Title Format: "Volume I_Lead Org", "Volume II_Lead Org", "Supporting Document Lead Org". The maximum page count for Volume 1 is thirty (30) pages. This includes sections A-E

described below (Executive Summary, Goals and Impact, Technical Plan, Management Plan and Capabilities). Sections F-I below are not included in the page count (Statement of Work (SOW), Schedule and Milestones, Technology Transfer Plan, and References). However, for all sections, ARPA-H encourages conciseness to the maximum extent practicable. No other supporting materials may be submitted for review. Volume I should include the following components:

A. Volume I, Technical and Management Proposal

Section I: Administrative

Cover Page

1. ISO number (ARPA-H-SOL-24-101):
2. Technical area:
3. Proposal title:
4. Prime Awardee/entity submitting proposal:
5. Type of organization, selected among the following categories: LARGE BUSINESS, SMALL DISADVANTAGED BUSINESS, OTHER SMALL BUSINESS", Historically Black Colleges and Universities (HBCUs), Minority Institution (MI), OTHER EDUCATIONAL, OR OTHER NONPROFIT (including non-educational government entities) (*NOTE:* The Small Business Administration's (SBA) size standards determine whether or not a business qualifies as small.). Size standards may be found here: https://www.ecfr.gov/current/title-13/chapter-I/part-121#121.201
6. Date of submission:
7. Other team members (if applicable), organization and type of organization for each:
Example: Jane Doe, ACME, Other Small Business
8. Technical point of contact (POC) to include: salutation, last name, first name, street address, city, state, zip code, telephone, email:
9. Administrative POC to include: salutation, last name, first name, street address, city, state, zip code, telephone, email:
10. Total funds requested from ARPA-H, and the amount of cost share (if any).

Section II: Detailed Proposal Information

A. Executive Summary: Provide a synopsis of the proposed effort, including answers to the following questions:

- What is the proposed work attempting to accomplish or do?
- How is it done today, and what are the limitations?
- What is innovative in your approach?
- What are the key technical challenges in your approach, and how do you plan to overcome these?
- Who or what will be affected, and what will be the impact if the work is successful?
- How much will it cost, and how long will it take?

B. Goals and Impact: Clearly describe what the team is trying to achieve and the difference it will make (qualitatively and quantitatively) if successful. Provide an overview of the current and previous R&D efforts related to the proposed research and identify any challenges associated with such efforts, including any scientific or technical barriers encountered in the course of such efforts or challenges in securing sources of funding, as applicable. Describe the innovative aspects of the effort in the context of existing capabilities and approaches, clearly delineating the uniqueness and benefits of this effort in the context of the state of the art,

alternative approaches, and other efforts from the past and present. Describe how the proposed work is revolutionary and how it significantly rises above the current state-of-the-art. Describe the deliverables associated with the proposed work and any plans to commercialize the technology, transition it to a customer, or further the work.

C. Technical Plan: Outline and address technical challenges inherent in the approach and possible solutions for overcoming potential problems. This section should provide appropriate measurable milestones (quantitative if possible) at intermediate stages of the program to demonstrate progress, a plan for achieving the milestones, and a simple process flow diagram of the final system concept. The technical plan should demonstrate a deep understanding of the technical challenges and present a credible (even if risky) plan to achieve the program goal. Discuss mitigation of technical risk.

D. Management Plan: Provide a summary of the expertise of the team, including any subproposers, and key personnel who will be performing the work. A PI for the proposal must be identified, along with a description of the team's organization, including the breakdown by TA. All teams are strongly encouraged to identify a Project Manager/Integrator to serve as the primary POC to communicate with the ARPA-H PM, IV&V team, and OT/Grant Officer's Representative equivalent for each award instrument (e.g., Grants Management Specialist), coordinate the effort across co-performer, vendor, and subproposer teams, organize regular performer meetings or discussions, plans for data sharing, and ensure timely completion of milestones and deliverables.

Provide a clear description of the team's organization including an organization chart that includes, as applicable: the programmatic relationship of team members; the unique capabilities of team members; the task responsibilities of team members, the teaming strategy among the team members; and key personnel with the amount of effort to be expended by each person during each year. Provide a detailed plan for coordination, including explicit guidelines for interaction among collaborators/subproposers of the proposed effort. Include risk management approaches. Describe any formal teaming agreements required to execute this program.

E. Capabilities: Describe organizational experience in relevant subject area(s), existing intellectual property, specialized facilities, and any Government-furnished materials or information. Describe any specialized facilities to be used as part of the proposed work, the extent of access to these facilities, and any biological containment, biosafety, and certification requirements. Discuss any work in closely related research areas and previous accomplishments by the team.

F. Statement of Work (SOW): The SOW should provide a detailed task breakdown, citing specific tasks for each TA, and their connection to the milestones and program metrics. Each Phase of the program should be separately defined. The SOW must not include proprietary information. The SOW will not be evaluated as part of the technical evaluation.

For each task/subtask, provide:

- A detailed description of the approach to be taken to accomplish each defined task/subtask.
- Identification of the primary organization responsible for task execution (prime awardee, subproposer(s), by name).
- A measurable milestone, i.e., a deliverable, demonstration, or other event/activity that marks task completion. Include completion dates for all milestones. Include quantitative metrics.

- A definition of all deliverables (e.g., data, reports, software) to be provided to the Government in support of the proposed tasks/subtasks.

It is recommended the SOW be developed so that each TA and Phase of the program is separately defined.

G. Schedule and Milestones: Provide a detailed schedule showing tasks (task name, duration, work breakdown structure element as applicable, performing organization), milestones, and the interrelationships among tasks. The task structure must be consistent with that in the SOW. Measurable milestones should be clearly articulated and defined in time relative to the start of the effort.

H. Technology Transfer Plan: Provide information regarding the types of partners (e.g., government, private industry) that will be pursued and submit a timeline with incremental milestones toward successful engagement.

I. References: Add a list with the cited literature

B. Volume II, Cost Proposal

(1) All proposers must submit the following:

Cover Page

1. ISO number (ARPA-H-SOL-24-101):
2. Technical area:
3. Prime Awardee/entity submitting proposal:
4. Type of organization, selected among the following categories: LARGE BUSINESS, SMALL DISADVANTAGED BUSINESS, OTHER SMALL BUSINESS", Historically Black Colleges and Universities (HBCUs), Minority Institution (MI), OTHER EDUCATIONAL, OR OTHER NONPROFIT (including non-educational government entities)
5. Proposer's reference number (if any).
6. Other team members (if applicable) and type of organization for each:
7. Proposal title:
8. Technical POC to include: salutation, last name, first name, street address, city, state, zip code, telephone, email:
9. Administrative POC to include: salutation, last name, first name, street address, city, state, zip code, telephone, and email:
10. Award instrument requested: Cooperative Agreement or OT:
11. Place(s) and period(s) of performance:
12. Total proposed cost separated by base and option(s) (if any):
13. Name, address, and telephone number of the proposer's cognizant auditor (as applicable):
14. Date proposal was prepared:
15. Unique Entity Identification (UEI) number:
16. Commercial and Government Entity (CAGE) Code:
18. Proposal validity period (Minimum of 120 days).

Cost Proposal Information

The Government requires that the provided MS Excel ARPA-H Standard Cost Proposal Spreadsheet be utlized in the development of cost proposals. Proposers and subproposers requesting a Cooperative

Agreement must also complete the MS Excel SF-424A Budget Information for Non-Construction Programs. All tabs and tables in the cost proposal spreadsheet should be developed in an editable format with calculation formulas intact to allow traceability of the cost proposal. Cost proposal spreadsheets should be used by the prime organization and all subproposers. In addition to using the cost proposal spreadsheet, the cost proposal still must include all other items required in this announcement that are not covered by the editable spreadsheet. Subproposer cost proposal spreadsheets may be submitted directly to the Government by the proposed subproposer via email to the address in the Part I *Overview Information*.

NOTE: Non-conforming submissions that do not address the TAs as outlined under Section 1.2.1 and/or do not follow instructions herein may be rejected without further review.

Cost Breakdown Information and Format

Detailed cost breakdown to include[2]:

1. **Total Program Costs**
    a. Broken down by major cost items (e.g., direct labor, including labor categories; sub-agreements; travel; materials; other direct costs; overhead charges, etc.). For materials exceeding $5,000, a backup (screenshot, quote, etc.) is required.
    b. Further broken down by task and phase
2. **Major Program Tasks by Fiscal Year**
3. **An Itemization of Major Sub-agreements**
    a. In the same detail as the total program cost breakdown, and equipment purchases.
4. **Equipment**
    a. Documentation supporting the reasonableness of the proposed equipment costs (e.g., vendor quotes, past purchase orders/purchase history, detailed estimates from technical personnel, etc.) shall be provided.
5. **Itemization of Any Information Technology (IT) Purchases** (as defined by FAR 2.101)
    a. Documentation supporting the reasonableness of the proposed equipment costs (e.g., vendor quotes, past purchase orders/purchase history, detailed estimates from technical personnel, etc.) shall be provided.
6. **Summary of Projected Funding Requirements**
    a. By month
7. **Any Industry Cost-Sharing (if applicable)**
    a. Include the source, nature, and amount.
8. **Identification of Pricing Assumptions**
    a. Use of Government Furnished Property/Facilities/Information, access to Government Subject Matter experts, etc.

Tables included in the cost proposal must be in editable (e.g., MS Excel) format with calculation formulas intact.

NOTE: If PDF submissions differ from the Excel submission, the excel will take precedence.

C. Supporting Cost and Pricing Data

[2] While cost and pricing data is required, certified cost and pricing data is not required for any award instruments resulting from this R&D Solicitation.

Respondents to the ISO should include supporting cost and pricing information in sufficient detail to substantiate the summary cost estimates and should include a description of the method used to estimate costs and supporting documentation. For other direct costs (ODCs) (e.g., equipment, IT) greater than $5,000, please provide screenshots/quotes. For indirect costs, if one has been negotiated with the federal government, please provide the most current indirect cost agreement (e.g., Colleges and Universities Rate Agreement, Forward Pricing Agreement, Provisional Billing Rates, etc.). The proposer must provide the point of contact (email and phone number) for the rate agreements (FPRA or Provisional Billing rates).

Sub-proposer Proposals

The awardee is responsible for compiling and providing all subproposer proposals for the Grants or OT Agreement Officer as applicable. Subproposer proposals should include Interdivisional Work Transfer Agreements or similar arrangements between the awardee and divisions within the same organization as the awardee. Where the effort consists of multiple portions which could reasonably be partitioned for purposes of funding, these should be identified as option periods with separate cost estimates for each. A cost workbook is required for ALL subproposers.

All proprietary subproposer proposal documentation, prepared at the same level of detail as that required of the respondent's proposal and which cannot be uploaded with the proposer's proposal, shall be provided to the Government either by the proposer or by the subproposer when the proposal is submitted. Subproposer proprietary proposals may be submitted directly to the Government. See Section 4.2.4. of this ISO for Proposal Submission information.

D. Other Documents

Proposers should include any other required documents, as applicable, in Volume II. This should include, as applicable, OCI disclosures, OCI mitigation plans, Human Subjects and Animal Subjects Research documentation, intellectual property representations and assertions, etc.

4.2.3. Additional Proposal Information

Proprietary Markings

The government will protect any submissions marked as proprietary. Proposers are responsible for clearly identifying proprietary information. Submissions containing proprietary information must have the cover page and each page containing such information clearly marked with a label such as "Proprietary."

NOTE: "Confidential" is a classification marking used to control the dissemination of U.S. Government National Security Information as dictated in Executive Order 13526 and should not be used to identify proprietary business information.

Human Subjects Research (HSR)

All entities applying for funding that involves human subjects research (as defined in 45 CFR § 46) must provide documentation of one or more current Assurance of Compliance with federal regulations for human subject protection, including at least a Department of Health and Human Services (HHS), Office of Human Research Protection Federal Wide Assurance (https://www.hhs.gov/ohrp/index.html). All human subjects research must be reviewed and approved by an Institutional Review Board (IRB), as applicable under 45 CFR § 46. The human subjects research protocol must include a detailed description of the research plan, study population, risks and benefits of study participation, recruitment and consent process, data collection,

and data analysis. Recipients of ARPA-H funding must comply with all applicable laws, regulations, and policies for the ARPA-H funded work. This includes, but is not limited to, laws, regulations, and policies regarding the conduct of human subject research, such as the U.S. federal regulations protecting human subjects in research (e.g., 45 CFR § 46, 21 CFR § 50, § 56, § 312, § 812) and any other equivalent requirements of the applicable jurisdiction.

The informed consent document must comply with all applicable laws, regulations, and policies, including but not limited to U.S. federal regulations protecting human subjects in research (45 CFR § 46, and, as applicable, 21 CFR § 50). The protocol package submitted to the IRB must contain evidence of completion of appropriate human subject research training by all investigators and personnel directly involved with the contemplated human subject research. Funding cannot be used toward human subject research until ALL approvals are granted.

Animal Subjects Research

Award recipients performing research, experimentation, or testing involving the use of animals shall comply with the laws, regulations, and policies on animal acquisition, transport, care, handling, and use as outlined in: (i) 9 CFR parts 1-4, U.S. Department of Agriculture rules that implement the Animal Welfare Act of 1966, as amended, (7 U.S.C. § 2131-2159); (ii) the Public Health Service Policy on Humane Care and Use of Laboratory Animals[3] , which incorporates the "U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training,"[4] and "Guide for the Care and Use of Laboratory Animals" (8th Edition).[5]

For all proposed research anticipating animal use, proposals should briefly describe plans for Institutional Animal Care and Use Committee (IACUC) review and approval. Proposers must also submit the Vertebrate Animals Section (VAS) as required by the NIH Office of Laboratory Animals Welfare. See here for requirements for the VAS: https://olaw.nih.gov/guidance/vertebrate-animal-section.htm).

Section 508 of the Rehabilitation Act (29 U.S.C. § 749d)/FAR 39.2

All electronic and information technology acquired or created through this ISO must satisfy the accessibility requirements of Section 508 of the Rehabilitation Act (29 U.S.C. § 749d).

Cooperative Agreement Summary

Proposers requesting Cooperative Agreements awards must submit a Program Solution Summary (use current version in Grants.gov). The one (1) page summary may be publicly posted and explains the program or project to the public. The proposer should sign the bottom of the summary confirming the information in the Solution Summary is approved for public release. Proposers are advised to provide both a signed PDF copy, as well as an editable (e.g., Microsoft word) copy. Summaries contained in Cooperative Agreements proposals that are not selected for award will not be publicly posted. The document will only be requested if a full proposal is requested.

Note: This does not apply to OTs.

[3] olaw.nih.gov/sites/default/files/PHSPolicyLabAnimals.pdf
[4] olaw.nih.gov/policies-laws/gov-principles.htm
[5] olaw.nih.gov/sites/default/files/Guide-for-the-Care-and-Use-of-Laboratory-Animals.pdf

Intellectual Property

All proposers must provide a good faith representation or documentation that the proposer either owns or possesses the appropriate licensing rights to all intellectual property that will be utilized under the proposed effort. The information should be provided as part of a full proposal.

Proposers responding to this ISO requesting a Cooperative Agreement or OT should appropriately identify any desired restrictions on the Government's use of any Intellectual Property contemplated under the award instrument in question. This includes both noncommercial items and commercial items. Respondents are encouraged to use a format like that shown in the table below. If no restrictions are intended, then the proposal should state "NONE."

Technical Data Computer Software To be Furnished With Restrictions	**Summary of Intended Use in the Conduct of the Research**	**Basis for Assertion (e.g., developed exclusively at private expense, developed exclusively with mixed funds, etc.)**	**Asserted Rights Category (e.g., Unlimited, Limited, Restricted, or negotiated, as defined in FAR 27.401)**	**Name of Person Asserting Restrictions**
(LIST)	(NARRATIVE)	(LIST)	(LIST)	(LIST)

In addition, the evaluation will take into consideration the extent to which the proposed intellectual property (IP) rights structure will potentially impact the Government's ability to transition the proposed technology.

System for Award Management (SAM) and Unique Identifier Requirements

Regardless of award type, all proposers must be registered in SAM before submitting a full proposal. Entities that are not currently registered in SAM are advised that the process can take time and are encouraged to begin the registration process as soon as possible. International entities can register in SAM by following the instructions in this link: https://www.fsd.gov/sys_attachment.do?sys_id=c08b64ab1b4434109ac5ddb6bc4bcbb8.

4.2.4. Submission Information for Solution Summary and OT Proposals

Proposers are responsible for submitting Solution Summary and proposals for OTs to the electronic Contract Proposal Submission (eCPS) website at https://ecps.nih.gov/ and ensuring receipt by the date and time specified. Proposers must use this electronic transmission method. No other method of Solution Summary submission is permitted. Instructions on how to submit a proposal into eCPS are available at https://ecps.nih.gov/howtosubmit. Proposers may also reference Frequently Asked Questions regarding online submissions at https://ecps.nih.gov/faq.

For each of the requested files, please create a new business PDF and submit it as a new business document. If unable to do so, please consolidate these documents and include them at the end of "Supporting Document Lead Org".

Be advised that registration is required to submit a Solution Summary into eCPS and registration may take several business days to process. It is highly recommended that offerors plan to register through eCPS well in advance of the Solution Summary submission deadline, late Solution Summary submissions resulting from delays with eCPS registration may not be accepted or considered.

*NOTE: Submissions received after these dates and times will **not** be reviewed.*

A. Proposers Requesting Other Transaction Agreements

Proposers requesting an OT must provide a document describing Current and Pending Support. The document is mandatory for all Senior/Key Personnel including the PD/PI. This document should include the following information:

- A list of all current programs and projects the individual is working on, in addition to any future support the individual has applied to receive, regardless of the source.
- Title and objectives of the other research programs/projects.
- The percentage per year to be devoted to other programs/projects.
- The total amount of support the individual receives in connection to each of the other research efforts or will receive if other proposals are awarded.
- Name and address of the agencies and/or other parties supporting the other research efforts.
- Period of performance for the other research efforts.

This document should be included in the Cost Proposal volume.

B. Proposers Requesting Cooperative Agreements

Full proposal applications for cooperative agreements must be submitted in https://www.grants.gov/. In addition to the volumes requested elsewhere in this ISO, proposers submitting a requested full proposal must also submit the three (3) forms listed below. The forms do not count toward the page limitations.

Form 1: SF 424 *Research and Related (R&R) Application for Federal Assistance*, available on the Grants.gov website at https://www.grants.gov/web/grants/forms/r-r-family.html. This form must be completed and submitted.

To evaluate compliance with Title IX of the Education Amendments of 1972 (20 U.S.C. § 1681 et seq.), HHS is collecting certain demographic and career information to be able to assess the success rates of women who are proposed for key roles in applications in science, technology, engineering, or mathematics disciplines. HHS is using the forms below to collect the necessary information to satisfy these requirements. Detailed instructions for each form are available on Grants.gov.

Form 2: The Research and Related Senior/Key Person Profile (Expanded) form, available on the Grants.gov website at https://www.grants.gov/web/grants/forms/r-r-family.html, will be used to collect the following information for all senior/key personnel, including Project Director (PD)/PI and Co-Project Director/Co-PI, whether or not the individuals' efforts under the project are funded by HHS. The form includes 3 parts: the main form administrative information, including the Project Role, Degree Type and Degree Year; the biographical sketch; and the current and pending support. The biographical sketch and current and pending support are to be provided as attachments:

- Biographical Sketch: Mandatory for PDs and PIs, optional, but desired, for all other Senior/Key Personnel. The biographical sketch should include information pertaining to the researchers:

  - Personal Statement
  - Positions and Honors
  - Contributions to Science
  - Additional Information: Research Support and/or Scholastic Performance

- Current and Pending Support: Mandatory for all Senior/Key Personnel including the PD/PI. This attachment should include the following information:
  - A list of all current programs/projects the individual is working on, in addition to any future support the individual has applied to receive, regardless of the source.
  - Title and objectives of the other research programs/projects
  - The percentage per year to be devoted to other programs/projects.
  - The total amount of support the individual receives in connection to each of the other research programs/projects or will receive if other proposals are awarded.
  - Name and address of the agencies and/or other parties supporting the other research programs/projects.
  - Period of performance for the other research programs/projects

Additional senior/key persons can be added by selecting the "Next Person" button at the bottom of the form. If ARPA-H receives an application without the required information, ARPA-H may determine that the application is incomplete and may cause your submission to be rejected and eliminated from further review and consideration under this ISO. ARPA-H reserves the right to request further details from the applicant before making a final determination on funding the effort.

Form 3: Research and Related Personal Data, available on the Grants.gov website at https://www.grants.gov/web/grants/forms/r-r-family.html. Each applicant must complete the name field of this form, however, provision of the demographic information is voluntary. Regardless of whether the demographic fields are completed or not, this form must be submitted with at least the applicant's name completed.

4.3. FUNDING RESTRICTIONS

Pre-award costs will **not** be reimbursed unless a pre-award cost agreement is negotiated prior to the award.

4.4. QUESTIONS

Interested entities may submit questions to the ISO Coordinator at **PRINT**@ARPA-H.gov. Answers to questions received will be posted to the same website. ARPA-H will likely post answers to all relevant non-duplicative questions at intervals.

5. Application Review Information

5.1. EVALUATION CRITERIA

Solution Summary will be evaluated based on Evaluation Criteria #1, #2 and #3. The Solution Summary will undergo an initial review for responsiveness.

Solution Summaries that are outside the scope of the ISO will not be evaluated further. In addition, Solution Summaries that do not meet the submission requirements or do not contain one (1) or more of the required items listed above may be deemed nonresponsive and will not be evaluated further.

Full proposals will be evaluated using Evaluation Criteria #1 – #4, listed in descending order of importance.

5.1.1. Evaluation Criteria #1: Overall Scientific and Technical Merit

The proposed technical approach is innovative, feasible, achievable, and complete. Task descriptions and associated technical elements provided are complete and in a logical sequence with all proposed deliverables clearly defined such that a final outcome that achieves the goal can be expected as a result of the award. The proposal identifies major technical risks and planned mitigation efforts are clearly defined and feasible.

5.1.2. Evaluation Criteria #2: Proposer's Capabilities and/or Related Experience

The proposed technical team has the expertise and experience to accomplish the proposed tasks. The proposer's prior experience in similar efforts clearly demonstrates an ability to deliver products that meet the proposed technical performance within the proposed budget and schedule. The proposed team has the expertise to manage the cost and schedule. Similar efforts completed/ongoing by the proposer in this area are fully described including identification of other Government entities.

5.1.3. Evaluation Criteria #3: Potential Contribution and Relevance to the ARPA-H Mission

The proposed solution addresses potential future R&D, commercial, and/or clinical applications, including whether the solution has the potential to address areas of currently unmet needs within biomedicine and improve health outcomes. The proposed solution has the potential to transform biomedicine via an interdisciplinary approach.

5.1.4. Evaluation Criteria #4: Cost Realism

Cost realism will be performed to ensure proposed costs are realistic for the technical and management approach, accurately reflect the technical goals and objectives of this ISO, are consistent with the proposer's SOW, and reflect a sufficient understanding of the costs and level of effort needed to successfully accomplish the proposed technical approach. The costs for the prime proposer and subproposers will be substantiated for realism by the details provided in the proposal (e.g., the type and number of labor hours proposed per task, the types and quantities of materials, equipment and fabrication costs, travel and any other applicable costs and the basis for the estimates).

It is expected that the effort will leverage all available relevant prior research to obtain the maximum benefit from the available funding. ARPA-H recognizes that undue emphasis on cost may motivate proposers to offer low-risk ideas with minimum uncertainty and to staff the effort with junior personnel to be in a more competitive posture. ARPA-H discourages such cost strategies.

5.2. REVIEW OF SOLUTION SUMMARY AND FULL PROPOSALS

5.2.1. Review Process

It is ARPA-H policy to ensure impartial, equitable, comprehensive Solution Summary/proposal evaluations based on the evaluation criteria listed in Section 5.1. and to select the source(s) whose proposed solution meets the Government's technical, policy, and programmatic goals.

ARPA-H will conduct a scientific/technical review of each conforming Solution Summary/proposal. Conforming Solution Summary/proposals comply with all requirements detailed in this ISO; Solution Summary/proposals that fail to do so may be deemed non-conforming and may be removed from consideration. Solution Summary/proposals will not be evaluated against each other since they are not submitted in accordance with a common work statement. ARPA-H's intent is to review Solution Summary/proposals as soon as possible after they arrive; however, Solution Summary/proposals reviews may be delayed.

Award(s) will be made to proposers whose Solution Summary/proposals are determined to be the most advantageous to the Government, consistent with instructions and evaluation criteria specified in the ISO.

5.2.2. Handling of Source Selection Information

ARPA-H policy is to treat all submissions as selection sensitive information, and to disclose their contents only for the purpose of evaluation. During the evaluation process, submissions may be handled by support contractors for administrative purposes and/or to assist with technical evaluation. All ARPA-H support contractors performing this role are expressly prohibited from performing ARPA-H sponsored technical research and are bound by appropriate nondisclosure agreements. Input on technical aspects of the Solution Summary/proposals may be solicited by ARPA-H from non-Government consultants/experts who are strictly bound by the appropriate non-disclosure requirements.

Information may also be provided to Courts and the U.S. Government Accountability Office, to the extent that the information is necessary for compliance with federal law or a court order.

5.2.3. Federal Awardee Performance and Integrity Information (FAPIIS)

Per 41 U.S.C. § 2313, as implemented by 2 CFR § 200.205, prior to making an award above the simplified acquisition threshold, ARPA-H is required to review and consider any information available through the designated integrity and performance system (currently SAM.gov). Entities can comment on any information about themselves entered in the database, and ARPA-H will consider any comments, along with other information in FAPIIS or other systems, prior to making an award.

6. Award Administration Information

6.1. SELECTION NOTICES AND NOTIFICATIONS

6.1.1. Solution Summary

ARPA-H will respond to each Solution Summary. At that time, the proposer will be notified and informed of one of the following decisions:

1) ARPA-H has not selected the proposer to move forward with the submitted Solution Summary.
2) ARPA-H requests that the proposer submit a full proposal.
3) ARPA-H will contact the proposer for explanation on any unclear elements in the submitted Solution Summary to determine whether the Solution Summary will be selected or not.

6.1.2. Full Proposals

ARPA-H will review all conforming full proposals using the published evaluation criteria and without regard to any comments resulting from the review of an Solution Summary. As soon as the evaluation of a full proposal is complete, the proposer will be notified that:

1. ARPA-H has not selected the proposal.
2. ARPA-H has selected the proposal for funding pending award negotiations, in whole or in part. Official notifications will be sent via email to the Technical POC and/or Administrative POC identified on the proposal coversheet.
3. ARPA-H requires an explanation of any unclear elements in the submitted proposal. Based on that discussion, ARPA-H may not select the proposal, select, and enter into negotiations, or require proposal revisions prior to making a selection decision.

6.2. ADMINISTRATIVE AND POLICY REQUIREMENTS

6.2.1. Meeting and Travel Requirements

There may be a program kickoff meeting after award and all awardees are required to attend. Performers should also anticipate regular program-wide PI Meetings and/or periodic site visits at the PM's discretion.

6.2.2. Award Clauses, Terms and Conditions

Specific terms and conditions will be negotiated for each OT. Cooperative Agreement terms and conditions will be as required by applicable regulation and policy and as supplemented by unique requirements of the program/project.

6.3. REPORTING

In addition to the reports noted above in the technical section, the number and types of reports will be specified in the individual award document. ARPA-H expects the reporting to include monthly financial status reports, monthly technical status reports, quarterly reports, and an end-of-phase report. The reports shall be prepared and submitted in accordance with the procedures contained in the award document and mutually agreed on before the award. Reports and briefing material will also be required as appropriate to document progress in accomplishing program metrics. A Final Report that summarizes the effort and tasks will be required at the conclusion of the performance period for the award, notwithstanding the fact that the research may be continued under a follow-on vehicle. If applicable based on funding amount, reporting requirements specified in 45 CFR Part 75 Appendix XII will be incorporated into a Cooperative Agreement.

6.4. ELECTRONIC SYSTEMS

6.4.1. Payment/Funding Receipt

The Government anticipates performers will be required to register in the Payment Management Services (PMS) system at https://pms.psc.gov. Performers requesting an OT agreement may be required to register with the Invoice Processing Platform (IPP), this will be determined at the time of award.

6.4.2. i-Edison

The award document for each proposal selected for funding will contain a mandatory requirement for patent reports and notifications to be submitted electronically through i-Edison (https://public.era.nih.gov/iedison).

7. Agency Contacts

Points of Contact:

The ISO Coordinator for this effort may be reached at **PRINT**@ARPA-H.gov.

Collaborative efforts/teaming are encouraged. Parties interested in teaming should submit a one-page profile with their contact information to the teaming site, a brief description of their technical capabilities, and the desired expertise from other teams, as applicable.
https://arpa-h.gov/engage/programs/**PRINT**/teaming/

8. Other Information

ARPA-H will host a Proposers' Day in support of the **PRINT** Program on the date listed in Part I., *Overview Information* of this ISO. The purpose is to provide potential proposers with information on the **PRINT** program, promote additional discussion, and encourage team networking.

Interested proposers are not required to attend, and materials formally presented on Proposers' Day will be posted to SAM.gov.

ARPA-H will not reimburse potential proposers for participation at the Proposers' Day or time and effort related to submitting Solution Summary/full proposals. To participate in the event, proposers must complete the online registration form located at https://solutions.arpa-h.gov/Events/PRINT/.

Participants are required to register no later than the date listed in Part I., *Overview Information* of this ISO. This event is not open to the press or patients. To facilitate easier access to underserved communities, Proposers' Day will be a hybrid event.