INNOVATIVE SOLUTIONS OPENING

FOR

BIOSTABILIZATION SYSTEMS

BOSS

SCALABLE SOLUTIONS OFFICE (SSO)

ARPA-H-SOL-26-136

December 2, 2025

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INNOVATIVE SOLUTIONS OPENING (ISO) SUMMARY INFORMATION

FEDERAL AGENCY: Advanced Research Projects Agency for Health (ARPA-H)

PROGRAM TITLE: BioStabilization Systems (BoSS)

ANNOUNCEMENT TYPE: Innovative Solutions Opening (ISO)

ISO SOLICITATION NUMBER: ARPA-H-SOL-26-136

ISO CONTACT: BoSS@arpa-h.gov

ANTICIPATED AWARDS: Multiple Other Transaction (OTs) Agreements

DATES: (All times listed are Eastern Time)

Proposer's Day: January 29th, 2026 8:00 AM to 5:00 PM ET
Questions & Answers (Q&A) due date: Jan 22nd, 2026 5:00 PM ET

For consideration as a Performer:
Solution Summary due date: February 19th, 2026 5:00 PM ET
Solution Pitch due date: March 26th, 2026 5:00 PM ET

For consideration as an IV&V partner:
Solution Summary due date: April 17th, 2026 5:00 PM ET
Solution Pitch due date: May15th, 2026 5:00 PM ET

WHERE TO SUBMIT:

Solution Summaries: https://solutions.arpa-h.gov/Submit-Solution/
Solution Pitch materials: https://solutions.arpa-h.gov/Submit-Solution/
Questions: https://solutions.arpa-h.gov/Ask-A-Question/

PROPOSERS' DAY

The Scalable Solutions Office (SSO) of ARPA-H is sponsoring a Proposers' Day (PD) and sidebar discussions for the planned Proposer community in support of the BoSS program as described in Special Notice ARPA-H-SN-26-137. The purpose is to provide potential Proposers with information on BoSS, promote additional discussions, and encourage teaming and networking.

Interested Proposers are encouraged to attend the PD and schedule an optional sidebar to discuss any clarifying questions with the Program Manager and team. Materials formally presented during PD will be posted to the ARPA-H Program Website.

ARPA-H will not reimburse potential Proposers for participation at Proposers' Day (or time and effort related to submissions in response to this ISO).

1. INTRODUCTION TO BOSS

The BioStabilization Systems (BoSS) program aims to transform how live cell-based therapies are stabilized, manufactured, and distributed. At its core, BoSS addresses a foundational bottleneck in the delivery of advanced cell and gene therapies (CGTs): the critical dependence on ultra-cold conditions (-80 to -196˚C) for storage and transport. BoSS will yield a bioprocessing system that enables scalable production of thermally stable cells, paving the way for a new era of efficient and resilient manufacturing and distribution of biologics without any need for cold storage. BoSS-developed technologies will also accelerate many other avenues in biotechnology that directly impact healthcare, including bio-surveillance, regenerative medicine, large-scale genetic testing, blood product supply, and wound repair, in addition to improving access to a wide range of existing biotherapeutics.

This ISO is intended to solicit:

1) Performer teams that can pioneer breakthrough cell stabilization technologies and integrate these technologies into a commercially viable system for producing cell therapy products at scale. Strategic partnerships are encouraged to best position technologies for commercialization success, such as assembling multidisciplinary teams that may include experts from academic, industry, regulatory, commercialization, and non-traditional backgrounds.
2) An Independent Verification and Validation (IV&V) partner to reliably provide well-characterized, clinically relevant, government-selected cells to Technical Area Performers. This partner will also assess cell viability and system performance at critical junctures throughout the program.

1.1 Background

This year approximately 150 million Americans will use at least one thermally unstable biologic, such as a monoclonal antibody, vaccine, or cell therapy[1,2]. The instability of these medicines necessitates a reliance on cold chain, which jeopardizes product effectiveness, escalates costs, and limits access due to complex, temperature-dependent manufacturing and distribution schemes. Furthermore, costly ultra-cold cryopreservation is the standard approach to extending shelf-life stability for life saving biologics such as CGTs. However, demand for CGTs continues to surge, powered by their transformative impact on healthcare and reflected in rapid market expansion. Globally, there are now >3000 CGTs in the development pipeline, ranging from pre-clinical through pre-registration phases[3]. Innovative solutions that relieve cold chain requirements while preserving shelf-life stability are crucial to meeting this rising demand, as FDA approval and widespread patient access to CGTs rely on maintaining product quality throughout storage and distribution.

BoSS aims to develop innovative technologies that preserve cells at ambient temperatures, a breakthrough approach we will subsequently refer to as *biostabilization*. Achieving

[1] *Centers for Disease Control and Prevention. Weekly Flu Vaccination Dashboard | FluVaxView. National Center for Immunization and Respiratory Diseases, 7 May 2025, www.cdc.gov/fluvaxview/dashboard/index.html.*
[2] *Centers for Disease Control and Prevention. Aggregated data from "Vaccination Trends for Respiratory Viruses". CDC. https://www.cdc.gov/respiratory-viruses/data/vaccination-trends.html. Accessed April 2025.*
[3] *American Society of Gene & Cell Therapy. Gene, Cell, & RNA Therapy Landscape Report: Q3 2025. Nov. 2025, www.asgct.org/uploads/files/general/Landscape-Report-2025-Q3.pdf.*

biostabilization remains a two-fold challenge that has yet to be overcome. The first challenge requires cellular interventions to preserve the integrity and function of vital elements prior to undergoing stabilization, enabling cells to withstand physical changes that would otherwise cause irreversible damage. This could include delivering protectants into cells and/or altering cells in other ways to improve processing and storage resilience. To maintain the clinical utility of cell products, cellular interventions to prepare and deploy biostabilization must be both biocompatible and reversible. The second challenge involves implementing aseptic, cell-friendly handling instrumentation to deploy stabilization techniques across various production scales.

One approach to address the first challenge is to adopt nature's strategies to accomplish biostabilization. For example, 'anhydrobiotes' can tolerate extreme loss of water and persist in a dehydrated state for years (e.g., tardigrades, rotifers, brine shrimp), quickly regaining full function after rehydration. Molecular contributors to this resilience have been elucidated such as amorphous trehalose glass and special classes of intrinsically disordered proteins (IDPs)[4]. Recent studies have revealed cell structure re-arrangements and stress-induced formation of molecular condensates that may be essential for surviving the stresses of dry processing[5]. Other discoveries from the genomic to the organismal scale form the natural basis of desiccation tolerance[6] and may be adapted or improved upon for biostabilization. Solutions inspired by chemistry and materials science advances are also encouraged along with approaches that employ biocompatible polymers, scaffolds, multi-organic frameworks, or cell encapsulation to protect and stabilize cells.

Addressing the second challenge requires development of new processing approaches and potentially new instrumentation that can yield products suitable for ambient storage. Current gold standard methods for batch processing like lyophilization (freeze-drying) are energy-intensive, slow, and challenging to apply to complex biologics. While appropriate for proteins, antibodies, and even some vaccines, lyophilization is a risky and unproven approach for high-value cell products that are widely used in the biopharma industry as starting materials, manufacturing intermediates, host cells, and cell-based therapies[7]. Nascent technologies like microwave-assisted vacuum foam-drying, thin film freeze-drying, and polymerization gelation exhibit potential for processing complex biologics but remain at a low manufacturing readiness level (MRL), i.e., early-stage development and requires significant development to establish full-scale production[8,9,10]. Established technologies with high MRL, such as spray-drying, commonly used for food production, offer the advantage of continuous processing and may have potential for adaptation to biologics[11].

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[4]Belott, CJ, et al. "Membraneless and membrane-bound organelles in an anhydrobiotic cell line are protected from desiccation-induced damage". Cell Stress Chaperones. 2024; 29(3):425-436.Nicholson, et al. "Osmolyte-IDP interactions during desiccation". Prog Mol Biol Transl Sci. 2025; 211:39-61.

[5]Marks, RA, et. al. "Life on the dry side: a roadmap to understanding desiccation tolerance and accelerating translational applications". Nat Comm. 2025; 16(1):3284.

[6] Nicholson, et al. "Osmolyte-IDP interactions during desiccation". Prog Mol Biol Transl Sci. 2025; 211:39-61.

[7] BioPharm International. Lyophilization Presents Complex Challenges. Published February 16, 2023.

[8] AboulFotouh, K, et al. "Inhalable dry powders of microRNA-laden extracellular vesicles prepared by thin-film freeze-drying". Int J Pharm. 2024;651:12375.7

[9] Osanloo, DT, et al. "Formulation factors affecting foam properties during vacuum foam-drying". Int J Pharm. 2024; 652:123803.

[10] McNally, DL, et al. "Reversible Intracellular Gelation of MCF10A Cells Enables Programmable Control Over 3D Spheroid Growth". Adv Healthc Mater. 2024; 13(7):e2302528.

[11] Dantas, A, et al. "Innovations in spray drying technology for liquid food processing: Design, mechanisms, and potential for application". Appl Food Res. 2024; 4(1):100382.

Successful completion of BoSS will yield a bioprocessing system designed as a platform technology for stabilizing cell biologics capable of easy integration into biomanufacturing pipelines. The bioprocessing system will enable scalable production and distribution of thermally stable cells benefiting the biopharmaceutical ecosystem that uses cells as starting materials, manufacturing intermediates, and CGTs. Breakthroughs from BoSS are expected to yield biostabilization innovations including intracellular and extracellular protectants and stabilizers, enabling bioprocessing technologies, and re-animation products. Together, BoSS bioprocessing system and biostabilization technologies will be commercially viable solutions that will establish a new paradigm for biomanufacturing designed to reduce costs and ensure that biological medicines are accessible to patients, including those living in the most remote and resource-limited communities.

1.2 Technical Areas

BoSS envisions that successful solutions will converge from extremophile biology, biomaterials science, biomanufacturing, pharmaceutical formulation, process engineering, and device development to unlock new bioprocessing and biostabilization solutions, bridging historical silos in biostasis science and advancing biological medicines. Proposals are required to address solutions to **both** technical areas:

(1) Technical Area 1 (TA1): BioPrep

Approaches to BioPrep include preparing, protecting, and other methods of intervention to allow cells to endure and recover from biostabilization at room temperature. BioPrep solutions should be reversible interventions that support the suspension of biological activity while ensuring cellular health and integrity upon reanimation. BioPrep solutions may also include the development of re-animation techniques and solutions that rapidly restore biological activities after biostabilization.

(2) Technical Area 2 (TA2): Bioprocessing

Bioprocessing technologies (e.g., instruments, devices) should enable the deployment of biostabilization concepts at scale. Activities may include the scale-up of an early MRL, cell-friendly processing technology, or the adaptation of scaled systems that can be re-designed to safely and gently handle cells. The proposed solution should mitigate stress on cells while achieving biostabilization with preserved quality and function for extended durations at ambient temperatures.

The following list of in-scope examples for TA1 is not exhaustive. Innovative solutions beyond this list, but theoretically capable of meeting the program metrics, will be considered.

The examples out-of-scope are considered incremental from the current state of the art, impractical from an implementation standpoint, or unlikely to lead to market adoption and therefore are not of interest.

Table 1. *In-scope and out-of-scope approaches*

Examples In-scope	Examples Out-of-scope
• Methods for altering cell structures in reversible ways (chemical, hormonal, physical) • Trehalose and IDPs used as part of a larger bioprotection scheme • Methods for inducing formation of protective membraneless organelles • Techniques that enable intracellular delivery of protectant or intervention molecules (sonoporation, mechanoporation, electroporation, other emerging approaches) • Additives to rehydration solutions that can improve recovery • Bio-polymerization approaches • Encapsulation methods (gelation, ensilication, metal-organic frameworks) • Processing techniques that can be adapted for cells (spray drying, microwave drying, supercritical fluid drying, thin-film freezing, vacuum foam-drying, combination systems) • Scalable and multiplexed microfluidic devices • Methods that allow characterization of biostabilization at the genomic, molecular, and cellular level • Application of AI or DOE methodologies that enhance research outcomes • Process analytical technologies • In vitro and in vivo models to interrogate cell function • Re-animation solutions	• Trehalose or IDPs deployed in an incremental manner • Standard lyophilization approaches • Slow (>4 hours) cellular interventions • Slow (>1 day) processing approaches • Storage solutions that achieve incremental advances in shelf-life (days instead of months) • Processing methods that cannot be scaled or adapted to aseptic Good Manufacturing Practice (GMP) manufacturing • Re-animation solutions that require complex processing steps prior to end-use • Techniques that do not address (or assess) preservation of intracellular complexity • Demonstrations on red blood cells or microbial species • Approaches that are not generalizable to other cells • Approaches that cannot be easily integrated into existing workflows with standardized industry-accepted containers • Genetic manipulation of cells

Dangerous gain-of-function research, per the definition in Section 8 of Executive Order (E.O.) 14292 on Improving the Safety and Security of Biological Research, **will not be considered**.

Proposers must submit proposals to both TAs. A conforming proposal will account for all program requirements outlined in this ISO, both TA-specific and overall program milestones and metrics.

Advancement to Phase 2 will be at the sole discretion of the Government and is dependent on the TA1 and TA2 members within each multi-party team working together to develop and demonstrate a cohesive solution. This includes jointly deciding on stabilization strategies,

sharing materials and instruments, and integrating their work to produce a fully functional system. Individual team members or sub-teams that have met or exceeded the metrics for one of the two TAs may have the opportunity to join another multi-party team that has met or exceeded metrics in the other TA. These newly formed teams may submit a revised program plan, reflecting the new teaming arrangement, to the Government for consideration for advancement to Phase 2. Decisions regarding continued performance may be based on several factors, including technical progress measured against the metrics and milestones defined in this ISO, and availability of funding. Solutions to TA1 and TA2 must include the use of robust, cost-effective materials and supplies with proven safety and quality. Importantly, re-animation procedures that require minimal manipulation of cell products and do not require post-manufacturing processing are highly preferred. Re-animation approaches can be developed as combination products with stabilized cell products, and the re-animation process is preferred to take under one hour with minimal manipulation to cell products. For all approaches, the goal is to develop a novel platform technology that demonstrates scalable production of stabilized cells using innovative methods. The resulting technology must be suitable for commercial use and meet FDA regulations for human cells, tissues, and cellular and tissue-based products (HCT/Ps).

1.3 Program Overview

Technology commercialization is a critical part of achieving the ARPA-H mission to improve health outcomes for all Americans. To support this goal, progress will be measured by strategic metrics and milestones that must be met to advance through subsequent phases. Technologies will advance across three integrated phases designed to drive both technical advancement and commercial translation:

- **Phase 1** focuses on establishing the scientific feasibility of ambient biostabilization. This proof-of-concept stage includes developing innovative cell preparation approaches with enabling instrumentation that, together, are capable of inducing biostabilization as well as re-animation methods to restore function after biostabilization.
- **Phase 2** emphasizes integrated capability demonstrations, converging biological and manufacturing innovations into a cohesive bioprocessing system that can produce stabilized cells under simulated commercial conditions.
- **Phase 3** advances to scaled solution development and industry transition, preparing the bioprocessing system for market entry through GMP-compliant production, strategic industry partnerships, and validation in real-world use cases.

Performer teams must meet increasingly stringent technological capability requirements and stabilized cell quality metrics during each phase (see phase-end metrics in **Table 3**) to demonstrate progress on biostabilization technology development. Performers will choose cells used for end of phase demonstrations from a list of government-selected cell types, which will be identified at the start of the performance period. Sub-phase milestones may be demonstrated on cell types chosen by the Performer, with consideration to the restrictions identified in Table 1. In later stages, end of phase demonstrations will be permitted on cells that are aligned with Phase 3 transition partners. Ideal transitional partners for Performers are organizations equipped with established distribution networks to seamlessly integrate the

developed bioprocessing system into their existing biomanufacturing pipelines for cell biologics, accelerating the path from innovation to implementation.

At the end of the program, biostabilization technologies will demonstrate capability, scalability, and applicability of commercially viable platform technologies that enable room temperature storage and distribution of stabilized cells agnostic of cell type, supporting widespread access to biologic medicines. The ideal bioprocessing system will integrate seamlessly with biomanufacturing and fill-finish systems. Ultimately, partnerships will culminate into early adoption of a new commercially viable bioprocessing system capable of scalable production of stabilized cell products that meet Good Laboratory Practice (GLP) and GMP standards with a path paved for commercialization to support broad industry adoption.

1.4 Program Structure

The BoSS program is structured as a 4-year effort (48 months) consisting of three phases (Figure 1). Phase 1 will be 15 months to allow multi-disciplinary coordination, interactive parallel development of technical approaches to both TAs, and iteration on various operational elements to demonstrate proof-of-concept by the end of the phase. Because of the range of possible approaches, multiple awards may be initially funded with a planned down-select at the end of Phase 1.

Down-selects are evaluation points resulting in the selection of Performers that proceed or do not proceed to the next phase of the program. The Program Management Team will evaluate the progress of each Performer against the program milestones, metrics, and deliverables. Additionally, IV&V will provide technology assessments on Performer technologies and their output (i.e., stabilized cells) to support the evaluation by Program Management Team.

Individual team members or sub-teams that have met or exceeded the metrics for one of the two TAs may have the opportunity to join another multi-party team that has met or exceeded metrics in the other TAs. These newly formed teams may submit a revised program plan, reflecting the new teaming arrangement, to the Government for consideration for advancement to Phase 2.

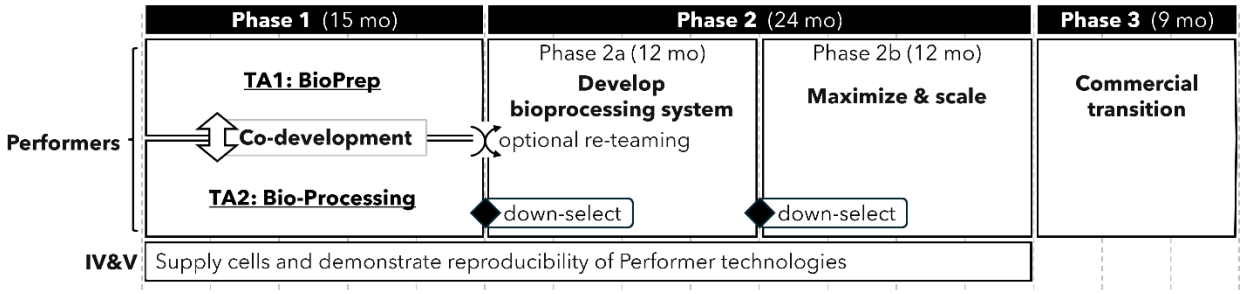
Phase 2 is a total of 24 months to develop a novel bioprocessing technology based on the integrated approaches from Phase 1. The first 12 months (Phase 2a) will focus primarily on design iterations to maximize performance of the system at small-scale. Performers are also expected to integrate regulatory considerations through engagements with the FDA and refine commercialization plans with a transition partner identified by the end of Phase 2a (see 3.3 Program Metrics for details). A second down-select at the end of Phase 2a will be based on demonstrations of increased cell function at longer storage times, with consideration also given to system scalability which will be key demonstrations in Phase 2b. At the end of Phase 2b, Performers will be assessed on the system performance on large-scale production, with a down-select to advance Performers to Phase 3.

Finally, Phase 3 will be 9 months focused on transition of the successful technology to commercial partners. This final phase is necessary to connect BoSS technology with the best commercial adopters given its potential as a market disruptor. Without a focused effort on commercialization there is the potential for successful BoSS technologies to be delayed, or even unsuccessful, in implementation. Resource-share is encouraged in Phase 3 and could

include strategic demonstration of the technology on a cell product for clinical use, with the intent of assessing the BoSS system for in-licensing, acquisition, or other partnership. Performers are encouraged to consider potential resource-share opportunities with transition partners as part of their transition strategy. However, resource-share is not required at this stage, and proposals are not expected to specify resource-share amounts or types

Continued performance of awardees through all phases of the program will be at the sole discretion of the government, and may be based on several factors, including technical progress measured again the metrics and milestones defined in this ISO, and availability of funding.

Figure 1. *BoSS program structure*



2. INDEPENDENT VALIDATION AND VERIFICATION (IV&V) PARTNER

The IV&V partner will be a commercial entity that will support the government's Program Management Team to assess the performing teams' progress, as required by the government. This commercial entity must be technically, managerially, and financially independent of all developmental performing teams. An IV&V partner will ensure reproducibility and credibility of data generated by Performers at critical assessment points throughout the program. Additionally, IV&V will supply government-selected cell types to Performers to be used for technology demonstrations. Proposers selected to receive funding related to research and development under TA1 or TA2 are not eligible to work as an IV&V partner. The objectives for IV&V are to:

Manufacture and supply Performers with authenticated human cell types and supporting documentation of donor testing to certify safe use (

- **Table 2**).
- Generate and supply standard operating procedures (SOP) for standard culture practices for metabolically active cells and characterize each cell type as benchmarks for Performers.
- Perform re-animation method according to SOPs generated by Performers and subsequently assess the quality of stabilized cells produced by all Performers.
- Generate technical reports that summarize validation results, identify discrepancies, and provide recommendations for development.

- Engage with Program Management Team via email or meetings to share information and data at critical assessment points (e.g., end-of-phase).
- Facilitate transparency and reproducibility with Performers and Program Management Team using experience and oversight.

***Table 2**. Examples of government-selected cells supplied by IV&V for use in Performer demonstrations*

Category	Example cell types
Clinical cells (e.g., cell therapies)	• T lymphocytes • Hematopoietic stem cells • Mesenchymal stem/stromal cells
Cells used in biomanufacturing	• Chinese hamster ovarian (CHO) cells • Human endothelial (HEK) cells
Cells as emerging regenerative medicines	• induced Pluripotent Stem Cells (iPSC) • iPSC-derived cells • Primary cells (e.g., hepatocytes, neurons)

2.1 IV&V Scope of Work

Prior to the initiation of Phase 1 demonstrations, IV&V will manufacture, authenticate, and bank cells according to ICH Guideline Q5D. IV&V will be responsible for maintaining comprehensive records of all cell line development traceable from initial starting materials, including donor screening for adventitious agents, batch records, reagent quality assurance documentation (e.g., certificate of compliance (COA), certificate of origin), and executed SOPs. IV&V will generate COAs for all cell lines to certify safe use and verify batches meet all release specifications. Authenticated cells will be banked until coordinating the transfer of materials to Performers for use in demonstrations.

Critical assessment points for IV&V include the end of Phase 1, Phase 2a, and Phase 2b. At these times prescribed amounts of stabilized cell samples and re-animation materials, along with SOPs generated by Performers, will be provided to IV&V to objectively determine the effectiveness of different biostabilization approaches on the same BoSS-selected cell types (

Table 2). IV&V assessments of Performer technologies and their outputs (i.e., stabilized cells) will be used as criteria at down-select points in the program to assess performer technology effectiveness and reproducibility. At the end of Phase 2a, access to the bioprocessing system will also be provided to the IV&V to assess usability, scalability, and fitness for purpose. IV&V will also play a supporting role to Performers by providing relevant feedback on system usability, scalability, and economic feasibility.

The following tasks and deliverables will be performed at the initiation of the study and/or at critical assessment points:

Task 1: Harmonization of Program Metrics by Establishing SOPs, Cellular Benchmarks, and Supplying Authenticated Cells (at program initiation)

- Develop, standardize, and document SOPs for characterization experiments to be shared with Performers for execution.
- Establish characterization benchmarks for metabolically active cells directly after manufacturing (i.e., before cryopreservation) and after cryopreservation.
- Supply Performers with cells with supporting documentation (e.g., COA).

Deliverables:

- Comprehensive SOPs for all cell culture activities and cell assessments based on phase-end metrics (Table 3) (initial delivery: Month 1; updates as needed).
- Benchmark documentation of cell characterization (initial and updated as needed)
- COA related to supplied cell lines.
- Supply GLP compliant cells for demonstrations.

Task 2: Receipt of Materials (at critical assessment points)

- Log, inventory, and inspect all incoming materials (stabilized cell samples, re-animation products) and documents (e.g., SOPs) developed by Performers.
- Maintain an inventory management system for tracking all materials.

Deliverables:

- Email notification of materials receipt to the Program Management Team.
- Chain-of-custody logs for all materials (updated upon every receipt).
- Inventory management reports (as needed).

Task 3: Material Assessments (at critical assessment points)

- Execute re-animation of stabilized cells according to corresponding re-animation SOPs from Performers.
- Perform assessments based on phase-end metrics (**Table 3**) relevant to cell type following re-animation.
- Document all procedures and deviations from Performer SOPs.

Deliverables:

- Overview of each Performer's cell assessment workplan.
- Records of procedures and executed tests / assays performed under each Performer's workplan.
- Documentation of the results based on phase-end metrics (**Table 3**) relevant to cell type following re-animation.
- Documentation of discrepancies, anomalies, or concerns related to assessment of stabilized cells (if applicable).

Task 4: Technology Assessments (at critical assessment points)

- In-person execution of Performer SOPs to operate bioprocessing systems used to produce stabilized cells.
- Assess usability, scalability, and fitness for purpose of bioprocessing systems based on performing biostabilization on at least 2 different cell types according to Performer SOP.

- Assess reproducibility of bioprocessing systems based on performing biostabilization on 3 separate lots of a single cell types.
- Document all procedures and deviations from Performer SOPs.

Deliverables:

- Documentation related to the operations of the bioprocessing systems including objective assessment of usability, scalability, fitness for purpose, and reproducibility.
- Documentation of discrepancies, anomalies, or concerns related to assessment of bioprocessing systems (if applicable).

Task 5: Data analysis and reporting (at critical assessment points)

- Analyze assessment data using appropriate statistical and computational methods.
- Compare results to established benchmarks.
- Prepare comprehensive technical reports summarizing findings, including:
  - Description of test materials and methodologies.
  - Results, interpretation, and assessment of reproducibility.
  - Highlight of any discrepancies, anomalies, or performance concerns.
  - Recommendations for further investigation or process improvement.

Deliverables:

- Draft cell assessment reports for each Performer (within 4 weeks of completion).
- Summary validity and reproducibility report for each Performer (at the end of assessment point).

Task 6: Communication and Coordination (throughout program)

- Maintain a secure, organized repository for all reports, data, and supporting documents.
- Communicate with Program Management Team to review progress, present findings, and reassess priorities.
- Provide rapid response or support (within 3 business days) in the event of critical findings or at the request of Program Management Team.

Deliverables:

- Notification reports for critical scientific issues or safety concerns.
- Submission of data and reports to ARPA-H.

Within 90 days of Program kick-off, all participating parties must establish and execute Material Transfer Agreements (MTAs) to govern the transfer, use, and management of biological materials and related data. These agreements are required to ensure compliance with institutional, legal, and regulatory standards, and to clarify the rights, responsibilities, and obligations of each party regarding the materials exchanged. To ensure unbiased assessments and deliverables, Independent Verification & Validation (IV&V) organizations must be wholly independent from Technical Performers. For the purposes of this requirement, organizational independence means that the IV&V entity must have no direct or indirect ownership, control, partnership, or affiliation with any Technical Performer under this program. This includes, but is

not limited to, subsidiaries, parent companies, affiliates, or entities under common ownership or control. The IV&V organization must provide a certified statement attesting to its independence after all technical performers have been awarded and prior to any IV&V award, as a condition of participation.

2.2 IV&V Qualifications

Required qualifications for IV&V include, but are not limited to, demonstrating the following:

- **Authenticated Cell Supplier**
    - Provides documentation of authentication results for each batch of supplied cells (e.g., Certificate of Analysis) with results of donor screening for adventitious agents.
    - Generates, stores, and ships a sufficient supply of well-characterized cells for Performers demonstrations (see
    -
    - Table **2**. Examples of government-selected cells).

Note: It is critical for IV&V to supply sufficient amounts of authenticated cells to Performers for iterating and demonstrating technology development along with supporting documentation (i.e., COA). For all cell types, IV&V is expected to manufacture each batch consistently, maintaining the characteristics that are initially defined and shared to Performers as stabilized cell metrics (see Table 3. Phase-end metrics). IV&V will supply each Performer with at least two cell types which will be supplied as cryopreserved vials of cells containing one to ten million cells for each small-scale demonstration (in Phase 1 and 2a) and up to 100 million cells for each large-scale demonstration (Phase 2b). Based on a high volume of iterations by multiple Performers in Phase 1 and Phase 2a, it is estimated that IV&V will supply up to 500 million cells per cell type. IV&V will be given advanced notice on the estimated amounts of cells needed for Phase 2b as this may vary depending on the number of succeeding Performers who may optionally outsource cells to strategically align with partnerships. It is important to note Performers will only thaw and recover cells in culture to a metabolically active state prior to use and will not further expand cells in culture.

If an IV&V partner does not have comprehensive capabilities as an Authenticated Cell Supplier, IV&V can satisfy this qualification by partnering with another entity. In this case, IV&V will be responsible for engaging the supplier to select, purchase, and store banks of multiple cell types and manage the shipping of cells to the Performers in addition to the remaining scope of work.

- **Technical Expertise in Cell Characterization**
    - Possesses experience with cell banking, cell line authentication, sterility testing, and advanced cell characterization methods (e.g., flow cytometry, bioassays).
    - Performs process development, analytical development, and product characterization for cell and gene therapy products.
- **Experience with Nonclinical Studies**
    - Possesses track record in supporting early-phase nonclinical studies, including project management, site monitoring, and oversight.

  - Provides integrated services from nonclinical development through clinical manufacturing and testing.

- **Regulatory and Compliance Knowledge**
  - Possesses familiarity with current standards, regulatory science, and guidance for cell-based products that are recognized by the FDA and established by Standards Development Organizations.
  - Maintains compliance with GLP and relevant quality standards for laboratory and clinical operations.

- **Data Analysis and Reporting Capabilities**
  - Possesses proficiency in data sourcing, dataset creation, and statistical analysis relevant to biologics.
  - Generates clear, actionable reports for technical and non-technical audiences.

- **Infrastructure and Capacity**
  - Provides access to state-of-the-art laboratory facilities and equipment for cell characterization.
  - Maintains sufficient staffing with qualified scientists, technicians, and project managers.

- **Independence and Objectivity**
  - Maintains organizational independence from stakeholders to ensure unbiased results.
  - Possesses history of third-party assessments and transparent reporting.

- **Track Record**
  - Demonstrates success in previous cell characterization projects, especially in support of biopharmaceutical, gene therapy, or cell therapy programs.
  - Provides references or case studies showing impact and reliability.

Preferred Qualifications:

- **Experience with Clinical Studies**
  - Possesses track record of supporting early-phase and late-phase clinical studies, including project management, site monitoring, and oversight.
  - Possesses ability to provide integrated services from nonclinical development through clinical manufacturing and testing.

- **Quality Assurance Systems**
  - Maintains robust quality management systems ensuring data integrity, traceability, and reproducibility.
  - Possesses experience with process validation, assay qualification, and verification of manufacturing capabilities.
  - Maintains documented protocols for assay validation, sample handling, and reporting.

- **Regulatory and Compliance Practices**
    - Implements current standards, regulatory science, and guidance for cell-based product assessments that are recognized by the FDA and established by Standards Development Organizations.
    - Maintains compliance with GMP regulations and relevant quality standards for laboratory and clinical operations.

For Proposers seeking consideration as the IV&V partner, please refer to the information in sections 4. ELIGIBILITY INFORMATION, 5. SUBMISSION PROCESS, 6. SUBMISSION REVIEW AND EVALUATION PROCESSES, and 7. POLICY REQUIREMENTS AND MISCELLANEOUS OTHER INFORMATION for details.

3. TECHNICAL PERFORMER TEAMS (TA1 AND TA2)

In addition to the fundamental expertise needed to develop solutions to TA1 and TA2, it is highly recommended that Performer teams include members or consultants with expertise in (but not limited to) regulatory, intellectual property, commercialization, biologics manufacturing, and medical device development. These expert advisors will be critical to the successful translation and commercialization of developed biostabilization technologies. Performers may opt to receive additional commercialization support and resources from the BoSS program, such as assistance forming strategic partnerships aimed at achieving the program deliverables and commercialization of products. It is encouraged to identify support needs early in the program and, by leveraging these optional resources, Performers can accelerate deployment of their innovative products, ensuring that breakthroughs reach the market efficiently.

NOTE: For this solicitation, ARPA-H will only accept multi-party teaming arrangements and will not accept prime/subcontractor teaming arrangements. Please refer to Section 4.6 for more details on teaming arrangements.

3.1 Performance Evaluations

Each BoSS phase will include regular performance evaluations. These evaluations will be informed by monthly progress reports, as well as other sources such as technical milestones and phase-end metrics (see Table 3). In addition to the technical requirements associated with each TA and phase, the BoSS program includes additional phase-end metrics designed to guide and monitor each Performer's commercialization plan, regulatory engagement, and accessibility efforts, which are integral components of the overall program design.

3.2 Progression Through BoSS Phases

The expectation is that Performers will develop plans that accommodate the rapid nature of the ARPA-H program schedule. We anticipate that innovative project management approaches by each team to achieve the fast timelines will be required. The iterations and feasibility demonstrations in Phase 1 require sufficient forecasting of risk and alternative methods to avoid delays in the programmatic schedule. Movement into Phase 2a, Phase 2b, and Phase 3 will be dependent on success in previous phases as determined by the ARPA-H Program

Manager and the availability of funding. Therefore, the Performer's ability to iterate quickly will be required to increase the chance of moving to subsequent phases. The specific goals, which align with the program milestones and metrics (**Table 3**), are described per phase below. It is the Proposer's responsibility to propose methods to accomplish the goals and mitigate potential risks and delays in the BoSS program.

3.3 Program Metrics

To evaluate how effectively a proposed solution is achieving the stated program objectives, the government will use the following program metrics to determine successful attainment of goals to warrant continued funding. Performance will be assessed against program objectives and metrics that fall into the following broad categories:

- Technology Process Metrics
- Technology Output Metrics (i.e., stabilized cells produced by biostabilization technologies)
- Commercialization
- Regulatory engagement

Although the program metrics are specified below, Proposers should note that ARPA-H 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 stated problem. Proposals should cite the quantitative and qualitative success criteria that the effort will achieve by each phase's milestone and intermediary metric measurement.

Progress toward program goals will be evaluated using regular milestones, metrics, and deliverables. ARPA-H specifies the following minimally required milestones, metrics, and deliverables, and Performers are expected to define additional quantitative and qualitative success criteria as needed. Due to rapid timelines and expedited research, such additional metrics and milestones will enable Performer-specific technology development to be tracked and measured in a way that suits the specific technology.

During the program, the Program Management Team will evaluate progress using defined metrics and milestones to assess the performance of the bioprocessing system and demonstrations of the systems' output (i.e., biostabilized cells). Technology development and demonstrations across multiple cell types will be subject to key phase-end metrics, as outlined in **Table 3**. For demonstrations, IV&V will supply each Performer with at least two cell types as cryopreserved vials of cells along with SOPs for all cell culture activities and assessment and supporting documentation of donor testing for adventitious agents to certify safe use. Performers are expected to manage the transport of materials directly with IV&V and recover cells to a metabolically active state in culture prior to use in demonstrations. Phase-level metrics will be validated at the end of Phase 1, Phase 2a, and Phase 2b by IV&V assessments of stabilized cells, re-animation methods, and technology usability. Additional milestones related to commercialization strategy, regulatory engagements, and technology readiness are subject to evaluation at the end of each phase.

The purpose of phase-end metrics is to assess the performance of TA1 and TA2 solutions for Phase 1 and the bioprocessing system development in Phase 2 and 3. Performers shall report

progress towards phase-end metrics (**Table 3**) in monthly progress reports and end-of-phase presentations to the Program Management Team. Additionally, SOP and performer results of stabilized cell metrics will be shared along with the IV&V partner to determine reproducibility. Together, end-of-phase performance will be assessed by the Program Management Team to adjudicate Performer teams that proceed to a subsequent Phase at down-select points, subject to availability of funding.

Proposed solutions to biostabilization, bioprocessing technologies, and re-animation methods must consider human clinical use, and thus biocompatibility testing on the re-animated cells following biostabilization - the bioprocessing technologies' output - is a key part of milestone and metrics throughout the program.

***Table 3**. Phase-end metrics*

Metrics	Phase 1	Phase 2	Phase 3
Biostabilization process:			
• Production speed	<6 hours	<4 hours	<2 hours
• Production scale	small (<10 mL)	small (<10 mL)	large (100 mL)
• Shelf-life at 20-25°C	>14 days	>1 month	>3 months
• Re-animation time	<24 hours	<12 hours	<1 hour
• Reproducibility	2 cell types	2 cell types	3 cell types
Technology output - stabilized cells:*			
• Cell viability	>30%	>60%	>90%
• Apoptotic cells	<70%	<40%	<10%
• Metabolic activity	>20%	>50%	>90%
• Cell identity	no change	no change	no change
• Biological function / potency	-	>50%	>90%

*Stabilized cell metrics are measured following re-animation of stabilized cells to metabolically active state.

Phase 1 (Months 1 through 15)

*The goal for Phase 1 demonstrations is to determine feasibility and reproducibility of the co-developed approaches for TA1 and TA2. Initially, IV&V will establish benchmarks for metabolically active cells for comparison to stabilized cells for demonstrations which will be based on the same assays used for assessing phase-end metrics (**Table 3**). These assays will measure cellular attributes using standard characterization assays appropriate for all cells (e.g., viability, apoptosis, metabolic activity) and specific to each cell type (e.g., identity, functional assays) (**Table 3**). Performers will choose 2 cell types for cell demonstrations to co-develop approaches which will be supplied by IV&V along with benchmarks (*

Table 2). Performers should be able to maintain metabolically active cells in culture which will be the starting materials for demonstrations and reproduce the benchmarks as IV&V. Thereafter, the benchmarks will serve solely as a reference, and phase-end metrics will be the target for demonstrating feasibility of approaches developed in TA1 and TA2.

The month next to each milestone and metric indicates the due date during the program.

Phase 1 Milestones and Metrics for TA1

- *Month 3:* Demonstrate ability to acquire and assess cells based on phase-end metrics (Table 3).
    - Maintain metabolically active cells in culture (starting material) by following IV&V-provided culture SOP culture.
    - Measure benchmarks comparable to IV&V assessments.
- *Month 4:* Demonstrate an ability to establish limits of toxicity related to Bio-Prep and re-animation.
- *Month 8:* Demonstrate feasibility of Bio-Prep and re-animation by achieving phase-end metrics (**Table 3**) of at least one cell type.
- *Month 12:* Demonstrate repeatability and reproducibility of Bio-Prep and re-animation by achieving phase-end metrics (**Table 3**) on two cell types.
    - Perform Bio-Prep and re-animation multiple times to show repeatability in assessments on two cell types.
    - Share samples of stabilized cells and assessments based on stabilized cell metrics (**Table 3**) as part of Deliverable 1 (**Table 4**) with IV&V.

Phase 1 Milestones and Metrics for TA2

- *Month 5:* Demonstrate capability of Bioprocessing instrument(s) to deploy BioPrep on at least one cell type and establish critical process parameters and operating limits.
- *Month 10:* Optimize performance of Bioprocessing to deploy BioPrep on two cell types based on phase-end metrics (Table 3).
- *Month 12:* Demonstrate repeatability and reproducibility of Bioprocessing performance based on phase-end metrics (Table 3).
    - Perform Bioprocessing multiple times to show repeatability in assessments on two cell types.
    - Share Bioprocessing instrument(s) as part of Deliverable 1 (Table 4) with IV&V.

Down-Select

- During *Months 13-15* Performers selected for Phase 2 will prepare detailed budgets and proceed to the next phase. Performers not proceeding will complete final reports. Re-teaming may occur during this period.

Phase 2a (Months 16 through 27)

The goal for Phase 2a is to develop a fully integrated bioprocessing system with feasible TA1 and TA2 solutions with functionality to manufacture stabilized cell products of the same two cell types used in Phase 1. The features of the bioprocessing system include, but are not limited to, deploying biostabilization on cells using generalizable process development for various cell types, closed system design with aseptic handling, and streamlined modular operations for rapid processing. Milestones and metrics incorporate considerations to scalability, batch size, and commercialization of the system which are necessary to advance to Phase 2b. Performers

will also continue to optimize re-animation methods as a post-manufacturing step to restore function of stabilized cells.

Phase 2a Milestones and Metrics

- *Month 16:* Demonstrate a feasible design of the bioprocessing system and develop a commercialization plan with regulatory engagements.
    - Bioprocessing system design should integrate TA1 and TA2 solutions.
    - Commercialization plan should consider market analysis of similar systems, potential industry partners for commercial transitions, and strategic IP protection.
    - Demonstrate ability to identify the type(s) of potential regulatory submission and requests to the FDA for the bioprocessing system (e.g., master files, designations).
    - Demonstrate ability to engage with FDA (e.g., INTERACT meeting request) by preparing materials outlining, at minimum, the bioprocessing system, commercialization plans, and specific questions to request feedback related to regulatory pathway, eligibility for designations (e.g., emerging technology), submitting master files, manufacturing requirements, and nonclinical studies.
- *Month 18:* Demonstrate functional capabilities of bioprocessing system for biostabilization.
    - Provide a description or schematic of all system components and associated engineering to support bioprocessing system operations (e.g., calibration, actuators, sensors, pumps).
    - Demonstrate functioning electrical framework and centralized interface for user operations and data computing.
- *Month 21:* Provide highlights from engagements with potential partners and FDA.
    - Pursue engagements with potential industry partners that may be interested in adopting or partnering in development of a commercial bioprocessing system.
    - Implement any feedback from FDA engagements to regulatory plan.
    - Demonstrate a feasible plan for further engagements (e.g., applying for pertinent designation(s)) to enhance regulatory support and communications with FDA.
- *Month 22:* Demonstrate capability of generalizable process development and assess performance of the bioprocessing system based on phase-end metrics.
    - Confirm closed system design and aseptic processing.
- *Month 24:* Demonstrate repeatability and reproducibility of bioprocessing system performance by achieving phase-end metrics (**Table 3**) on at least two cell types.
    - Perform biostabilization and re-animation on multiple samples for two cell types to show repeatability.
    - Share sample of stabilized cells, results based on stabilized cell metrics (Table 3), and Deliverable 3 (Table 4) with IV&V.
    - Confirm closed system design and aseptic processing.
- *Month 27:* Finalize a Phase 3 industry adopter/partner and commercialization plan and create an affordability plan.

- Formalize an agreement with an industry partner for commercial adoption or transition.
- Revise commercialization plan to update the timeline for adoption or transition with an industry partner to enable the development of a commercially viable bioprocessing system.
- Create an Affordability Plan to demonstrate accessibility of the bioprocessing system. The final manufacturer's suggested retail price (MSRP) is not to exceed $200K and, ideally, not to exceed $100K for small commercial-scale systems.

Phase 2b (Months 28-39)

The goal for Phase 2b is to maximize the process development and demonstrate scalability of the bioprocessing system. It is recommended that Performers engage with selected industry adopters/partners to identify a third cell type for Phase 2b demonstrations that aligns with product portfolios. Performers must gain approval from the Program Management Team to outsource a third cell type or, alternatively, IV&V may supply a third cell type for demonstrations if provided advanced notice prior to the start of Phase 2b.

Phase 2b Milestones and Metrics

- *Month 34:* Demonstrate progress related to process development optimization to scale-up bioprocessing system production and improve performance based on phase-end metrics.
  - Confirm closed system design and aseptic processing.
- *Month 37:* Demonstrate repeatability and reproducibility of bioprocessing system performance by achieving phase-end metrics (Table 3) on at least three cell types.
  - Perform biostabilization and re-animation multiple times for three cell types to show repeatability.
  - Share sample of stabilized cells, results based on stabilized cell metrics (Table 3), and Deliverable 5 (Table 4) with IV&V.
- *Month 39:* Demonstrate improvements to shelf-life stability of stabilized cells produced from at least three cell types following >1 months storage at 20-25°C based on stabilized cell metrics.

Phase 3 (Months 40-48)

- *Month 42:* Determine comparability of stabilized cells to cryopreserved counterparts based on stabilized cell metrics.
  - Compare assessments of stabilized cells stored for at least 3 months at 20 to 25°C to cryopreserved counterparts (supplied by IV&V and partner, if applicable) for all cell types. Identify any significant differences in assessments using statistical analysis.
  - Demonstrate a plan for improving comparability (if needed).
- *Month 43:* Determine technology readiness by assessing current capabilities of the bioprocessing system and create a roadmap of any enhancements and/or additional testing to demonstrate broader applications (e.g., other cell therapies) for commercialization.

- *Month 46:* Demonstrate progress towards commercialization with further enhancements to the bioprocessing system and/or activities performed according to commercialization plan.
- *Month 48:* Re-engage with FDA and finalize exit strategy.
    - Prepare meeting package (e.g., pre-submission meeting) describing the bioprocessing system for commercialization and specific questions to understand the needs for regulatory submissions for use of the bioprocessing system.
    - Engage with FDA for feedback on upcoming regulatory submissions for bioprocessing system.
    - Develop documents for prospective requests (e.g., platform technologies) for attracting technology adopters and accelerating regulatory pathways to commercialization.
    - Compile and protect data to be transferred as proprietary information, if applicable (e.g., biostabilization method, formulation of re-animation solution).

3.4 Programmatic Deliverables

Performers need to allot time and budget to fulfill obligations for travel to review meetings and the transmission of report documentation. A final list of deliverables will be included in any resulting OT award. A non-exhaustive list of expected deliverables is provided below:

- **Monthly status reports** that describe progress in each category, as well as the financial status of each BoSS project, will be required from the Performer and will be evaluated by the Program Management Team and discussed at monthly meetings. These reports shall be in the form of an editable Microsoft (MS) Excel™ file and shall provide financial data including, but not limited to:
    - Program spend plan by phase and task
    - Incurred program expenditures to date by phase and task
    - Invoiced program expenditures to date by phase and task

  Length and level of detail is at the discretion of the Program Manager who may also alter the cadence of such reports and meetings and may request additional Performer data as deemed necessary to evaluate technical and non-technical progress as deemed necessary. Other stakeholders (including IV&V) may participate in Performer reviews to provide feedback to the Program Management Team.

- **Transition Plan**: One month prior to the end of Phase 2a, Performers must present to the Program Management Team a detailed transition plan for their technology and bioprocessing system. This transition plan must include, at a minimum: identified stakeholders that would benefit from transitioning the technology including at least one partner that has agreed to support Phase 2b technology development, real-world sample sharing, and testing; commercial/industry support and capabilities to scale-up/produce commercial system; associated material(s)/reagent(s) necessary for continued system operations.

In addition to the above reporting requirements, the following deliverables are expected by Performers to ensure the timely preparation for commercialization of developing technologies and assess the credibility and reproducibility of progress by IV&V. For end-of-phase presentations, Leadership from each performer team (with additional key personnel at the discretion of the PI) will be required to present research progress in person at program review meetings. The purpose of these reviews is to ensure adequate engagement with the Program Management Team to discuss details that might otherwise fall outside the scope of a routine technical brief; progress towards milestones and scientific goals; and any ongoing technical or programmatic challenges that must be overcome to achieve the overarching program goals.

***Table 4**. Deliverables*

Deliverable	Description
1	*12 months:* SOP describing BioPrep, Bioprocess, and re-animation methods applied to two cell types. • To be shared with IV&V along with stabilized cell samples, re-animation materials, and enabling technologies for biostabilization.
2	*15 months:* End-of-phase 1 presentation demonstrating progress made towards methods of inducing and reversing biostabilization (TA1 results), deploying technology on cells (TA2 results), and current performance based on metrics.
3	*16 months:* Commercialization plan describing regulatory, market, and investment pathways.
4	*24 months:* SOP describing bioprocessing technology operations and process development used to induce biostabilization and re-animation procedures on cells and current performance based on phase-end metrics. • To be shared with IV&V along with stabilized cell samples and re-animation materials.
5	*27 months:* End-of-phase 2a presentation demonstrating progress made towards the development of a bioprocessing system to deploy methods of inducing cell biostabilization and re-animation procedures and current performance based on metrics.
6	*27 months:* Updated commercialization plan describing regulatory, market, and investment pathways.
7	*37 months:* SOP describing optimized bioprocessing technology operations and universal process development used to induce biostabilization on cells and re-animation procedures and current performance based on metrics. • To be shared with IV&V along with stabilized cell samples and re-animation materials.
8	*39 months:* End-of-phase 2b presentation demonstrating functionality and performance of the bioprocessing system to deploy methods of inducing cell biostabilization and re-animation procedures and current performance based on metrics.
9	*42 months:* Final commercialization plan describing the exit strategy with partners.

10	*48 months:* End-of-phase 3 presentation demonstrating the capabilities and performance of bioprocessing system and stabilized cells qualities based on metrics.

3.5 Commercialization and Regulatory Engagement

Each team will be required to submit a comprehensive **Commercialization Plan** (CP) at the initiation of Phase 2a with refinements expected throughout the program to ensure alignment with regulatory, market, and investment pathways. Within the CP, Performer teams must demonstrate measurable progress against defined commercialization metrics, thereby positioning BoSS-developed technologies for both regulatory success and sustainable market adoption.

Areas of Focus in the CP:

To ensure that BoSS-funded technologies not only reach the market but remain viable and impactful over the long term, the CP should address the following six interconnected areas:

1. **Corporate Structure and Governance**
   Define the Performer's organizational framework, governance, and long-term business model. This includes pathways for scaling operations, building commercialization capacity, and establishing a sustainable corporate structure capable of supporting technology adoption and growth.
2. **Sustainable Product Development**
   Map the trajectory of BoSS innovations from laboratory feasibility to commercially viable products. This includes development timelines, integration with existing biomanufacturing workflows, and plans to meet industry standards for scalability, reliability, and cost-effectiveness.
3. **Market, Customer, and Competition Analysis**
   Provide a rigorous market assessment to define target customers, adoption barriers, and competitive dynamics. This must include **Porter's Five Forces analysis** to evaluate industry pressures, potential disruptors, and competitive advantages, ensuring BoSS solutions are positioned for differentiation and market resilience.
4. **Intellectual Property (IP) Success Framework (IPSF)**
   Outline a layered IP strategy that ensures freedom to operate, defensibility in the marketplace, and attractiveness to investors or acquirers. The IPSF should include clear approaches to **IP Development and Management (IPDM)**, addressing ownership, cross-licensing, and protection of core innovations while enabling strategic partnerships.
5. **Regulatory Engagement and Compliance**
   Detail proactive strategies for regulatory alignment, including FDA interactions, pre-submission meetings, and early engagement with relevant authorities. The plan should include classification of technologies, risk assessments, and the

integration of regulatory requirements into experimental design—ensuring that BoSS innovations are positioned for a smooth approval pathway.

6. **Engagement with Venture and Industrial Partners**
   Identify opportunities for early collaboration with venture capital firms, biopharma companies, and industrial partners when technology progress justifies commercialization. Such engagements can provide critical resources, accelerate validation, and de-risk market entry.

Commercialization Plans (Deliverables 3, 6, and 9):
CPs must include sufficient detail to demonstrate not only the pathway to commercialization but also the strategy for sustaining market presence and delivering long-term health impact for all Americans. At a minimum, each CP deliverable should include quantifiable milestones, risk mitigation strategies, and a roadmap for bridging scientific achievement with regulatory approval, commercial adoption, and sustained public benefit. Once a transition partner has been identified, CPs should include the transition plans of the strategic partnership.

CP deliverables 6 and 9 should also include, at a minimum, the following elements to demonstrate a complete and credible pathway toward commercialization and sustained market presence:

- **Risk Assessments**
  A detailed identification of technical, regulatory, financial, and market risks that could affect the development and adoption of BoSS technologies. This should include probability, impact scoring, and prioritization of risks across the program lifecycle.
- **Risk Mitigation Plans**
  Concrete, actionable strategies to minimize or eliminate identified risks. These should include proactive measures, monitoring processes, and contingency planning to ensure project continuity in the face of unexpected challenges.
- **Alternative Strategies**
  Well-defined backup approaches that can be pursued if primary technical, regulatory, or commercial pathways fail. These may involve pivoting to alternative markets, modifying the technology design, or adjusting the commercialization model to preserve value.
- **Quality Management Systems (QMS) Approach**
  A comprehensive plan for implementing a QMS aligned with Good Manufacturing Practices (GMP) and international standards (e.g., ISO 13485 where relevant). This ensures that quality is embedded from early development through scale-up and commercial deployment.
- **Manufacturing Plans**
  Detailed strategies for scaling laboratory processes into robust, cost-effective, and GMP-compliant manufacturing systems. Plans should address facility requirements, modular or decentralized production models, supply chain integration, and long-term scalability.

- **Corporate Structure**
  Documentation of the Performer's corporate framework, including governance, legal structure, decision-making authority, and organizational roles that support commercialization and sustainable growth.
- **Intellectual Property (IP) Protection Strategy**
  A clear framework for securing and defending patents, trademarks, trade secrets, and licensing arrangements. This includes strategies to ensure freedom to operate, competitive defensibility, and alignment with the IP Success Framework (IPSF).
- **Non-Disclosure and Confidentiality Strategy (NDA)**
  Policies and protocols for protecting proprietary information during collaborations, partnerships, and external engagements. This ensures that sensitive know-how and competitive advantages are safeguarded while enabling necessary industry interactions.
- **Financing Plans**
  Structured funding strategies that detail capital requirements, anticipated sources of financing (venture capital, government grants, strategic partnerships), and timelines. These plans should demonstrate financial sustainability beyond the program lifecycle and readiness to attract private-sector investment.

Within the CP, each Performer will be required to develop a comprehensive infographic timeline that clearly overlays the start and end periods of all key Research & Development (R&D) activities. This visual roadmap must integrate and align milestones across the following domains:

- **Regulatory** (as defined by the program's regulatory metrics, including anticipated FDA or equivalent agency interactions),
- **Commercialization** (partnership development, corporate structuring, and funding strategies),
- **Intellectual Property (IP) Filings** (patent submissions, IP management milestones, and licensing activities),
- **Pricing, Market Analysis, and Accessibility** (including cost-modeling, customer segmentation, competitive positioning, and equitable access considerations).

The infographic will serve as both a program management tool and a compliance checkpoint, enabling ARPA-H to evaluate the alignment of technical progress with commercialization objectives. It should highlight dependencies, potential bottlenecks, and critical decision points, ensuring that each Performer's R&D efforts remain on track to achieve successful transition to market.

This infographic should present detailed, step-specific timelines that extend well beyond the general goals outlined in the BoSS metrics. The sequence of events must follow a logically structured and realistic progression that reflects established regulatory and commercialization timelines (e.g., Intellectual Property filings, Food and Drug Administration (FDA) interactions, and related activities).

Specifically, the overlayed timelines should include, at a minimum:

- the projected period for R&D and integration of the first TA1 and TA2 technologies,
- the expected date of invention disclosure filings,
- the anticipated issuance of a provisional patent,
- the timing for recruitment of a Commercialization Advisory Board (CAB),
- the initiation of a pre-submission meeting request with the FDA,
- the submission of a technology designation request to the FDA, and
- the scheduling of any subsequent informational or follow-up meetings with the FDA (as deemed necessary).

By requiring these specific milestones, the infographic will function not only as a program management tool but also as a compliance checkpoint, ensuring that Performers maintain clear alignment with regulatory, IP, and commercialization best practices.

Notably, the example provided is intended solely as guidance to assist Performers in developing their infographic timelines. Each Performer is expected to design a bespoke Commercialization Plan and corresponding overarching infographic that reflects their specific technologies, institutional capabilities, and proposed development pathways. Where appropriate, Performers should also identify opportunities to truncate or streamline timelines based on unique institutional processes, available resources, or demonstrated efficiencies.

The BoSS program requires state-of-the-art technology development for stabilizing cell products, with all work conducted in alignment with current Good Manufacturing Practices (cGMP) and GLP standards. Meeting these requirements will demand not only rigorous scientific innovation in Phase 1 but also proactive partnerships to ensure seamless progression into later phases.

The Commercialization Plan and accompanying infographic are designed to help Performers streamline the pathway from laboratory discovery to GLP and cGMP-compliant manufacturing. These tools will clarify critical decision points, protocol tradeoffs, and partnership strategies needed to maintain momentum toward commercialization.

Because timelines and manufacturing scalability are central to program success, Performers are expected to outline realistic yet ambitious strategies for achieving these milestones. For example, transition to IND-enabling studies will require timely access to GLP-compliant manufactured products. Demonstrating the feasibility of these manufacturing milestones—through both planning and evidence of capacity—will be essential to aligning technical progress with regulatory and commercial goals.

By articulating a clear, actionable approach to manufacturing within the CP and infographic, Performers not only strengthen their own commercialization pathway but also reinforce the BoSS program's overarching mission: to ensure that stabilized cell technologies are ready for safe, scalable, and impactful adoption.

As outlined above and detailed in the metrics tables below, BoSS Performers are expected to meet rigorous milestones that ensure successful translation of technologies into the clinic.

Maintaining a strict regulatory timeline is essential to support timely submissions for one or multiple designations. The regulatory timelines for this project are outlined in the program metrics; however, ARPA-H recognizes that ongoing R&D and interactions with the FDA may necessitate adjustments. ARPA-H is committed to accelerating regulatory approvals by leveraging dedicated metrics and emphasizing both commercialization and regulatory milestones, while maintaining the highest standards of safety and efficacy. To support this, ARPA-H and the BoSS Program Manager may provide additional resources and guidance, assisting Performers in achieving these challenging objectives in alignment with ARPA-H's mission to improve health outcomes for all Americans.

Ultimately, success in BoSS extends beyond the development of revolutionary technologies; it also requires achieving regulatory, accessibility, and commercial milestones that ensure these innovations enter the FDA regulatory pipeline and reach stakeholders equitably, regardless of socioeconomic status. To support this, BoSS Performers will develop an Affordability Plan demonstrating how technologies will be priced for accessibility. The final MSRP for a small commercial-scale system should not exceed $200K, with a preferred target below $100K (see metrics tables). These price points are based on comparable commercial technologies with similar unit operations and capabilities. The government recognizes that MSRP assessments may vary depending on the technical approach used to meet the TA1 and TA2 metrics. Overall, BoSS success is defined by the creation of accessible, transformative technologies that maximize adoption across the biopharmaceutical ecosystem.

4. ELIGIBILITY INFORMATION

4.1 Eligible Proposers

All responsible sources capable of satisfying the government's needs may submit a proposal to this ISO. Specifically, universities, non-profit organizations, small businesses and other than small businesses are eligible and encouraged to propose to this ISO.

4.2 Prohibition of Performer Participation from Federally Funded Research and Development Centers (FFRDCs) and other Government Entities

ARPA-H is primarily interested in responses to this solicitation from commercial Performers, academia, non-profit organizations, etc. In certain circumstances, FFRDCs and Government Entities may have unique capabilities that are not available to proposing teams through any other resource. Accordingly, the following principles will apply to this solicitation.

- FFRDCs and government entities, including federal government employees, are not permitted to respond to this solicitation on a proposed Performer team.

- If an FFRDC or government entity has a unique research idea that is within the technology scope of this solicitation that they would like considered for funding; OR, if an FFRDC or government entity, including a federal government employee, is interested in working directly with the government team supporting the research described by this solicitation, contact BOSS@arpa-h.gov.

- If a potential Performer believes an FFRDC has a unique capability without which their solution is unachievable, they may provide documentation as part of their Solution Summary submission demonstrating they have exhausted all other options. ARPA-H will consider the documentation to determine if inclusion of the FFRDC as a team member necessary for the solution.

4.3 Current Professional Support

Those individuals/entities currently providing contracted support services to ARPA-H have an organizational conflict of interest (OCI) that cannot be mitigated and thus are ineligible for award.

4.4 Non-U.S. Entities

ARPA-H will prioritize awards to entities (organization and/or individuals) that will conduct funded work in the United States. Non-U.S. entities may participate to the extent that such participants comply with any necessary nondisclosure agreements, security regulations, export control laws, and other governing statutes applicable under the circumstances. In accordance with these laws and regulations, 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. Ch 44 § 3059)]; a foreign entity of concern meeting any of the criteria in section 10638(3) of the CHIPS and Science Act of 2022; an individual that is party to a malign foreign talent recruitment program, as defined in Section 10638(4) of the CHIPS and Science Act of 2022; or entities suspended or debarred from business with the government.

4.5 System for Award Management (SAM)

All Proposers must have an active registration in SAM.gov and have a valid Unique Entity ID (UEI) number for their Solution Pitch to be found conforming. Proposers must maintain an active registration in SAM.gov with current information at all times during which a Solution Pitch is under consideration and/or a current award from ARPA-H is held. Information on SAM.gov registration is available at SAM.gov.

NOTE: New registrations as well as renewals may take more than 14 business days to process in SAM.gov. SAM.gov is independent of ARPA-H and thus ARPA-H representatives have no influence over processing timeframes. Although Proposers are not required to have an active SAM.gov registration when submitting a Solution Summary (Step 1 of the submission process), ARPA-H strongly encourages submitting registration in SAM.gov well in advance of the Solution Pitch deadline to reduce the risk of being found non-conforming (Step 2 of the submission process).

4.6 Proposer Team Structure

The multi-party teaming arrangement is anticipated to be utilized in a team wherein a group of organizations and/or Performers work together to accomplish a common goal, with members sharing resources, knowledge, and expertise. While one team member is usually elected to serve as the lead member or authorized agent for administrative purposes, such as executing documents or receiving payment on behalf of the team, each member must be bound to the team membership agreement and must be a party to the resultant OT award with

ARPA-H. In this type of team structure, each member must perform substantive technical work as part of the team. Unlike a prime/sub arrangement where the prime Performer is the leader of the team throughout the duration of the program, the multi-party teaming structure allows different members of the team to take the lead role at different stages of the program life cycle based on expertise and experience, as needed. Additionally, the team structure allows for changes in team membership whenever necessary. The multi-party team arrangement allows for dynamic changes as needed throughout the course of performance, allows for open communication between the government and all Performers on a team, and ensures that all team members are responsible for performance and invested in the success of the program. A multi-party team is formed by having all team members sign a teaming agreement (also referred to as "articles of collaboration"), a contract which binds signing members together as a team and which identifies team members, roles, responsibilities, etc. The government is not a party to this teaming agreement and is not involved in the negotiation of the terms amongst the team members. This is a private arrangement amongst the team members with no government-dictated terms. Most teaming arrangements allow for members to leave the team during performance or for new members to join when needed but those options are at the discretion of the team members. Team members have a wide range of options regarding how they establish and internally handle the teaming arrangement and the teaming agreement.

A multi-party team does NOT need to be established as a separate legal entity as the teaming agreement serves to bind all members to the team. The team must choose one member to act as the agent and/or lead member to handle administration duties on behalf of the team. For example, although the government contract is between the multi-party team and the government, the lead member will sign the contract as the representative for the team. Additionally, the lead member is usually the direct payee, receiving funds from the government and distributing payment to team members. A multi-party team structure has many advantages over a typical prime/sub-performer team. Because the team has chosen to work together in a collaborative manner, the multi-party team approach is usually advantageous to all members and oftentimes, teams forge relationships and alliances that continue beyond the program. This type of team structure also gives the government privity of contract with all team members, allowing the government insight and visibility into all levels of technical and management actions, providing for direct communication between all team members and the government, ensuring that all team members are responsible for successful performance, and enabling seamless leadership changes of the effort and/or addition of new team members (e.g. product sponsors), if necessary, as the program evolves.

At a minimum, a proposing team must:

1. Not be a prime/sub-performer team. While a multi-party team may still choose to subcontract with commercial vendors and consultants not performing essential components of the program, entities that are performing substantive work should be members of the team, not sub-contractors.
2. Identify a team member to perform administrative functions and act as an agent or lead member for the team. The agent does not need to be the lead performing organization, but the agent should perform substantive technical

work on the program beyond program management and administrative functions.

3. Execute, prior to award, a teaming agreement that details the team structure, roles, and responsibilities and which binds the team members to the agreement. All members of the team will be party to the OT agreement with the government. Whatever the team structure, the lead performing organization must be able to change during performance or between phases, if necessary. The teaming agreement must account for the full scope of the BoSS program. The government is not a party to and will not approve the teaming agreement, however ARPA-H will require evidence that the teaming agreement has been fully executed by all team members in order to make an award to the team.

ARPA-H recognizes that this approach may be unfamiliar or new to many Performers. ARPA-H strongly encourages Performers who are interested in a deeper explanation of this approach and how it can be fully utilized by teams to attend the BoSS Proposers' Day and ask any questions they may have.

5. SUBMISSION PROCESS

5.1 Submission Process Overview

Submissions as a Performer or IV&V partner are as follows:

- ✓ **Step 1:** Submit Solution Summary (Proposers are encouraged / discouraged to move to Step 2).
- ✓ **Step 2:** Submit Solution Pitch presentation and schedule a virtual oral presentation.

Optional Staggered Submission Pathway

To maximize participation and assemble the most capable teams, ARPA-H is implementing staggered submission deadlines for applicants seeking consideration as either a Technical Performer or an IV&V partner. Because the due date for Solution Summary submission as a potential Technical Performer precedes the due date for Solution Summary submission as an IV&V partner, those who are discouraged as a Technical Performer at this review phase may elect to discontinue the Technical Performer path and submit a Solution Summary as the IV&V partner. Proposers cannot submit Solution Pitch materials for virtual oral presentations as a Technical Performer and as an IV&V partner. Refer to page 4 of this solicitation for due dates pertaining to all submissions for both Performer and IV&V partner roles.

5.2 Solution Summary Submissions

Solution Summary submissions are required and are due by the date listed in the ISO Summary Information Section on page 4.

- See Appendix A for the required Solution Summary format and instructions for proposing as a Performer.
- See Appendix B for the required Solution Summary format and instructions for proposing as an IV&V partner.

ARPA-H will review conforming submissions and provide feedback to Proposers to encourage or discourage proceeding to Step 2, Solution Pitch Presentations. Proposers may proceed to Step 2, regardless of whether encouraged or discouraged in Step 1

5.3 Solution Pitch Presentations

Based on the Solution Summary, ARPA-H will provide feedback that either encourages or discourages Proposers to submit Solution Pitch materials for virtual oral presentations.

- See Appendix C for the Solution Pitch presentation format and instructions and Attachment 1 for the Solution Pitch slide deck template for proposing as a Performer.
- See Appendix D for the Solution Pitch presentation format and instructions and Attachment 2 for the Solution Pitch slide deck template for proposing as an IV&V partner.

5.4 Submission Information

All submissions in response to this solicitation must be written in English and must be consistent with the content and formatting requirements of Appendix A (Performer Solution Summary Format and Instructions), Appendix B (IV&V Solution Pitch Format and Instructions), Appendix C (Performer Solution Pitch Presentation Format and Instructions), and Appendix D (IV&V Solution Pitch Presentation Format and Instructions).

Proposers are responsible for submitting all written submissions via the ARPA-H Solution Submission Portal and ensuring receipt by the date and time specified in the ISO. No other method of submission is permitted.

Registration is required to submit via the ARPA-H Solution Submission Portal and registration may take several business days to process. Plan to register well in advance of the solution summary submission deadline as late submissions resulting from delays with registration may not be accepted or considered.

5.5 Proprietary Information

Proposers are responsible for clearly identifying proprietary information in any submissions. 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.

ARPA-H is responsible for handling submissions in accordance with applicable federal law, including the Freedom of Information Act (FOIA).

6. SUBMISSION REVIEW AND EVALUATION PROCESSES

6.1 Conforming Submissions

Conforming submissions contain all requirements detailed in this ISO. Submissions that fail to include required information may be deemed non-conforming and may be removed from further consideration and/or rejected without further review. A submission may be deemed non-conforming under this ISO if it fails to meet one or more of the following solicitation requirements:

- The proposed concept is applicable to the BoSS program.
- The Proposers meet the eligibility requirements.
- The submission meets the submission requirements, including content and formatting requirements in the attached instructions.
- The Proposer's concept has not received funding or been selected for award negotiations for another funding opportunity (whether from ARPA-H or another Government agency).

Proposers will be notified of non-conforming determinations via email correspondence.

Please note that ARPA-H reserves the right, at its discretion, to reject as non-conforming submissions that it determines are duplicative of previous submissions under this or other ARPA-H solicitations.

6.2 Solution Summary Review Process

ARPA-H will review and respond to all Proposers submitting conforming Solution Summaries. Solution Summaries will be reviewed to provide potential Proposers with feedback on whether ARPA-H is interested in the proposed solution/concept. At a minimum the response will indicate whether a Proposer is encouraged or discouraged from submitting a Solution Pitch. Although potential Proposers may submit a Solution Pitch regardless of the feedback provided in response to a Solution Summary, ARPA-H Solution Summary feedback is provided to ensure that potential Proposers are making an informed decision on the investment of time and resources to a Solution Pitch. Feedback will be provided to the administrative and technical points of contact noted on the Solution Summary cover page.

6.3 Solution Pitch Review Process

ARPA-H will respond to all Proposers submitting a Solution Pitch deck and completing a virtual oral presentation. ARPA-H will conduct a scientific and technical review of each conforming Solution Pitch and associated submission materials and evaluate how well the submitted and presented content meets the criteria stated in this ISO. At a minimum, Proposers will be provided with notification of the government's decision on whether the Solution Pitch was selected for negotiation of an award. Notification of the government's decision will be provided to the administrative and technical points of contact noted on the pitch deck cover page.

6.4 Evaluation Criteria

All Solution Pitches will be evaluated using the following evaluation criteria, listed in descending order of importance.

6.4.1 Criteria 1: Overall Scientific and Technical Merit

The proposed technical approach is innovative, feasible, complete, technically resolute, and able to pass regulatory muster in keeping with program metrics*. Comprehensive technical approach and granular technical elements provided are complete and in a logical sequence with proposed deliverables clearly defined such that a final outcome that achieves the goal can be expected as a result of the award. The Solution Pitch identifies major technical risks; planned mitigation efforts are clearly defined and feasible.

The Solution Pitch includes a clear commercialization strategy and addresses the Proposer's intended intellectual property (IP) rights structure. 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 technology.

*Note: Program metrics include scientific/technical, regulatory, and commercial.

6.4.2 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 and; similar efforts completed/ongoing by the Proposer in this area are fully described, including identification of other government or commercial activities where they have led or participated.

If the Proposer is not a commercial entity with the capability to facilitate at least early commercialization efforts, the Solution Pitch should describe the proposed teaming arrangement and how it is structured to support commercialization objectives. Proposers should outline how their teaming approach will enable compliance with applicable requirements and facilitate effective collaboration among all team members (e.g., intended multi-party teaming agreement between academic teams and commercial entities).

In terms of capability, the government may assess the bio-sketches provided for the Performer team members including the Principal Investigator, Project Manager, regulatory expert, commercialization experts, and any other key personnel on the project team as requested by ARPA-H.

6.4.3 Criteria 3: Potential Contribution to Relevance to the ARPA-H Mission and User Experience

Solution Pitches will be evaluated on the potential future R&D, commercial, and/or clinical applications of the project proposed, including whether such applications may have the potential to address areas of currently unmet need within biomedicine and improve health outcomes; the degree to which the proposed project has the potential to transform biomedicine; and/or the potential for the project to take an interdisciplinary approach. Further, the proposed solution contemplates the end user and reflects an understanding of the direct needs and benefits for stakeholders, whether they are patients, providers, health systems or payers. For example, how would this solution fit inside the clinical workflow? Or how will this be accessible to users in all geographies, and at an affordable cost?

6.4.4 Criteria 4: Assessment of Proposed Cost/Price

All Solution Pitches and cost proposals will be evaluated to determine the reasonableness or value of the estimated price/cost proposed to accomplish the work. Analysis may be performed to ensure proposed costs are realistic for the proposed scientific and technical approach and capabilities/related experience, accurately reflect the technical goals and objectives of the solicitation, the proposed costs are consistent with the Proposer's Solution Pitch and reflect a sufficient understanding of the costs and effort needed to successfully accomplish the proposed technical approach. The costs for all parties should be substantiated by the details provided in the Solution Pitch and cost 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 including the basis for the estimates).

It is expected the effort will leverage all available relevant prior research to obtain the maximum benefit from the available funding. For efforts with a likelihood of commercial application, appropriate resource sharing may be a positive factor in the evaluation.

NOTE: Proposers are encouraged to propose the best technical solution. For example, Proposers are discouraged from proposing low-risk ideas with minimum uncertainty or to staff the proposed effort with junior personnel to be more appealing from a budget perspective. ARPA-H seeks novel solutions that are reflective of the level of effort and risk proposed.

6.5 Handling Selection Sensitive Information

It is the intent of ARPA-H to protect all proposals as selection sensitive information and to disclose their contents only for the purpose of evaluation, and only to screened personnel for authorized reasons, in accordance with applicable federal laws and regulations, including FOIA. Restrictive notices notwithstanding, submissions may be handled by ARPA-H support contractors during the evaluation process for administrative purposes and/or to assist with technical evaluation.

ARPA-H support contractors are expressly prohibited from performing ARPA-H-sponsored technical research and are bound by appropriate non-disclosure agreements. Input on technical aspects of a proposal may be solicited by ARPA-H from non-government consultants/experts who are strictly bound by appropriate non-disclosure requirements. No submissions will be returned.

6.6 Award Information

The ISO constitutes a merit-based solicitation, and the number of awards made will depend on the quality of the proposals received and the availability of funds. Proposals are expected to use innovative approaches that include novel technology, enabling revolutionary advances in medicine and healthcare. The ISO uses merit-based competitive procedures to the maximum extent practicable.

The government reserves the right to select for negotiation all, some, one, or none of the proposals received in response to this ISO. In the event the government desires to award only portions of a proposal, negotiations will commence upon selection notification. The government reserves the right to fund proposals with phases or options for continued work, as applicable.

The government reserves the right to request any additional necessary documentation to support the negotiation and award process. The government reserves the right to remove a proposal from award consideration should the parties fail to reach agreement on award terms, conditions, price, and/or if the Proposer fails to provide requested additional information in a timely manner.

In all cases, the government Agreements Officer (AO) will have sole discretion to negotiate all terms and conditions with Proposers. ARPA-H will apply publication or other restrictions, as necessary, if it is determined the research resulting from the proposed effort will present a high likelihood of disclosing sensitive information including Personally Identifiable Information (PII), Protected Health Information (PHI), financial records, proprietary data, any information marked Sensitive, etc. Any award resulting from such a determination will include a requirement for ARPA-H concurrence before publishing any information or results on the effort.

7. POLICY REQUIREMENTS AND MISCELLANEOUS OTHER INFORMATION

7.1 CONTROLLED UNCLASSIFIED INFORMATION (CUI) ON NON-FEDERAL INFORMATION SYSTEMS

Information on Controlled Unclassified Information (CUI) identification, marking, protection, and control is incorporated herein and can be found at 32 CFR § 2002.

7.2 Organizational Conflicts of Interest (OCI)

The Proposer, through submission of a proposal, is required to identify and disclose all facts relevant to any potential OCI involving the Proposer, its organization, and/or any proposed team member. Along with the disclosure, the Proposer may be required to submit a mitigation plan, which is a description of the action the Proposer has taken to avoid, neutralize, or mitigate the stated OCI. The government may require the Proposer to provide additional information to assist the government in evaluating the OCI mitigation plan.

If the government determines the Proposer failed to fully disclose an OCI; or failed to provide the affirmation of ARPA-H support; 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.

7.2.1 Agency Supplemental OCI Policy

ARPA-H restricts Performers from concurrently providing professional support services, including Advisory and Assistance Services or similar contracted support services, in addition to performing as an R&D technical Performer. Therefore, the Proposer must affirm whether it or any proposed team member is providing professional support services to any ARPA-H office(s) under: (1) a current award or subaward; or (2) a past award or subaward that ended within one calendar year prior to the proposal's submission date.

If any professional support services are 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 number, and
- Identification of proposed team member providing the support.

7.2.2 Research Security Disclosures

In accordance with NSPM-33, research organizations should identify and mitigate conflicts of commitment (COCs) and conflicts of interest (COIs) to receive federal funding. A research organization proposing to this ISO must provide additional documentation as requested for Senior/Key Personnel for ARPA-H to determine the existence of any risk. The format for this submission can be found in the Administration and National Security Document Template (Appendix E).

7.3 Intellectual Property

Proposers must provide a good faith representation that the Proposer either owns or possesses the appropriate licensing rights to all IP that will be utilized for the proposed effort. ARPA-H strongly encourages IP rights to be negotiated in a manner that promotes team collaboration and ultimately commercialization and adoption of the integrated BoSS system and associated products. Further, it is desired that all non-commercial software (including source code), software documentation, and technical data generated and/or developed under the proposed project is provided as a deliverable to the government. IP delivered to the government should align with program goals and should be aligned with the level of government funding provided to generate and/or develop the IP.

7.4 Electronic Invoicing and Payments

Performers will be required to register in, and submit invoices for payment through, the Payment Management Services (PMS) https://pms.psc.gov.

7.5 Software Component Standards

The health- and healthcare data eco-system is complex and multi-dimensional with a variety of standards for data models, data transmission protocols, data routing methods, etc. that are similar to and extend the International Standards Organization (ISO) Open Systems Interconnection Model (OSI). ARPA-H programs are likely to involve research that touches on multiple layers of the OSI model, from low-level radio frequency (RF) based protocols for transmission of data from implantable devices (potentially OSI layers 1-5), to secure and fault tolerant networking protocols for medical devices (potentially OSI layers 3-6), to the exchange of health information including Electronic Health Records, lab results, and medical images related to a patient between healthcare facilities and health data brokers, including (but not limited to) Health Information Exchanges (HIE) and Trusted Exchange Framework and Common Agreement (TEFCA) Qualified Health Information Networks using protocols such as HL7 FHIR (Fast Healthcare Interoperability Resources, OSI Layer 7). This diversity requires careful consideration of the most appropriate standards to be used for the specific technologies in development and the layer at which they operate.

ARPA-H is committed to advancing interoperability in today's health ecosystem through the adoption of open, consensus-driven standards and laying the foundation for emerging technologies to interoperate in the health ecosystem of the future through the evolution of these standards across all layers of the health data information technology (IT) eco-system. With that in mind, we anticipate that the Performer will develop software and data communication components that fall into three categories:

(1) components that can leverage today's existing standards without impeding the R&D,

(2) components where extensions to existing standards will be necessary to unlock new capabilities in an interoperable way, and
(3) components in areas where consensus-based standards do not yet exist or where use of standards would seriously limit the ability to efficiently conduct R&D.

Whenever such an existing standard is available that meets the scientific, technical, and research needs of the proposed effort, Proposers must use the existing standard instead of creating their own. In cases where an existing standard provides only partial functionality, Proposers should expand upon the existing standard, ideally in a way that does not prohibit or interfere with backward compatibility, and create sufficient documentation for the Office of the National Coordinator for Health Information Technology (ONC), and the U.S. Department of Health and Human Services (HHS) agencies or standards organizations, to evaluate extensions for potential inclusion in the standard (including open Application Programming Interfaces (APIs) and open data formats).

In the case of information relating to health- and healthcare data at higher layers of the OSI model, all health IT components should adhere to or (as needed) expand upon applicable national standards adopted by HHS, including the ONC (e.g., Fast Healthcare Interoperability Resources (FHIR) and United States Core Data for Interoperability (USCDI)).

For technical solutions that contain software elements, commercial-friendly open-source licenses (e.g., MIT, BSD, or Apache 2.0) are preferred. If an open, consensus-based standard does not yet exist, the Proposer should identify the aspects that lack an open standard, describe a plan to develop a general-purpose open data model and to prototype new open APIs. A strong proposal will explain how the Performer will enhance data interoperability (including semantic interoperability) and expand the availability of open, consensus-based standards and data models.

A proposal must include a technical plan to align with applicable standards based on the OSI layer at which they are operating including (but not limited to) HHS-adopted health IT standards (45 CFR Part 170 Subpart B). For the full description of standards adopted in CFR Part 170, Subpart B, please review the complete text of the regulations; a strong technical solution will also outline integration with the Trusted Exchange Framework and Common Agreement (TEFCA). Adhering to international standard ISO/IEEE 11073 will enable broad support for current and future devices, especially those developed internationally. At other layers of the OSI model, and for software components operating outside the network stack (e.g., health databases, Picture Archiving and Communication Systems (PACS), etc.) other standards will be relevant, and strong technical solutions will seek to utilize or expand upon appropriate open, consensus-based standards.

If a technical solution requires an extension of existing standards or development of technologies outside of the standards, the Proposer must schedule a meeting with ARPA-H representatives prior to proposal submission to discuss the deviation to the standards.

7.6 RESEARCH SECURITY DISCLOSURES

Proposals selected for negotiations of a potential award will undergo a Research Security Review (RSR). The RSR involves a review of the Proposer's disclosures made as part of the

Administrative & National Policy Document and a validation and comparison of those disclosures utilizing publicly available information and commercially available information tools. Section 10631 of the CHIPS and Science Act of 2022 prohibits federal research agencies, such as ARPA-H, from providing R&D awards on any proposal in which a covered individual is participating in a malign foreign talent recruitment program (MFTRP). It also requires Federal agencies to require recipient entities to prohibit covered individuals participating in MFTRPs from working on projects supported by federal R&D awards.

In accordance with NSPM-33, research organizations should identify and mitigate conflicts of commitment (COCs) and conflicts of interest (COIs) to receive federal funding. COCs and COIs involving foreign countries of concern (FCOCs), including the People's Republic of China, the Russian Federation, the Islamic Republic of Iran, and the Democratic People's Republic of Korea (also known as North Korea), will require risk mitigation plans. A research organization proposing to this ISO must research security disclosures as described in the Administrative and National Policy Document and the Office of Science and Technology Policy identified Common Forms. The Common Forms are required for all senior or key personnel.

ARPA-H will conduct an RSR of each Proposer and their senior or key personnel **after** a proposal is selected for negotiations of a potential award. The reviews include assessments of potential risks associated with covered individuals' disclosed or undisclosed participation in MFTRPs, funding received from FCOCs, collaboration with FCOC entities (including researchers and research institutions that have been identified on various entity lists), foreign ownership control or influence with regards to FCOCs identified in proposals, and the pursuit of foreign patents stemming from U.S. Government funded research prior to obtaining U.S. patent protections. The RSR is not part of the ARPA-H scientific merit review process outlined in this ISO.

If ARPA-H determines the Proposer fails to provide all requisite research security disclosures or reasonably provide additional information requested by ARPA-H to assist in evaluating the Proposer's disclosures and/or research security mitigations, ARPA-H may remove the proposal from award consideration.

7.7 Government-Furnished Property/Equipment/Information

Government-furnished property/equipment/information will not be provided under this ISO.

7.8 Human Subjects Research

A proposal for funding that will involve engagement in human subjects research (HSR)(as defined in 45 CFR § 46) must provide documentation of one or more current *Assurance(s) of Compliance* with federal regulations for human subjects' protection, including at least a Department of Health and Human Services (HHS), Office of Human Research Protection Federal Wide Assurance. All HSR must be reviewed and approved by an Institutional Review Board (IRB), as applicable under 45 CFR § 46 and/or 21 CFR § 56. The entity's HSR 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 ARPA-H funded work. This includes, but is not limited to, laws, regulations, and policies regarding the conduct of HSR, 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 utilized in HSR funded by ARPA-H 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 HSR training by all investigators and key personnel who will be involved in the design or conduct of the ARPA-H funded HSR. Funding cannot be used toward HSR until ALL approvals are granted.

7.9 Animal Subjects Research

All entities submitting a proposal for funding that will involve engagement in animal subjects research (award recipients performing research, experimentation, or testing involving the use of animals) must comply with the laws, regulations, and policies on animal acquisition, transport, care, handling, and use as outlined in:

- 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); and,

- the Public Health Service Policy on Humane Care and Use of Laboratory Animals, which incorporates the "U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training," and "Guide for the Care and Use of Laboratory Animals" (8th Edition)."

Proposers must provide documentation of a current Animal Welfare Assurance (AWA) on file with the Office of Laboratory Animal Welfare (OLAW).
The Proposer must complete and submit the Vertebrate Animal Section worksheet for all proposed research anticipating Animal Subject Research (ASR).
All Animal Use Research must undergo review and approval by the local Institutional Animal Care Use Committee (IACUC) prior to incurring any costs related to the animal use research. For all proposed research anticipating animal use, proposals should briefly describe plans for IACUC review and approval.