The Advanced Research Projects Agency for Health (ARPA-H)

Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Broad Agency Announcement (BAA)

IMPORTANT DATES:

Virtual Proposer's Day. All potential proposers are encouraged to attend the ARPA-H webinar for this opportunity. The webinar will highlight important aspects of the SBIR/STTR Program, ARPA-H's mission, Topic Areas, and this solicitation. The webinar is being held on June 11, 2026.

Deadline for Questions. Questions must be received by June 25, 2026. All questions shall be submitted online via https://solutions.arpa-h.gov/ask-a-question.

Deadline for Receipt of Solution Summaries. The BAA will be open through September 30, 2027, with specific open/close dates for topics. It is anticipated that additional topics will be added to the BAA via amendment. Late Solution Summaries and Technical Presentations will not be accepted.

Stage 1 - Solution Summary Deadline: Topics 01 – 07: July 10, 2026

Stage 2 – Proposal Package and Technical Presentation Deadline: Topics 01 – 07: To be determined at a future date.

Please read the entire BAA carefully prior to submitting questions and/or Solution Summaries. Paper proposals or proposals sent via email will not be accepted.

Proposers are encouraged to periodically check for updates to the BAA for amendments, including additional topics, date changes, or administrative changes. Any updates will be published on SAM.gov and https://arpa-h.gov/explore-funding/sbir.

Questions? Please contact: https://solutions.arpa-h.gov/ask-a-question/

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1 Program Description

The Advanced Research Projects Agency for Health (ARPA-H) invites small businesses to submit research proposals under this Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) solicitation. All eligible organizations with relevant expertise are encouraged to apply (See section 2 for eligibility requirements). The topics are described in *Section 8 Research Topics*, and new topics may be added periodically.

The mission of ARPA-H is to accelerate better health outcomes by supporting the development of high-impact solutions to society's most challenging health problems. Innovative small businesses can contribute to this mission through the ARPA-H Small Business Program (SBP). ARPA-H holds small business performers to the same rigorous technical standards as other ARPA-H performers. Commercialization and transition are key elements of the ARPA-H SBP, and ARPA-H provides tailored support to help performers overcome a range of challenges.

This solicitation contains specific topic areas where ARPA-H is seeking proposals from small businesses for high-impact solutions. Proposals are expected to use novel approaches to achieve revolutionary advances in science, technology, or systems. Specifically excluded are proposals for open-ended research projects or that represent an incremental advance in the current state of the art. Additionally, proposals directed towards policy changes, traditional education and training, or construction of physical infrastructure are outside the scope of the ARPA-H mission and will not be considered.

SHORTCUT TO TECHNICAL TOPICS

1.1 Program Phases

The SBIR/STTR program organizes projects into three phases:

- **Phase I**: Feasibility
- **Phase II**: Full Research / Research & Development (R&D) Effort
- **Phase III**: Commercialization (Not part of this solicitation)

These phases build on each other, with each subsequent phase the maturity of the technology should advance so that the final output is ready for commercialization. Once a performer has successfully completed a Phase I, ARPA-H (or any other agency) can invite them to submit a Phase II proposal to continue development.

Note: This solicitation does not accept Phase III proposals.

1.1.1 Phase I: Feasibility

The objective of Phase I is to determine the scientific or technical and commercial feasibility of the proposed solution. Typically, a Phase I proposer has a solution concept but has not yet built a prototype to test technical feasibility.

This phase is intended to de-risk the effort and is substantially smaller in scope and cost than subsequent phases. At ARPA-H, a typical Phase I lasts 6-12 months but may last longer in rare circumstances. The result of a Phase I is a proof-of-concept or early-stage prototype.

NOTE: Performers with a Phase I award from ARPA-H may submit a Phase II proposal to ARPA-H to continue the development of their technology. This usually occurs in the last quarter of the period of performance or shortly after contract completion. The performer should notify the ARPA-H SBP of their intention to submit a proposal, and ARPA-H will provide submission instructions. While all Phase I participants are welcome to submit a Phase II proposal, not all will be selected for a Phase II award. ARPA-H may also invite performers to submit a Phase II proposal outside of specified solicitation timeframes.

1.1.2 Phase II: Full Research/Research & Development (R&D) Effort

The objective of Phase II is to further develop a technology or R&D effort initiated in Phase I. During Phase II, performers advance from a proof-of-concept into a commercially viable prototype. Phase II awards are larger in scope and cost than Phase I efforts and typically last 12-24 months, although they can be longer or shorter. Individual topics may include estimates regarding the anticipated project duration which are meant to guide proposers rather than be hard requirements.

While the specific Phase II activities in a project are case-specific, they usually include continued improvement of the technology along with evidence generation. This may

include completing pre-clinical work, conducting enabling studies for an Investigational New Drug (IND), or even first-in-human trials. At ARPA-H, it is common for a Phase II to conclude with an FDA submission (when applicable).

Additional emphasis is placed on commercialization during Phase II. Performers must submit a detailed Commercialization Plan and provide regular updates. This is a key activity of Phase II efforts at ARPA-H and necessary to prepare for a successful transition. During Phase II, performers often develop or initiate strategic partnerships, manufacturing plans, regulatory engagements, go-to-market strategies, and user-testing (these examples are meant to be illustrative rather than exhaustive or prescriptive).

A Phase II may be awarded as (a) a follow-on to a Phase I award, (b) a Direct-to-Phase II, or (c) integrated into a Fast Track project.

1.2 Award Types

In some instances, ARPA-H will consider **Fast Track** proposals that combine Phases I and II, or **Direct-to-Phase II** proposals that skip Phase I. Not all phases or award types are eligible for all topics; proposers must check which types will be considered for their intended topic.

All awards will be made on a Firm-Fixed-Price (FFP) basis.

Note: This solicitation is only accepting proposals for Phase I, Direct-to-Phase II, and Fast Track. This solicitation is not accepting Phase III proposals.

Refer the information for individual topics at the end of this document to determine which phase will be considered. Submissions for phases not eligible for the associated topic will not be considered.

1.2.1 Phase I

A Phase I award is intended for proposers who have a promising concept aligned with the solicitation topic but have not yet demonstrated its technical feasibility or developed a working prototype. Phase I proposals should clearly outline the planned approach to establish feasibility and address the key risks associated with the concept. These awards are limited in scope and duration and are designed to support early-stage R&D efforts that lay the groundwork for potential advancement to Phase II. Not all topics in this solicitation may accept Phase I proposals, so confirm eligibility before applying.

1.2.2 Direct-to-Phase II

In some instances, ARPA-H may permit proposers to bypass Phase I and submit a Direct-to-Phase II proposal. This is intended for projects that already have evidence

demonstrating their feasibility and where a Phase I would be unnecessary. Direct-to-Phase II proposers must have already created a proof-of-concept or prototype and demonstrated its technical feasibility. Not all topics in this solicitation will accept Direct-to-Phase II proposals, so be sure to confirm that the topic is accepting Direct-to-Phase II proposals.

1.2.3 Fast Track

A Fast Track award combines both Phase I and Phase II into a single project. This streamlines the process and reduces the likelihood of a gap between Phases I and II. Fast Tracks are intended for early-stage projects that straddle Phases I and II. These projects require some development to complete the proof-of-concept and de-risk their approach (Phase I), yet enough work has been done to clearly define the Phase II activities.

To receive a Fast Track award, a proposer must submit a proposal that contains both their Phase I and Phase II activities and all the required contents specified in *Section 3: Proposal Preparation Instructions and Requirements*. If selected, the resulting award contains a base scope with the initial Phase I with an option containing the Phase II activities. The Government can exercise this option to initiate Phase II without needing to re-solicit the topic or request a new proposal. However, the Government is not required to fund the Phase II Option and the performer may only begin executing Phase II if the Government exercises the contract-option for Phase II.

> **Note:** Receiving a Fast Track award is not a guarantee that ARPA-H will exercise Phase II. ARPA-H may **down-select** performers between Phases I and II.

1.3 ARPA-H's Commercialization Support and Entrepreneur-in-Residence Program

ARPA-H offers commercialization resources and support to Small Business Program performers. Participation is not mandatory, is at the discretion of the ARPA-H Program Manager (PM), and is contingent on funding availability. This support includes but is not limited to commercialization needs assessments, regulatory consultations, Entrepreneurs-in-Residence (EIR), and networking support.

The EIR Program provides experts to advise and support small businesses. EIRs are seasoned experts with experience commercializing innovative healthcare technologies. They provide strategic guidance in technology development, market analyses, intellectual property, and regulatory and reimbursement needs. All EIRs operate under a Non-Disclosure Agreement (NDA) to ensure confidentiality. The EIR program is designed to shorten the commercialization timeline by assisting

SBIR/STTR companies as they navigate critical inflection points like regulatory pathways, FDA meetings, Good Manufacturing Practice (GMP) manufacturing, clinical trial design, and fundraising.

Example EIR Support Services:

- Technology validation
- Assistance with customer discovery and stakeholder introductions
- Confirmation of regulatory and reimbursement strategies
- Market, customer, and competition research
- Review and provide recommendations of regulatory submission drafts
- IP and licensing strategy, freedom to operate analyses

Note: ARPA-H may offer Technical and Business Assistance (TABA) funding to selected performers during performance. ARPA-H does not guarantee or entitle performers that request TABA funding to utilize ARPA-H Entrepreneur-in-Residence (EIR) program and resources. Requests for EIR services will be provided on a case-by-case basis.

ARPA-H will offer SBIR/STTR awardees the option to request participation in I-Corps programs. Requests will be approved by ARPA-H depending on budget and I-Corps programming availability.

1.4 Program Deliverables

In addition to the completion of technical milestones, SBP performers must complete the following deliverables and reports to fulfill administrative and SBA/HHS reporting requirements:

• Funding Agreement Certification • Kickoff Presentation • Quarterly Reports • (Phase II Only) Annual Commercialization Plan Update • Draft Commercialization Report • Draft Final Report	• Contract Impact & Outcomes Report • Final Commercialization Report • Final Report • Final Presentation • Lifecycle Certification • Final Invention Statement • Invention Disclosure Report

1.5 Fixed Payment Milestones

The ARPA-H Small Business Program only uses fixed payment milestones. These are fixed payments based on (1) submission and Government acceptance of the required deliverables and (2) successful completion of the associated technical milestones and objectives in the statement of work. Payment milestones evenly divide the overall cost of the project and are quarterly (<u>not monthly</u>), except for the kickoff, draft final deliverables, and final deliverables. Quarters are set reporting periods tied to the calendar year (as detailed below), not individualized to the period of performance.

Payment milestones will be defined in the awarded contract and may include kickoff, quarterly, draft final, and final milestones. Amounts may be equal or prorated as specified in the contract schedule. The table below illustrates a sample payment structure for a Phase I SBIR with a 1-year period of performance.

Example Phase I Payment Schedule	
Description	**Payment Amount**
Kick-off Presentation (Month 1)	[1/6th total contract amount]
Quarterly Report 1 (Quarter 1)	[Prorated by weeks on contract during the quarter]
Quarterly Report 2 (Quarter 2)	[1/6th total contract amount]
Quarterly Report 3 (Quarter 3)	[1/6th total contract amount]
Draft Final Reports (Month 11)	[1/6th total contract amount]
Final Report & Associated Deliverables (Month 12)	[1/6th total contract amount + any remaining pro-rated amount]

Reporting/Quarterly Periods:

- January 1 to March 31
- April 1 to June 30
- July 1 to September 30
- October 1 to December 31

2 Eligibility & Certifications

This section describes the eligibility requirements for participating in the ARPA-H SBIR/STTR Program and the certifications that must be completed by proposers and performers. These certifications are required by SBA and HHS to fulfill reporting requirements. Some are completed during the proposal process, while others are completed during performance.

Copies of all the certification forms mentioned in the following sections can be found at: https://grants.nih.gov/grants/forms.htm?filter=small-business

Note: NIH maintains the small business certification forms for all of HHS. Only the forms specified in this section must be completed by the Proposer. Forms that are not listed, such as the *SF424 Grant Application*, are not required.

2.1 Summarized Small Business Eligibility Requirements

To be eligible for SBIR or STTR awards, proposers must be valid Small Business Concerns (SBCs) that meet the eligibility requirements in 13 CFR 121.702 and the SBA's SBIR/STTR Policy Directive (summarized in bullets below). Proposers attest to their eligibility by completing the *Funding Agreement Certification*.

Summarized Eligibility Requirements:

- SBC has no more than 500 employees
- Majority ownership by U.S. Citizens or another U.S.-based Small Business
- All work will be performed in the United States
- SBIRs:
  - Primary Investigator is >50% employed by the Small Business
  - Phase I: ≥66% of work performed by Small Business*
  - Phase II: ≥50% of work performed by Small Business*
- STTR:
  - Small Business has a Research Institution partner (RI)
  - Primary Investigator is >50% employed by the Small Business or RI
  - Phase I & Phase II: ≥40% of the work performed by Small Business and ≥30% of the work must be performed by the RI

*The required work distribution applies to the subcontractors performing activities that involve meaningful programmatic decision making, contributions to scholarly/scientific conduct of the project, and/or requires considerable discretionary judgment and the unique expertise of the subcontractor in the performance of the work. This does not include standard goods or services such as those provided by a consultant, clinical research organization, or another fee-for-service organization that operate in a competitive environment and routinely provide similar goods/services to other organizations. The percentage of work is determined by the amount of project funding going to an entity.

2.2 SBA Company Registry *(Required at Proposal Submission)*

All proposers to this solicitation are required to register in the SBA Company Registry prior to proposal submission. The ARPA-H Solutions site requires proposers to input their SBC Control ID and upload their proof of registration (.pdf) as part of the proposal submission.

Follow the steps listed below to register and download your proof of registration:

- If you are a previous SBIR/STTR awardee from any agency, go to www.sbir.gov and login to your SBIR.GOV user account. Click on DASHBOARD and select 'Download SBC Registration (Proof of Registration/Certification)' from MY DOCUMENT BOX.

- If you are a first-time applicant, navigate to the SBA Company Registry and use the registration tool to complete your company's registration (may take approximately 1 business day to get approval).
- Download and save your SBA registry PDF locally. The name will be in the format of SBC_123456789.pdf, where the 9-digit number reflects your firm's SBC Control ID.
- Upload a copy of the completed SBA Company Registration for your organization when submitting your proposal to the ARPA-H Solutions site.

2.3 Registration in the System for Award Management (SAM) *(Required at Proposal Submission)*

All proposers must have an active SAM.gov registration with current information at the time of proposal submission, at award, and at all times during performance. Information on SAM.gov registration is available at SAM.gov. A Unique Entity Identifier (UEI) number will be assigned upon registration with SAM.gov. A UEI is required to submit your proposal to the ARPA-H Solutions site.

NOTE: New registrations and renewals may take more than 14 business days to process in SAM.gov. ARPA-H has no influence over SAM.gov processing times.

2.4 Required Disclosures of Foreign Affiliations or Relationships to Foreign Countries *(Required at Proposal Submission)*

All proposers must disclose all funded and unfunded relationships with foreign countries, using the Required Disclosures of Foreign Affiliations or Relationships to Foreign Countries form (referred to as the "Disclosure Form" hereafter), for all owners and covered individuals.

A "covered individual" is defined as all senior key personnel identified by the Small Business Concern (SBC) in the application (i.e., individuals who contribute to the scientific development or execution of a project in a substantive, measurable way).

This certification must be uploaded to the ARPA-H Solutions site along with your proposal. The SBIR-STTR Foreign Disclosure form and instructions can be found at: https://grants.nih.gov/grants-process/write-application/forms-directory/required-disclosures-foreign-affiliations-or-relationships-foreign-countries

2.5 Disclosure of Foreign Relationships Reporting Requirements *(Required throughout performance period)*

Performers are responsible for monitoring their relationships with foreign countries of concern for any changes that may impact previous disclosures. SBCs receiving an

award under the SBIR-STTR program are required to submit an updated Disclosure Form if there is:

- any change to a disclosure on the Disclosure Form;
- any material misstatement that poses a risk to national security; and
- any change of ownership, change to entity structure, or other substantial change in circumstances of the SBC that is determined to pose a risk to national security.

Note: this is reported using the same disclosure form listed in section 2.4.

Detailed Terms & Conditions

For changes that occur between progress reports, recipients must request prior approval for legal actions such as merger, acquisition, and successor-in-interest or any other change in ownership, entity structure, covered individual, or other substantive changes in circumstances no later than 30 calendar days before the proposed change. Disclosure Forms are required for any changes as described above.

If the contractor reports a covered foreign relationship that meets any of the risk criteria prohibiting funding described in this solicitation, ARPA-H may withhold funding until the covered relationship has been dissolved. The contractor will be required to submit documentation verifying the relationship has been terminated. If the risk cannot be resolved, ARPA-H may deem it necessary to terminate the award for material failure to comply with the federal statutes, regulations, or terms and conditions of the federal award. Contractors are encouraged to monitor their covered foreign relationships post-award and avoid entering into relationships, both funded and unfunded, that may pose a security risk and jeopardize their ability to retain their award.

Agency Recovery Authority and Repayment of Funds
An SBC will be required to repay all amounts received from ARPA-H under the award if either of the following determinations are made upon assessment of a change to their disclosure:

- the SBC makes a material misstatement that ARPA-H determines poses a risk to national security; or
- there is a change in ownership, change in entity structure, or other substantial change in circumstances of the SBC that ARPA-H determines poses a risk to national security.

2.6 Funding Agreement Certification *(Required at Proposal Submission)*

All proposers must submit either the SBIR or STTR Funding Agreement Certification form (links below) along with their proposal. Fast Track performers will need to re-submit this certification before beginning Phase II. This is required by SBA's reporting requirements.

All proposers to this solicitation must submit this form despite the instructions on the form indicating otherwise.

SBIR Funding Agreement Certification: https://grants.nih.gov/grants-process/write-application/forms-directory/sbir-funding-agreement-certification

STTR Funding Agreement Certification: https://grants.nih.gov/grants-process/write-application/forms-directory/sttr-funding-agreement-certification

Detailed Terms & Conditions

The SBA SBIR/STTR Policy Directive requires the collection of funding agreement information from firms at time of award and potentially during the award life cycle through the use of the SBIR or STTR Funding Agreement Certification. For purposes of this solicitation and contrary to the information found on the certification forms, all proposers are required to submit the appropriate and completed funding agreement certification document with the Solution Summary materials in accordance with this solicitation. This includes checking all applicable boxes and having an authorized officer of the awardee sign and date the certification each time it is requested in accordance with this solicitation.

The Federal government relies on this information to determine whether the business is eligible for a SBIR or STTR award. A similar certification, the Life Cycle Certification, will be used to ensure continued compliance with specific program requirements during the life of the funding agreement.
The definitions for the terms used in this certification are set forth in the Small Business Act, SBA regulations (13 CFR 121), the SBIR Policy Directive, and any statutory and regulatory provisions referenced in those authorities.

If the Contracting Officer believes that the business may not meet certain eligibility requirements at the time of award, the SBC/Proposer is required to file a size protest with the U.S. Small Business Administration (SBA), who will determine eligibility. At that time, SBA will request further clarification and supporting documentation to assist in the verification of any of the information provided as part of a protest.

If the Contracting Officer believes, after award, that the business is not meeting certain requirements the agency may request further clarification and supporting documentation to assist in the verification of the information provided. Even if correct information has been included in other materials submitted to the Federal government, any action taken with respect to this certification does not affect the Government's right to pursue criminal, civil, or administrative remedies for incorrect or incomplete information given in the certification. Each person signing this certification may be prosecuted if false information has been provided.

2.7 Life Cycle Certification (Required throughout performance period)

SBA requires the collection of information from all performers through the SBIR or STTR Life Cycle Certification Form. All SBIR/STTR Phase I and Phase II recipients must complete this certification the following times:

1. For Phase I Recipients: at the time of final invoice or receiving final payment.
2. For Phase II Recipients: prior to receiving more than 50% of the total award amount and prior to final payment.

Note: There are separate forms for SBIR and STTR recipients. Links to the forms and instructions are below.

SBIR Life Cycle Certification: https://grants.nih.gov/grants-process/write-application/forms-directory/sbir-life-cycle-certification

STTR Life Cycle Certification: https://grants.nih.gov/grants-process/write-application/forms-directory/sttr-life-cycle-certification

2.8 Majority Ownership in Part by Multiple Venture Capital, Hedge Fund, and Private Equity Firms Certification *(Required at Proposal Submission)*

Small Businesses that are owned in majority part by multiple venture capital operating companies (VCOCs), hedge funds, or private equity funds are only eligible for SBIR opportunities under this solicitation – they are not eligible for STTR opportunities. These businesses must complete the "SBIR Application VCOC Certification" and upload it to the ARPA-H Solutions site when submitting their proposal.

Note: SBC's that do not meet these criteria should NOT complete or submit the "SBIR Application VCOC Certification" form.

VCOC Form: https://grants.nih.gov/grants-process/write-application/forms-directory/sbir-vcoc-venture-capital-operating-companys-application-certification

Detailed Terms & Conditions

Small businesses that are owned in majority part by multiple venture capital operating companies (VCOCs), hedge funds, or private equity funds are eligible to submit proposals for SBIR opportunities under this solicitation but are required to submit a "SBIR Application VCOC Certification" at time of their proposal submission per the SBIR Policy Directive. Download the "SBIR Application VCOC Certification.pdf" at the NIH SBIR Forms webpage. Answer the 3 questions and check the certification boxes. The authorized business official must sign the certification. The signed SBIR Application VCOC Certification must be submitted with the Solution Summary materials.

Applicant small business concerns who are NOT owned in majority by multiple venture capital operating companies (VCOCs), hedge funds, or private equity funds, as described above, should NOT fill out a "SBIR Application VCOC Certification" and should NOT attach it to their application package.

NOTE: SBC that are more than 50% owned by multiple venture capital operating companies, hedge funds, private equity firms, or any combination of these are NOT eligible to apply to the ARPA-H/NIH STTR program.'

3 Proposal Preparation Instructions and Requirements

Submissions will follow a two-step process. This is a phased approach that reduces paperwork and effort for both proposers and ARPA-H. All eligible SBIR/STTR mechanisms (Phase I, Direct-to-Phase II, and Fast Tracks) will follow the same process.

3.1 Stage 1: Solution Summary

The Solution Summary is an abstract that concisely describes the proposed solution and implementation approach. The Solution Summary is 4 pages of technical content with exceptions noted in the following paragraphs. It is required to use the Solution Summary Template provided with this BAA. Proposers must clearly describe what they are developing and how they will do it. It must detail their overall approach and explain the technical challenges and innovations entailed. It must address how the proposer will achieve the metrics and milestones in the topic.

Direct-to-Phase II Only: Feasibility Statement. Proposers must address the scientific basis underpinning the proposed approach and provide evidence (whether from literature or prior work) that it will be successful. While ARPA-H seeks ambitious projects (not incremental advances), there should still be specific technical evidence underpinning the approach. This should not exceed 1-page of additional content.

Direct-to-Phase II and Fast Track Only: Commercialization Plan Statement. Commercialization is an essential goal of the SBIR/STTR program and performers are required to conduct commercialization activities during Phase II. Proposers must describe their commercialization objectives and plans. This includes their strategy, customers/buyers/markets, regulatory objectives, and any anticipated transition challenges to overcome. This should not exceed 1-page of additional content.

See *Section 5: Method of Selection and Evaluation Criteria*, for how solution summaries are evaluated.

3.2 Stage 2: Proposal Package with Technical Presentation

Proposers will be notified if they are invited to continue to Stage 2 after the Government completes the review of the Solution Summaries. The Technical Presentation is a 50-minute technical presentation with the first 20-minutes set aside for the proposer's presentation followed by 30-minutes for Q&A and technical discussion with the evaluation team. All presentations will be virtual, in-person, or hybrid as agreed upon between the Government and Proposer. Proposers will be limited to 3 virtual or in-person attendees, which must include the Principal Investigator (PI) for the project. STTR proposers must also include (virtually or in person) a representative from the participating research institution. Any associated travel costs or preparation expenses will not be reimbursed by the government.

ARPA-H expects to notify invited proposers 1-month before the Technical Presentation.

Proposers must provide advance copies of their slides, a Task Description Document (TDD), a GANTT chart, a key personnel worksheet, and a cost proposal. These are due approximately 2-weeks before the scheduled presentation following the instructions provided by ARPA-H. The evaluation team will use these as reference materials and to prepare questions (Note: questions will not be shared in advance).

Technical Presentation Content

Proposers should note that this is a *technical presentation*, not a *sales pitch*. This is Proposers' opportunity to voice-track their technical approach, their proposed statement of work, and why they will be successful. They should explain not only *what they will do*, but also *how they will do it, why it will work,* and *why they will be successful*. As necessary, the presentation should incorporate evidence to substantiate claims being made.

Presentations must also include slides describing the expertise of the organizations and key personnel participating in the project. Proposers must explain why they are qualified to not only create the technical innovation, but also to bring them to market and patients / users.

A maximum of 16 slides is permitted for the Technical Presentation. Proposers must use the template accompanying this solicitation and address each of the sections listed below. The suggested number of slides are also provided for each section.

- **Technical Merit & Novelty** (3 slides): Describe the technical merit and novelty of the solution being developed, the health problem being addressed, current limitations, the unique approach, expected impact, etc.
- **Technical Milestones & Project Timeline** (3 slides): Present the tasks and milestones from the TDD in a GANTT chart. The proposer should address the overall timeline and the most important milestones, but is not required to discuss all of them during the presentation.
- **Technical Risks & Mitigation Strategies** (2 slides): Identify the major technical risks and associated mitigation strategies to addressing them.
- **Commercialization Plan** (2-3 slides): Address the commercialization plans for the proposed solution. Includes the long-term vision commercialization and activities that will be executed during the proposed project. The content should include the anticipated end-state and additional steps that need to be taken to bring their project (if successful) to market. Proposers must also describe their overall strategy, key stakeholders, customer acquisition plans, market data, and articulate the key commercialization challenges and

mitigation plans that need to be overcome to successfully transition their solutions.

- **Team** (2 slides): Detail your team's qualifications by highlighting relevant expertise, roles, and experience supporting project success and commercialization.
- **Research Organization Partner - STTR Only (1 slide)**: Describe the relationship with your partner research institution, the details of your agreement, and the proposed division of labor and activities.
- **Project Summary** (1 slide): provides a high-level overview of the project and commercialization potential

4 Submissions

4.1 Submission via ARPA-H Solutions site

All submissions must occur using the ARPA-H Solutions site. The first time an individual uses the site, registration is required. Instructions for registration and troubleshooting issues are available on the Solution site landing page. The site for this solicitation contains a form and fields to upload all required documents and required certification forms. It is recommended that applicants register on the site and review the form contents early in the proposal preparation process. Additionally, a site submission resource will be posted with the special notice to help applicants prepare for the form fields in the site.

4.2 Documents required at submission

Proposal Page/Length Limit Table

Stage	Submission Item	Applies To	Limit	Notes
Stage 1	Solution Summary – core technical content	All proposers	4 pages	Must use the Solution Summary Template.
Stage 1	Feasibility Statement	Direct-to-Phase II only	+1 page max	Additional content beyond the 4-page Solution Summary. Must provide scientific basis and feasibility evidence.
Stage 1	Commercialization Plan Statement	Direct-to-Phase II and Fast Track only	+1 page max	Additional content beyond the 4-page Solution Summary.
Stage 1	SBA Proof of Registration	All proposers	No page limit	Required upload; administrative document.
Stage 1	SBIR Funding Agreement Certification	SBIR only	No page limit	Required upload.
Stage 1	STTR Funding Agreement Certification	STTR only	No page limit	Required upload.

Stage	Submission Item	Applies To	Limit	Notes
Stage 1	Foreign Disclosure Form	All proposers	No page limit	Required upload.
Stage 1	VCOC Certification	If applicable	No page limit	Required only for applicable SBIR proposers.
Stage 2	Technical Presentation Slides	Invited proposers	16 slides max	This is a slide limit, not a page limit.
Stage 2	Technical Presentation session	Invited proposers	50 minutes total	20 minutes presentation + 30 minutes Q&A. Not a page limit, but a formal length limit.
Stage 2	Task Description Document (TDD)	Invited proposers	No page limit stated	Required 2 weeks before presentation.
Stage 2	GANTT Chart	Invited proposers	No page limit stated	Required 2 weeks before presentation.
Stage 2	Cost Proposal	Invited proposers	No page limit stated	Required 2 weeks before presentation.
Stage 2	Key Personnel Worksheet	Invited proposers	No page limit stated	Required 2 weeks before presentation.

Total Solution Summary Page Limits:

Phase I	4 page max
Fast Track	5 page max
Direct to Phase II	6 page max

4.3 Submission Timeline

ARPA-H will notify all proposers about the status of their solution summary submission within 60 calendar days after the closing date for the topic. At that time, ARPA-H will inform the proposer as follows:

a. ARPA-H has discouraged the proposer to provide a presentation; or

b. ARPA-H encouraged the proposer to submit a proposal package and participate in a technical presentation. If selected for a presentation, additional instructions for scheduling a presentation session will be provided.

After the proposal package submission, ARPA-H will respond to each proposer who has submitted a proposal package and completed their technical presentation within 60 days to inform the proposer that:

a. ARPA-H has not selected the proposer to move forward with the solution; or

b. ARPA-H is recommending the proposal for award, which may or may not require negotiations.

ARPA-H intends to make awards for a topic within 180 calendar days of its closing date. If this changes, ARPA-H will notify proposers of the delay and provide a revised

timeline. Proposals packages submitted shall be valid for 180 calendar days after submission.

ARPA-H will not provide feedback during solution summary evaluations or after solution summaries have been evaluated and instead will provide an encourage/discourage designation. However, ARPA-H may provide Stage 2 proposal package feedback in the form of a written debrief after final Stage 2 selection decisions have been announced. If a written debrief is requested, ARPA-H will endeavor to provide a technical evaluation narrative to the proposer for each proposal package submitted to a topic.

4.4 Reducing Administrative Burden

The **Small Business Innovation and Economic Security Act** requires each agency head to set a maximum number of Phase I or Phase II proposals that a small business (including affiliates) may submit to each agency in a single fiscal year. Unless otherwise stated in this solicitation, HHS sets the number of SBIR/STTR proposals that a small business including its affiliates can submit per fiscal year to 9 proposals across all HHS Operating Divisions. This includes submitting a Phase II proposal to continue development of a Phase I project. Proposers should note that some topics may be waived from this requirement. **This section only applies to proposals submitted on or after October 1, 2026, through the closing date of the solicitation.**

5 Method of Selection and Evaluation Criteria

Conforming submissions will be evaluated using the method of selection and evaluation criteria detailed in this section. Submissions that do not meet the SBIR/STTR eligibility requirements (Section 2: Eligibility & Certifications), do not contain/conform to the required technical content (Section 3: Proposal Preparation Instructions and Requirements), or do not adhere to the submission instructions (Section 4: Submissions) will not be recommended to progress to Stage 2 or will not be evaluated nor considered for award. Proposers must make a complete Stage 1 submission by the topic deadline to be eligible to participate in Stage 2.

Stage 1: "Solution Summary" Basis of Evaluation

Solution Summaries will be evaluated for technical merit and novelty against the specific topic, not against other Solution Summaries. All conforming Solution Summaries submitted by the deadline will be evaluated against the criteria below:

1.) Non-Cost Evaluation Criteria: Technical Merit (see section 5.1.1)
2.) Non-Cost Evaluation Criteria: Technical Novelty (see section 5.1.2)

Based on the evaluation, applicants will be encouraged or discouraged from progressing to Stage 2. This is intended to save the time and cost of associated with preparing a full proposal package for Stage 2 when significant issues have been identified in the Solution Summary. While not recommended, "discouraged" companies have the option to progress to Stage 2. To do so, they must provide written notification to the contracting officer within 48 hours of receiving their Stage 1 recommendation.

Note: ARPA-H is not obligated to provide detailed feedback to Stage 1 submissions or to offer proposers an opportunity to correct errors.

Stage 2: Proposal Package Basis of Evaluation

In stage 2, proposal packages will be evaluated using the criteria below; they will be evaluated on their own merits and not in comparison to one another. The proposal package includes the technical presentation, the task description document (TDD), cost proposal, key personnel worksheet, and GANTT chart. The contents of the proposal package will be evaluated along with the oral presentation and Q&A using the following criteria:

1.) Non-Cost Evaluation Criteria: Technical Merit (see section 5.1.1)
2.) Non-Cost Evaluation Criteria: Technical Novelty (see section 5.1.2)
3.) Non-Cost Evaluation Criteria: Team & Relevant Experience (see section 5.1.3)
4.) Non-Cost Evaluation Criteria: Path to Impact and Health Outcomes (see section 5.1.4)
5.) Cost Evaluation Criteria (see section 5.1.5)

The Government will evaluate each proposal package in its entirety, documenting strengths and weaknesses relative to each evaluation criteria. Based on these identified strengths and weaknesses, the Government will determine the proposal's overall selectability for funding.

For the purposes of this evaluation process, a selectable proposal is defined as follows:

> **Selectable:** A selectable proposal is a proposal that the Government has evaluated against the evaluation criteria listed in the BAA, and the strengths of the overall proposal outweigh its weaknesses. Additionally, there are no accumulated weaknesses that would require extensive negotiations and/or a resubmitted proposal.

For the purposes of this proposal evaluation process, a non-selectable proposal is defined as follows:

> **Non-Selectable:** A proposal is considered non-selectable when the Government has evaluated the proposal against the evaluation criteria listed in

the BAA, and the strengths of the overall proposal do not outweigh its weaknesses or if there are accumulated weaknesses that would require extensive negotiations and/or a resubmitted proposal.

The government reserves the right to limit the number of proposers to be awarded a contract (with or without negotiations). As such, a proposer's submission may be evaluated as "Selectable" but not invited to negotiate or receive an award.

5.1 Evaluation Criteria

The following non-cost evaluation criteria will be used to evaluate the stages:

5.1.1 Technical Merit

The proposed technical approach meets or exceeds the objectives of the corresponding topic. The proposed technical approach is feasible and complete. Task descriptions and associated technical elements provided are complete and in a logical sequence with all proposed deliverables clearly defined such that an outcome that achieves the goal can be expected because of the award. The proposal identifies major technical risks and planned mitigation efforts are clearly defined and feasible. All claims should be substantiated with evidence provided. In addition, the evaluation may take into consideration the extent to which the proposed intellectual property (IP) rights structure and software components will potentially impact the ability to commercialize the technology and adhere to open-source solutions and/or standards.

5.1.2 Technical Novelty

The proposed technical approach is novel, innovative and highly ambitious, not incremental or basic research. This includes the development of new technologies/capabilities, novel applications or adaptations of existing technologies, and new interdisciplinary approaches. The proposal clearly identifies the novel elements of the proposed approach and the associated advancements created. The proposals illustrate how these advancements improve upon the status quo, enhance the state of science, advance overall capabilities in the field, and meet unmet needs within biomedicine to improve health outcomes. The proposed approach aligns to the ARPA-H mission of funding transformative advancements and gaps that are not being funded by other government agencies or the private sector.

5.1.3 Team & Relevant Experience

The proposed technical team has the expertise and experience to accomplish the proposed tasks, to fulfill the objectives of the topic, and to successfully commercialize the capabilities being developed. The technical team includes Principal Investigators/Project Managers, supporting staff, consultants, and other

personnel/partners involved in completing or commercializing the work. The proposer's prior experience in similar efforts is articulated and clearly demonstrates an ability to deliver products that meet the proposed technical performance within the proposed budget and schedule and to overcome regulatory and commercialization challenges incumbent in fielding the technology. It is important that teams demonstrate their ability to work together and have a proven track record of successfully developing technologies. Because the small business program seeks to develop novel capabilities, not incremental research, track records of developing and fielding new biomedical technologies is more important than publication histories.

5.1.4 Path to Impact and Health Outcomes

The proposal clearly demonstrates an understanding of the pathway to field, commercialize, or otherwise transition the solution being developed. The proposal articulates the key stakeholders involved, such as beneficiaries, economic buyers, users, entrenched incumbents, etc. The proposer articulates a commercialization strategy that is viable and demonstrates an understanding of the challenges that must be overcome and the operational constraints that must be accommodated. Other considerations include notional business model, freedom to operate and intellectual property, regulatory pathway, payment / reimbursement, evidence of commercial potential, and indicators of market readiness.

> The ARPA-H Small Business Program seeks to fund performers and technologies that can 'survive in the wild' and are not perpetually reliant on government funding. Strong proposals will address how ARPA-H's funds will enable them to achieve an inflection point from which they can complete commercialization independently. ARPA-H recognizes that it is impossible and impractical to plan every detail of commercialization before the technology has been developed. Rather, ARPA-H is seeking proposals that demonstrate an understanding of relevant pathways to market, their trade-offs, and how to manage some of the potential risks to commercialization.

5.1.5 Cost Criteria

The Cost Proposal will be evaluated to determine whether the proposed costs:

- are reasonable for the technical and management approach,
- accurately reflect the technical goals and objectives of the topic,
- are consistent with the proposer's statement of work, and
- reflect a sufficient understanding of the level of effort needed to successfully accomplish the proposed technical approach.

The costs for the prime proposer and proposed sub-awardees should be substantiated by the details provided in the proposal (e.g., the type and number of labor hours proposed per task, the types and quantities of materials, equipment 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. The proposer should provide as much back-up documentation for each proposed cost category to support proposed costs (vendor quotes, paystubs, indirect rate pool and base/rate agreements, travel break-out). All proposed costs should be supported by some reasonable basis.

Proposers requesting TABA funding will be required to submit a narrative as part of their Cost Proposal. The TABA narrative must provide ARPA-H substantiating information on what the TABA funding will be utilized for. See section 1.3 for further information on TABA funding.

5.2 Award Decision

The Government will make awards to proposers based on the following factors:

- Results from the technical evaluation of the submissions
- Availability of funds
- Security risk as assessed by the HHS Due Diligence Program
- Cost/Price
- Alignment with executive orders and applicable HHS policies
- Awardee must be a valid and responsible Small Business Concerns (SBCs) that meet the eligibility requirements set forth in 13 CFR 121.702 and the SBA's SBIR/STTR Policy Directive.
- Awardee must have an active SAM registration.

5.3 Denial of Awards

Proposers are encouraged to consider whether their entity's relationships with foreign countries of concern will pose a security risk. Prior to issuing an award, ARPA-H will determine whether the SBC submitting the proposal:

- has an owner or covered individual that is party to a malign foreign talent recruitment program;
- has a business entity, parent company, or subsidiary located in a foreign country of concern; or
- has an owner or covered individual that has a foreign affiliation with a research institution located in a foreign country of concern.

A finding of foreign involvement with countries of concern will not necessarily disqualify a proposer. Final award determinations will be based on whether the applicant's involvement falls within any of the following risk criteria, per the Small

Business Innovation and Economic Security Act:

- interfere with the capacity for activities supported by ARPA-H to be carried out; or
- create duplication with activities supported by ARPA-H; or
- present concerns about conflicts of interest; or
- were not appropriately disclosed to ARPA-H; or
- violate Federal law or terms and conditions of ARPA-H; or
- pose a risk to national security.

Generally, ARPA-H will not provide proposers the opportunity to address any identified security risks prior to award. ARPA-H will not issue an award under the SBIR/STTR program if the covered relationship with a foreign country of concern identified in this guidance is determined to fall under any of the criteria provided. Note that the denial of an award due to foreign involvement in one cycle does not bar eligibility in a later cycle.

5.4 Pre-Award and Post Award Solicitation Protests

Interested parties have the right to protest via procedures in FAR Subpart 33.1; protests exclusively related to this solicitation's terms must be sent to the Contracting Officer: steven.snyder@arpa-h.gov

For protests filed with the Government Accountability Office (GAO), a copy of the protest shall be submitted to the email address listed above (pre-award ONLY) within one day of filing with the GAO.

For the purposes of a protest related to a particular topic selection, non-selection or award decision, protests should be served to the Contracting Officer.

6 Policy Requirements, Considerations, and Other Information

Submission of proposal materials does not guarantee that ARPA-H will make an award. Awards will be issued to applicants whose proposals best meet the Government's instructions, evaluation criteria, and available funding.

ARPA-H will not reimburse proposers for costs to prepare and submit responses to this solicitation.

By submitting a Solution Summary/Proposal, proposers agree that ARPA-H:

a. Shall reproduce the Solution Summary/Proposal, or any portions thereof, to the extent necessary to evaluate the submission
b. Shall use information contained for evaluation purposes

c. Shall not disclose, directly or indirectly, such information to any person including potential evaluators, unless that person has been authorized to receive such information
d. ARPA-H is under no obligation to proceed with any Solution Summary/Proposal or select a specific number of Solution Summaries/Proposals for each topic. ARPA-H may award more or fewer awards than the anticipated number listed on an individual topic.
e. During the evaluation process, submissions may be handled by support contractors for administrative purposes and/or to assist with technical evaluation. All support contractors performing this role are expressly prohibited from performing ARPA-H-sponsored technical research and are bound by appropriate non-disclosure agreements (NDAs).

6.1 Protecting proprietary information - Proposal Markings

Information contained in all submissions will remain the property of the proposer. The Government may, however, retain copies of all proposals. Public release of information in any proposal submitted will be subject to existing statutory and regulatory requirements. If proprietary information is provided by a proposer in a proposal, which constitutes a trade secret, commercial or financial information, it will be treated in confidence, to the extent permitted by law, provided that the proposal is clearly marked by the proposer as follows:

> *"This proposal contains information that shall not be disclosed outside the Federal Government and shall not be duplicated, used, or disclosed in whole or in part for any purpose other than evaluation of this proposal, unless authorized by law The Government shall have the right to duplicate, use, or disclose the data to the extent provided in the resulting contract if award is made as a result of the submission of this proposal. The information subject to these restrictions are contained on all pages of the proposal except for pages [insert page numbers or other identification of pages that contain no restricted information.]"*

6.2 Technical Data Rights

6.2.1 Rights in Data Developed Under SBIR Funding Agreement.

The Small Business Act (15 U.S.C. 638) provides for "retention by an SBC of the rights to data generated by the concern in the performance of an SBIR award."

(1) Each agency must refrain from disclosing SBIR technical data to outside the Government (except reviewers) and especially to competitors of the SBC, or from using the information to produce future technical procurement specifications that could harm the SBC that discovered and developed the innovation.

(2) SBIR agencies must protect from disclosure and non-governmental use all SBIR technical data developed from work performed under an SBIR funding agreement for a period of not less than twenty years from the award date under that agreement (either Phase I, Phase II, or follow-on non-SBIR Federal funding agreement) unless, subject to paragraph (b) (3) of this section, the agency obtains permission to disclose such SBIR technical data from the awardee or SBIR applicant. Agencies are released from obligation to protect SBIR data upon expiration of the protection period except that any such data that is also protected and referenced under a subsequent SBIR award must remain protected through the protection period of that subsequent SBIR award. For example, if a follow-on non-SBIR Federal funding award is issued within or after the Phase II data rights protection period and the follow-on non-SBIR Federal funding award refers to and protects data developed and protected under the Phase II award, then that data must continue to be protected through the award protection period. The Government retains a royalty-free license for Government use of any technical data delivered under an SBIR award, whether patented or not. This section does not apply to program evaluation.

(3) SBIR technical data rights apply to all SBIR awards, including subcontracts to such awards, that fall within the statutory definition of Phase I or II of the SBIR Program, or follow-on non-SBIR Federal funding award, as described in section 4 of the SBIR Policy Directive. The scope and extent of the SBIR technical data rights applicable to follow-on non-SBIR Federal funding awards is identical to the SBIR data rights applicable to Phases I and II SBIR awards. The data rights protection period lapses only:

(i) Upon expiration of the protection period applicable to the SBIR award; or

(ii) By agreement between the awardee and the agency.

SBIR data rights markings shall not be affixed to SBIR Proposals; only to SBIR technical data delivered under funding agreements.

6.2.2 Identification and Marking of SBIR/STTR Technical Data in Contract Reports and Deliverables

a. SBIR: Rights in Data – SBIR Policy Directive SBIR/STTR Data Rights Clause (May 3, 2023)

(a) Definitions.

(1) Computer Software. Computer programs, source code, source code listings, object code listings, design details, algorithms, processes, flow charts, formulae, and related material that would enable the software to be reproduced, recreated, or recompiled. Computer Software does not include Computer Databases or Computer Software Documentation.

(2) Data. All recorded information, regardless of the form or method of

recording or the media on which it may be recorded. The term does not include information incidental to contract or grant administration, such as financial, administrative, cost or pricing or management information.

(3) Form, Fit, and Function Data. Data relating to items, components, or processes that are sufficient to enable physical and functional interchangeability, and data identifying source, size, configuration, mating and attachment characteristics, functional characteristics, and performance requirements. For Computer Software it means data identifying source, functional characteristics, and performance requirements, but specifically excludes the source code, algorithms, processes, formulas, and flow charts of the software.

(4) Government Purpose. Any activity in which the United States Government is a party, including cooperative agreements with international or multi-national defense organizations or sales or transfers by the United States Government to foreign governments or international organizations. Government Purposes include competitive procurement, but do not include the rights to use, modify, reproduce, release, perform, display, or disclose Technical Data or Computer Software for commercial purposes or authorize others to do so.

(5) Operations, Maintenance, Installation, or Training Purposes (OMIT) Data. Data that is necessary for operation, maintenance, installation, or training purposes (but not including detailed manufacturing or process data).

(6) SBIR/STTR Computer Software Rights. The Federal Government's rights during the SBIR/STTR Protection Period in specific types of SBIR/STTR Data that are Computer Software.

(A) The Federal Government may use, modify, reproduce, release, perform, display, or disclose SBIR/STTR Data that are Computer Software within the Government. The Federal Government may exercise SBIR/STTR Computer Software Rights within the Government for:

(1) Use in Federal Government computers;

(2) Modification, adaptation, or combination with other Computer Software, provided that the Data incorporated into any derivative software are subject to the rights in § 3(ee) of the SBIR/STTR Policy Directive and that the derivative software is marked as containing SBIR/STTR Data;

(3) Archive or backup; or

(4) Distribution of a computer program to another Federal agency, without further permission of the Awardee, if the Awardee is notified of the distribution and the identity of the recipient prior to the distribution, and a copy of the SBIR/STTR Computer Software Rights included in the Funding Agreement is

provided to the recipient.

(B) The Federal Government shall not release, disclose, or permit access to SBIR/STTR Data that is Computer Software for commercial, manufacturing, or procurement purposes without the written permission of the Awardee. The Federal Government shall not release, disclose, or permit access to SBIR/STTR Data outside the Government without the written permission of the Awardee unless:

(i) The non-Governmental entity has entered into a non-disclosure agreement with the Government that complies with the terms for such agreements outlined in § 8 of the SBIR/STTR Policy Directive; and

(ii) The release or disclosure is–

(I) To a Federal Government support service contractor or their subcontractor for purposes of supporting Government internal use or activities, including evaluation, diagnosis and correction of deficiencies, and adaptation, combination, or integration with other Computer Software provided that SBIR/STTR Data incorporated into any derivative software are subject to the rights in § 3(ee) of the SBIR/STTR Policy Directive; or

(II) Necessary to support certain narrowly-tailored essential Government activities for which law or regulation permits access of a non-Government entity to a contractors' data developed exclusively at private expense, non-SBIR/STTR Data, such as for emergency repair and overhaul.

(7) SBIR/STTR Data. All Data developed or generated in the performance of an SBIR or STTR award, including Technical Data and Computer Software developed or generated in the performance of an SBIR or STTR award. The term does not include information incidental to contract or grant administration, such as financial, administrative, cost or pricing or management information.

(8) SBIR/STTR Data Rights. The Federal Government's license rights in properly marked SBIR/STTR Data during the SBIR/STTR Protection Period are as follows: SBIR/STTR Technical Data Rights in SBIR/STTR Data that are Technical Data or any other type of Data other than Computer Software; and SBIR/STTR Computer Software Rights in SBIR/STTR Data that is Computer Software. Upon expiration of the protection period for SBIR/STTR Data, the Federal Government has a royalty-free license to use, and to authorize others to use on its behalf, these data for Government Purposes, and is relieved of all disclosure prohibitions and assumes no liability for unauthorized use of these data by third parties. The Federal Government receives Unlimited Rights in Form Fit, and Function Data, OMIT Data, and all unmarked SBIR/STTR Data.

(9) SBIR/STTR Protection Period. The period of time during which the Federal Government is obligated to protect SBIR/STTR Data against unauthorized use and disclosure in accordance with SBIR/STTR Data Rights. The SBIR/STTR Protection Period begins at award of an SBIR/STTR Funding Agreement and ends not less than twenty years from that date (See § 8(b)(4) of the SBIR/STTR Policy Directive).

(10) SBIR/STTR Technical Data Rights. The Federal Government's rights during the SBIR/STTR Protection Period in SBIR/STTR Data that are Technical Data or any other type of Data other than Computer Software.

(A) The Federal Government may, use, modify, reproduce, perform, display, release, or disclose SBIR/STTR Data that are Technical Data within the Government; however, the Government shall not use, release, or disclose the data for procurement, manufacturing, or commercial purposes; or release or disclose the SBIR/STTR Data outside the Government except as permitted by paragraph (B) below or by written permission of the Awardee.

(B) SBIR/STTR Data that are Technical Data may be released outside the Federal Government without any additional written permission of the Awardee only if the non-Governmental entity or foreign government has entered into a non-disclosure agreement with the Federal Government that complies with the terms for such agreements outlined in § 8 of the SBIR/STTR Policy Directive and the release is:

(i) Necessary to support certain narrowly-tailored essential Government activities for which law or regulation permits access of a non-Government entity to a contractors' data developed exclusively at private expense, non-SBIR/STTR Data, such as for emergency repair and overhaul;

(ii) To a Government support services contractor in the performance of a Government support services contract for internal Government use or activities, including evaluation, diagnosis or modification, provided that SBIR/STTR Technical Data incorporated into any derivative Data are subject to the rights in § 3(ii) of the SBIR/STTR Policy Directive, and the release is not for commercial purposes or manufacture;

To a foreign government for purposes of information and evaluation if required to serve the interests of the U.S. Government; or

To non-Government entities or individuals for purposes of evaluation.

(11) Technical Data. Recorded information, regardless of the form or method

of the recording, of a scientific or technical nature (including Computer Software Documentation and Computer Databases). The term does not include Computer Software or financial, administrative, cost or pricing, or management information, or other data incidental to contract or grant administration. The term includes recorded Data of a scientific or technical nature that is included in Computer Databases.

(12) Unlimited Rights. The Government's rights to access, use, modify, prepare derivative works, reproduce, release, perform, display, disclose, or distribute Data in whole or in part, in any manner and for any purpose whatsoever, and to have or authorize others to do so.

(b) Allocation of SBIR/STTR Data Rights.

(1) An SBC retains ownership of all SBIR/STTR Data it develops or generates in the performance of an SBIR/STTR award. The SBC retains all rights in SBIR/STTR Data that are not granted to the Federal Government in accordance with the SBIR/STTR Policy Directive. These rights of the SBC do not expire.

(2) During the SBIR/STTR Protection Period, the Federal Government receives SBIR/STTR Technical Data Rights in appropriately marked SBIR/STTR Data that is Technical Data or any other type of Data other than Computer Software; and SBIR/STTR Computer Software Rights in appropriately marked SBIR/STTR Data that is Computer Software.

(3) After the protection period, the Federal Government may use, and authorize others to use on its behalf, for Government Purposes, SBIR/STTR Data that was protected during the SBIR/STTR Protection Period. Awards issued by the U.S. Department of Energy are subject to Unlimited Rights after the expiration of the SBIR/STTR Protection Period.

(4) The Federal Government receives Unlimited Rights in Form Fit, and Function Data, OMIT Data, and all unmarked SBIR/STTR Data

(c) Identification and Delivery of SBIR/STTR Data. Any SBIR/STTR Data delivered by the Awardee, and in which the Awardee intends to limit the Federal Government's rights to SBIR/STTR Data Rights, must be delivered with restrictive markings. The Federal Government assumes no liability for the access, use, modification, reproduction, release, performance, display, disclosure, or distribution of SBIR/STTR Data without markings.

The Awardee or its subcontractors or suppliers shall conspicuously and legibly mark all such SBIR/STTR Data with the appropriate legend.

(1) The authorized legend shall be placed on each page of the SBIR/STTR Data. If only portions of a page are subject to the asserted restrictions, the SBIR/STTR Awardee shall identify the restricted portions (e.g., by circling or underscoring with a note or other appropriate identifier). With respect to SBIR/STTR Data embodied in Computer Software, the legend shall be placed on: (1) the

printed material or media containing the Computer Software; or (2) the transmittal document or storage container. The legend shall read as follows:

SBIR/STTR DATA RIGHTS

Funding Agreement No.	
Award Date	
SBIR/STTR Protection Period	
SBIR/STTR Awardee	
SBIR/STTR Awardee Address	

This is SBIR/STTR Data (or is Computer Software or a Prototype that embodies or includes SBIR/STTR Data) to which the SBIR/STTR Awardee has SBIR/STTR Data Rights and to which the Federal Government has received SBIR/STTR Technical Data Rights (or SBIR/STTR Computer Software Rights) during the SBIR/STTR Protection Period and rights of use for Government Purposes after the SBIR/STTR Protection Period, as those terms are defined in the SBIR/STTR Funding Agreement. Awards issued by the U.S. Department of Energy are subject to Unlimited Rights after the SBIR/STTR Protection Period, as that term is defined in the SBIR/STTR Funding Agreement. Any reproduction of SBIR/STTR Data or portions of such data marked with this legend must also reproduce the markings.

Data submitted without correct or appropriate markings may be corrected within 6 months from the date the data is delivered.

6.2.3 Patents and Invention Reporting

Small business firms normally may retain the principal worldwide patent rights to any invention developed with Government support. The Government receives a royalty-free license for its use, reserves the right to require the patent holder to license others in certain limited circumstances, and requires that anyone exclusively licensed to sell the invention in the United States must normally manufacture it domestically. To the extent authorized by 35 USC 205, the Government will not make public any information disclosing a Government-supported invention to allow the awardee to pursue a patent.

The reporting of inventions is accomplished by submitting information through the Edison Invention Reporting System for those Awarding Components participating in "Interagency Edison", or iEdison. ARPA-H requires contractors to use iEdison, which streamlines the reporting process and greatly reduces paperwork. Access to the system is through a secure interactive Web site to ensure that all information submitted is protected.

Inventions must be reported promptly—within two months of the inventor's initial

report to the contractor organization.

This should be done prior to any publication or presentation of the invention at an open meeting, since failure to report at the appropriate time is a violation of 35 U.S.C. 202 and may result in loss of the rights of the small business concern, inventor, and Federal Government in the invention. All foreign patent rights are immediately lost upon publication or other public disclosure unless a United States patent application is already on file. In addition, statutes preclude obtaining valid United States patent protection after one year from the date of a publication that discloses the invention.

If no invention is disclosed or no activity has occurred on a previously disclosed invention during the applicable reporting period, a negative report shall be submitted to the Contracting Officer. Inquiries or information about invention reporting or requirements imposed by 37 CFR 401 may also be directed to: ARPA-HSBP_Proposals@arpa-h.gov.

6.3 Security Prohibitions and Exclusions Representations and Certifications.

(a) Definitions. As used in this provision-—

Backhaul, covered article, covered telecommunications equipment or services, critical technology, FASCSA order, Intelligence community, interconnection arrangements, national security system, roaming, sensitive compartmented information, sensitive compartmented information system, source, and substantial or essential component have the meanings provided in the clause 52.240-91, Security Prohibitions and Exclusions.

Business operations means engaging in commerce in any form, including by acquiring, developing, maintaining, owning, selling, possessing, leasing, or operating equipment, facilities, personnel, products, services, personal property, real property, or any other apparatus of business or commerce.

Marginalized populations of Sudan means—

(1) Adversely affected groups in regions authorized to receive assistance under section 8(c) of the Darfur Peace and Accountability Act (Pub. L. 109-344) (50 U.S.C. 1701 note); and

(2) Marginalized areas in Northern Sudan described in section 4(9) of such Act.

Restricted business operations means business operations in Sudan that include power production activities, mineral extraction activities, oil-related activities, or the production of military equipment, as those terms are defined in the Sudan Accountability and Divestment Act of 2007 (Pub. L. 110-174). Restricted business operations do not include business operations that the person (as that term is defined in Section 2 of the Sudan Accountability and Divestment Act of 2007) conducting the business can demonstrate—

(1) Are conducted under contract directly and exclusively with the regional government of southern Sudan;

(2) Are conducted under specific authorization from the Office of Foreign Assets Control in the Department of the Treasury, or are expressly exempted under Federal law from the requirement to be conducted under such authorization;

(3) Consist of providing goods or services to marginalized populations of Sudan;

(4) Consist of providing goods or services to an internationally recognized peacekeeping force or humanitarian organization;

(5) Consist of providing goods or services that are used only to promote health or education; or

(6) Have been voluntarily suspended.

Sensitive technology—

(1) Means hardware, software, telecommunications equipment, or any other technology that is to be used specifically—

(i) To restrict the free flow of unbiased information in Iran; or

(ii) To disrupt, monitor, or otherwise restrict speech of the people of Iran; and

(2) Does not include information or informational materials the export of which the President does not have the authority to regulate or prohibit pursuant to section 203(b)(3) of the International Emergency Economic Powers Act (50 U.S.C. 1702(b)(3)).

(b) Procedures.

(1) Covered telecommunications and video surveillance. The Offeror shall review the list of excluded parties in the System for Award Management (SAM) at https://www.sam.gov for entities excluded from receiving federal awards for "covered telecommunications equipment or services."

(2) FASCSA Orders.

(i) The Offeror shall search in SAM for the phrase "FASCSA order" for any covered article, or any products or services produced or provided by a source, if there is an applicable FASCSA order described in paragraph (e) of FAR 52.240-91, Security Prohibitions and Exclusions.

(ii) The Offeror shall review the solicitation for any FASCSA orders that are not in SAM but are effective and apply to the

solicitation and resultant contract (see FAR 40.204-1(c)(2)).

(iii) FASCSA orders issued after the date of solicitation do not apply unless added by an amendment to the solicitation.

(c) *Covered telecommunications equipment or services representations.* By submission of its offer, the Offeror represents that, after conducting a reasonable inquiry (that looks at any information in the Offeror's possession but does not need to include an internal or third-party audit)–

(1) It will not provide covered telecommunications equipment or services to the Government in the performance of any contract, subcontract or other contractual instrument resulting from this solicitation, except as waived by the solicitation, or as disclosed in paragraph (g); and

(2) It does not use covered telecommunications equipment or services, or use any equipment, system, or service that uses covered telecommunications equipment or services, except as waived by the solicitation, or as disclosed in paragraph (g).

(d) *FASCSA Representation.* By submission of this offer, the offeror represents that it has conducted a reasonable inquiry, and that the offeror does not propose to provide or use in response to this solicitation any covered article, or any products or services produced or provided by a source, if the covered article or the source is prohibited by an applicable FASCSA order in effect on the date the solicitation was issued, except as waived by the solicitation, or as disclosed in paragraph (g). A reasonable inquiry will look at any information in the offeror's possession but does not need to include an internal or third-party audit.

(e) *Sudan certification*. By submission of its offer, the offeror certifies, after conducting a reasonable inquiry (that looks at any information in the offeror's possession but does not need to include an internal or third-party audit), that the offeror does not conduct any restricted business operations in Sudan.

(f) *Iran Representation and Certifications*.

(1) Except as provided in paragraph (f)(2) of this provision or if a waiver has been granted in accordance with FAR 40.203-3, the offeror, after conducting a reasonable inquiry (that looks at any information in the offeror's possession but does not need to include an internal or third-party audit), by submission of its offer –

(i) Represents, to the best of its knowledge and belief, that the offeror does not export any sensitive technology to the government of Iran or any entities or individuals owned or controlled by, or acting on behalf or at the direction of, the government of Iran;

(ii) Certifies that the offeror, or any person (as defined at section 15 of the Iran Sanctions Act of 1996, Pub. L. 104-172, 50 U.S.C. 1701 note)

owned or controlled by the offeror, does not engage in any activities for which sanctions may be imposed under section 5 of the Act. These sanctioned activities are in the areas of development of the petroleum resources of Iran, production of refined petroleum products in Iran, sale and provision of refined petroleum products to Iran, and contributing to Iran's ability to acquire or develop certain weapons or technologies; and

(iii) Certifies that the offeror, and any person owned or controlled by the offeror, does not knowingly engage in any transaction that exceeds $15,000 with Iran's Revolutionary Guard Corps or any of its officials, agents, or affiliates, the property and interests in property of which are blocked pursuant to the International Emergency Economic Powers Act (50 U.S.C. 1701 et seq.) (see OFAC's Specially Designated Nationals and Blocked Persons List at https://www.treasury.gov/resourcecenter/sanctions/SDN-List/Pages/default.aspx)

(2) Exception for trade agreements. The representation and certification requirements of paragraph (f)(1) of this provision do not apply if—

(i) This solicitation includes a trade agreements notice or certification (e.g., 52.225-6, Trade Agreements Certificate); and

(ii) The offeror has certified that all the offered products to be supplied are designated country end products or designated country construction material.

(iii) The offeror shall email questions concerning sensitive technology to the Department of State at CISADA106@state.gov.

(g) Disclosure.

(1) If the Offeror is not able to represent compliance with the prohibitions in paragraphs (c) or (d), then the Offeror shall disclose within 72 hours to the contracting office identified in paragraph (g)(2) the following information for each product or service not compliant:

(i) Contract number and order number, if applicable;

(ii) Identification of whether this disclosure relates to paragraph (c) on covered telecommunication equipment or services, or to paragraph (d) on FASCSA orders;

(iii) A description of the products or services that the Contractor identifies or has reason to suspect is prohibited (include brand; model number, such as the original equipment manufacturer (OEM) number, manufacturer part number, or wholesaler number; and item description, as applicable);

(iv) The entity that produced the product or service (include entity

name, unique entity identifier, Contractor and Government Entity (CAGE) code, facilities responsible for design, fabrication, assembly, packaging, and test of the product, and whether the entity was the OEM or a distributor (provide manufacturer codes and distributor codes used for the product));

(v) Description of the functionality of the product or service and how that functionality impacts the risk to the product or service;

(vi) An explanation of any factors relevant to determining if the product or service should be permitted by an applicable exception, exemption, or waiver (if the offeror would like the Government to consider a waiver);

(vii) Whether alternative products or services are available that would be compliant with the prohibition;

(viii) If the product or service is related to item maintenance, include the following information on the item being maintained:

(A) Brand;

(B) Model number, OEM number, manufacturer part number, or wholesaler number; and

(C) Item description, as applicable.

(ix) Any readily available information about mitigation actions undertaken or recommended.

(2) If a disclosure is required to be submitted to a contracting office, the offeror shall submit the disclosure as follows:

(i) If a Department of Defense contracting office, the offeror shall submit the disclosure to the website at https://dibnet.dod.mil.

(ii) For all other contracting offices, the Offeror shall submit the disclosure to the Contracting Officer.

(3) If the disclosure provided does not contain any of the information required by paragraph (1), and the Offeror later discovers new information that is required by paragraph (1), then the Offeror shall submit a subsequent disclosure within 72 hours of discovering the new information.

(h) Executive agency review of disclosures. The Contracting Officer will review disclosures provided in paragraph (g) to determine if any applicable waiver may be sought. The Contracting Officer may choose not to pursue a waiver and may instead make an award to an Offeror that does not require a waiver.

7 Scientific and Technical Information Sources

7.1 Human Subject Research (HSR)

All entities submitting a proposal for funding that will involve engagement in human subjects research (as defined in 45 CFR § 46) must provide documentation of one or more current Assurance of Compliance with federal regulations for human subjects protection including at least a Department of Health and Human Services (HHS) Office of Human Research Protection Federal Wide Assurance. (Note: Processing times for new Federal Wide Assurances may take 60-90 days). All human subjects research must be reviewed and approved by an IRB, as applicable under 45 CFR § 46 and/or 21 CFR § 56. The entities human subjects research protocol must include a detailed description of the research plan, study population, risks and benefits of study participation, recruitment and consent process, data collection, and data analysis. Recipients of ARPA-H funding must comply with all applicable laws, regulations, and policies for the ARPA-H funded work. This includes but is not limited to laws, regulations, and policies regarding the conduct of human subjects research, such as the U.S. federal regulations protecting human subjects in research (e.g., 45 CFR § 46, 21 CFR § 50, § 56, § 312, § 812) and any other equivalent requirements of the applicable jurisdiction. The informed consent document utilized in human subjects research 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 human subjects research training by all investigators and key personnel who will be involved in the design or conduct of the ARPA-H funded human subjects research. Funding cannot be used toward human subjects research until ALL approvals are granted and the vendor receives express written permission from the Contracting Officer.

7.2 Animal Subject Research (ASR)

All entities submitting a proposal for funding that will involve engagement in animal subjects research (performers 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: (i) 9 CFR parts 1-4, U.S. Department of Agriculture rules that implement the Animal Welfare Act of 1966, as amended, (7 U.S.C. § 2131-2159); (ii) the Public Health Service Policy on Humane Care and Use of Laboratory Animals, 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).

Proposers must complete and submit the Vertebrate Animal Section (VAS) for all proposed research anticipating animal subjects research. A guide for completing the VAS can be found at https://olaw.nih.gov/sites/default/files/VASchecklist.pdf worksheet for all proposed research anticipating Animal Subject Research.

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. The vendor shall receive express written permission from the Contracting Officer prior to commencement of any ASR related tasks.

8 Research Topics

This section contains the research topics being solicited through this BAA. New topics may be added periodically and will be added to the table below. Note the deadline for submitting solution summaries for each topic.

Topic Number	Title	Solution Summary Deadline
Topic 1	Development of an annual test to inform women about their future fertility	TBD
Topic 2	Versatile Bioadhesives	TBD
Topic 3	Universal Platform for Living Adaptive Toxin-removal (UNI-PLAT)	TBD
Topic 4	Breaking Ground: The First Curative, Durable, Non-Surgical Therapy for Endometriosis	TBD
Topic 5	ARPA-H Lineage Topic	TBD
Topic 6	Rapid Comprehensive Diagnostic Test for Multi-System Autoimmune Disease	TBD
Topic 7	Virtual Human Brain for the Development of Neurosurgical Robotics	TBD

Topic 1: *Development of an annual test to inform women about their future fertility*	
Anticipated Awards	2
Anticipated Budget	$600k (Phase I), $3.5M (Phase II)
Anticipated Timeline	12 months (Phase I), 24 months (Phase II)
Type	SBIR and STTR
Eligible Phases	Phase I, Direct-to-Phase II, or Fast-Track

Background / Introduction

Infertility impacts between 9-15% of couples and, in the setting of historically low birth rates, improving fertility is imperative for our future economy. Currently, infertility is diagnosed only after a couple has failed to conceive for a year or more. Until then, women receive no personalized data regarding the best time to have a baby or when their personal fertility will end. This leaves little room for early interventions that may avoid the need for costly and invasive fertility treatments, such as in vitro fertilization (IVF). Finding a biomarker to give women additional information about when their natural fertility will decrease and end will provide women with critical guidance for family planning.

In the US, women are choosing to start families later in life, due to social and career circumstances. First birth rates for women aged 35-39 years old increased six-fold from 1973 to 2006. For women aged 40-44, they grew four-fold from 1985 to 2012 (Matthews 2014). While we know that the average age of sterility, meaning inability to conceive, is 44.7 years old, the range is wide with 20% of women becoming sterile at 40 years old and 80% of women not becoming sterile until 46 years old. As women plan childbearing, it's impossible to know how easy or hard it will be to start a family at a given age given the wide array of outcomes. Out of 100 women trying to become pregnant at (Leridon 2004):

> 30 years old: 91 will have a child without IVF, 3 will do so with IVF, 6 will remain childless.
>
> 35 years old: 82 will have a child without IVF, 4 will do so with IVF, 14 will remain childless.
>
> 40 years: 57 will have a child without IVF, 7 will do so with IVF, and 36 will remain childless.

Most attempts to quantify fertility have focused on assessments of ovarian reserve, defined as the number of oocytes remaining in the ovary. Biomarkers include ultrasound imaging of the follicles in an ovary and serum hormonal tests such as follicle stimulating hormone (FSH), estradiol (E2), and anti-mullerian hormone (AMH). Unfortunately, a 2024 cohort study found that these tests are not associated with infertility or probability of achieving a live birth in women aged 30-44,and are only predictive of IVF success. The article concludes that women highly desire a "fertility" test to predict whether they will have difficulty conceiving should they delay pregnancy attempts (Harris 2023).

Currently, age is the most accurate biomarker for fertility. Emerging technologies are primarily focused on genetic determinants, which strongly influence the timing of menopause, likely via variation in DNA damage repair mechanisms (Laven 2024). A 2025 paper in Nature Aging published a comprehensive single-nuclei multi-omics atlas of four young (ages 23-29 years) and four

reproductively aged (ages 49-54 years) human ovaries, revealing coordinated changes in regulatory variants across ovarian cell types (Jin 2025).

Purpose and Goals

In a time where couples are increasingly delaying conception, patients want to know more about their predicted fertility (Grootenhuis 2019) and having the information could help prevent involuntary childlessness (Laven 2024). Currently, there is no way to provide women with personalized recommendations for fertility planning. If successful, this work would enable a woman who is 30 years old and considering having a baby after 5 more years in her current job, to take a test and discover that her fertility will decline sharply at 33 years old. Armed with that information, she can either freeze her eggs now or decide to start a family now, instead of facing a high likelihood of involuntary childlessness had she waited until age 35 to begin trying.

Given that ovarian reserve biomarkers do not predict spontaneous pregnancy, the purpose of this topic is to discover new biomarkers that provide women with actionable data for fertility planning. Results from this work will help inform the program manager regarding the feasibility of future programs focused on enhancing natural fertility before the need of IVF and guiding the development of women's health monitoring and improvement tools. This work will develop a diagnostic test that can assess fertility status and generate an estimated timeline for the onset of infertility. This topic seeks to develop a test that is affordable, suitable for at least annual use, and provides user-friendly results for patients and care teams to support childbearing decisions.

Requirements Supported (In-Scope)

Solutions must propose and develop a biomarker-based method to evaluate a woman's fertility status and predict her future fertility. This could include, but is not limited to, biospecimen collection, imaging, or device diagnostics, provided the proposed solution meets the Target Product Profile defined below. The solution may be implemented in either a primary care or at home diagnostic setting and must provide interpretable, objective, and evidence-backed results. At home diagnostics should provide a plan for optional clinical collaboration with a medical provider and should have a pathway to be covered by insurance. Development may be accomplished using previously collected samples with known outcomes to assess the potential for new biomarkers. Solutions must be agnostic regarding menstrual phase or contraceptive use status.

Examples that would be considered in scope may include but are not limited to:

- A blood/urine/saliva test that can be performed at an annual visit that provides an objective measure of fertility status
- An at home diagnostic test that can provide a clear result to patient and provider with immediate or mail in results
- A low cost, non-invasive, point of care detection device that can be used at an annual exam
- Wearables requiring baseline data collection of 1 month or less

Out-of-Scope Requirements

Solutions around predicting or enhancing the success of IVF will not be accepted. Solutions that cannot feasibly be deployed in both urban and rural care settings, are invasive, or cumbersome to

the patient will not be accepted. Solutions positioned in the direct-to-consumer space will not be accepted.

Examples that would be considered out of scope may include but are not limited to:

- An imaging test that can monitor IVF that must be performed at an urban specialist clinic
- A surgical method to confirm a physiological state
- A biomarker that requires specialized equipment to detect at great financial cost making it inaccessible by the general population

Metrics and Milestones

Phase I Activities:

- Identify source of biospecimens and methodology for testing.
    - Specimen collection and testing must be performed in compliance with good clinical practice and institutional ethics requirements.
    - Collection method must be minimally invasive and able to be performed within 15 minutes (with the exception of wearables as above).
- Discover 5+ candidate biomarkers for fertility prediction.
    - Biomarkers or combination of biomarkers must have a sensitivity and specificity of 80% with respect to fertility status
    - Analysis of biomarker for fertility result must be able to be completed in under 1 hour of sample collection

Phase II Activities:

- Establish fertile, sub fertile, and infertile biomarker thresholds with AUC>0.85.
- Assess candidate biomarkers performance prospectively and maintain AUC>0.85.
    - Biomarkers or combination of biomarkers must have a sensitivity and specificity of 90% with respect to fertility status
    - Analysis of biomarker for fertility result must be able to be completed in under 15 min of sample collection
- Establish regulatory plan for FDA submission.
    - Pre-submission questions and discussion meeting with the FDA completed within 6 months of phase initiation.
    - Design controls implemented and data collected for verification and validation
- Target product profile:
    - Cost is less than $50 per test
    - Minimally-invasive - requiring at most an intravenous blood collection or skin prick
    - Result clearly interpretable by the patient and provider and describes both current and future fertility status.
    - In the case of a biospecimen-based biomarker:
        - Collection able to be performed at the bedside by a care provider (nurse, phlebotomist, technician, etc.) or at home by the patient (in the case of an at home diagnostic collection)
        - Analyzed result provided to the care team and patient (or just the patient in case of an at-home test) within 15 minutes, or the patient

- In the case of an imaging or device-based biomarker:
    - Device must be able to be incorporated into a standard primary care clinical workflow
    - Device must be mobile and able to be moved and operated by one person
    - Test able to be performed consistently with 95% repeatability
    - Analyzed result provided to the care team and patient (or just the patient in case of an at-home test) within 15 minutes.
- Covered by insurance with plan to establish mechanism of reimbursement

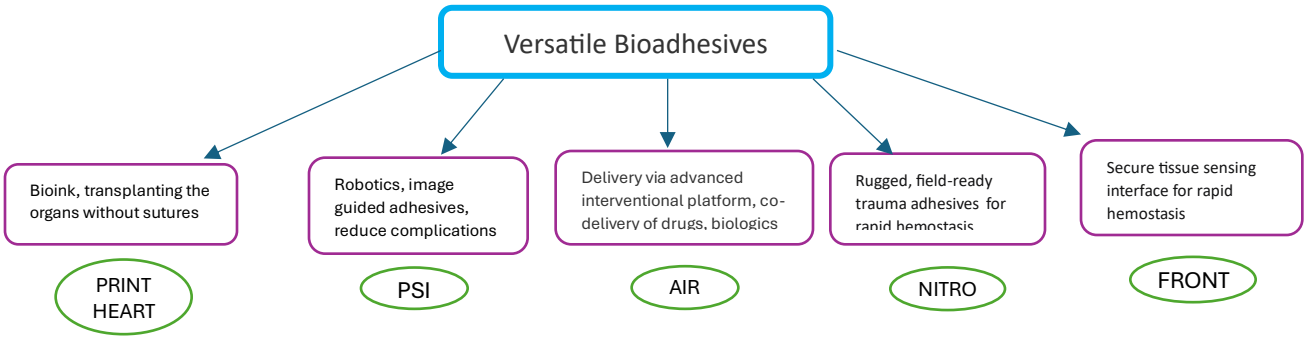
Topic 2: *Versatile Bioadhesives*	
Anticipated Awards	2
Anticipated Budget	$600k (Phase I), $3.5M (Phase II)
Anticipated Timeline	12 months (Phase I), 24-36 months (Phase II)
Type	SBIR and STTR
Eligible Phases	Phase I, Direct-to-Phase II, or Fast-Track

Background / Introduction

Bioadhesives are a class of adhesive materials derived from or inspired by biological systems that can bond to living tissues or other surfaces in wet, dynamic environments. Unlike conventional synthetic glues, bioadhesives are typically designed to be biocompatible, often biodegradable, and to function effectively in conditions where traditional adhesives fail, such as inside the human body or in marine settings. These materials draw inspiration from natural models like mussel byssal threads, gecko feet, and insect secretions, and are increasingly used in applications ranging from surgical sealants and wound dressings to environmentally friendly industrial glues.

Current medical glues have major limitations that restrict their clinical use. Many fail to adhere reliably in wet, bloody, or highly mobile environments and lack the strength and durability needed for high-pressure or long-term applications, so they are often relegated to adjunct roles. Safety and handling are problematic: some cyanoacrylate and synthetic products cause tissue toxicity or inflammation, curing can be too fast or too slow for precise use, and cured glues are often stiff, poorly integrated with healing tissue, and hard to remove without damage. Additional challenges include infection and biofilm risk, poor performance on difficult tissues (fatty, mucosal, calcified), suboptimal degradation. Practical issues such as complex preparation, storage requirements, short shelf life, and regulatory constraints, contribute to the overall challenge of developing safe, robust, and versatile medical glues.

This SBIR topic seeks innovative bioadhesive technologies. Proposed solutions should move beyond current single-use, tissue-limited glues to create modular, tunable platforms compatible with multiple clinical scenarios (e.g., hemostasis, leak prevention, anastomotic reinforcement, internal device fixation) and delivery modes (open, laparoscopic, endoscopic, and robotic).



The versatile medical bioadhesives SBIR topic is a cross-cutting platform that amplifies multiple ARPA-H efforts. With PRINT, it powers bioinks and adhesive tools for sutureless organ repair and transplantation. With PSI, it pairs robotics and image-guided adhesives to cut leaks, bleeding, and reoperations while standardizing high-performance closure. With AIR, it integrates into advanced interventional platforms to co-deliver biologics and devices on moving organs. With NITRO, it supplies rugged, field-ready trauma adhesives for rapid hemostasis and stabilization. With FRONT, it creates secure, low-profile tissue interfaces for advanced sensing and therapeutic delivery. Together, these interfaces accelerate translation and multiply impact across the ARPA-H portfolio.

Purpose and Goals

Develop and validate a new class of versatile, tissue-compatible bioadhesives that can safely and reliably seal, bond, and repair diverse tissues in wet, bloody, and mechanically dynamic environments, ultimately reducing complications and expanding treatment options across surgical, drug delivery and emergency settings.

Technical Areas Supported (In-Scope):

1. Create modular bioadhesive platforms that provide strong, predictable adhesion across key tissue types (e.g., lung, heart, vascular, solid organs, skin) and can be tuned for specific mechanical and healing requirements.
2. Engineer bioadhesives for safety, integration, and reversibility, ensuring biocompatibility, controlled degradation aligned with healing, and on-demand curing and debonding to support revision procedures and device removal.
3. Deliver clinically usable formats (e.g., sprays, patches, injectables, catheter/robot-compatible applicators) and generate preclinical data packages that enable regulatory progression and deployment in both advanced and resource-limited care environments.
4. Present a clear commercialization strategy for versatile bioadhesives, including defined initial indications, regulatory path, scalable GLP manufacturing, cost targets and reimbursement/market adoption plans (PMS, De Novo, 510K).

Out-of-Scope Technical Areas:

This topic will not support R&D efforts of surgical glues that are disease/tissue/organ specific or for standard product development work of existing surgical glue technology.

Metrics and Milestones

Phase I Objectives (examples):

- Demonstrate a proof-of-concept bioadhesive prototype with:
    - Strong, reproducible adhesion to at least two distinct tissue types (e.g., lung and heart, or vascular and solid organ) under physiologic moisture and motion.
    - Biocompatibility and controlled degradation in relevant in vitro and/or small-animal models.
- Develop at least one clinically relevant delivery format (e.g., spray, patch, or injectable system) and establish preliminary usability and handling characteristics.

Phase II Objectives (examples):

- Optimize formulations and applicators to support at least two priority indications (e.g., sealing pulmonary air leaks and reinforcing GI anastomoses, or trauma hemostasis and internal device anchoring).
- Demonstrate performance that meets or exceeds standard of care in relevant large-animal models (e.g., burst pressure, leak rate, time to hemostasis, durability under motion).
- Establish a scalable, GMP-compatible manufacturing strategy and generate a preclinical data package that supports a defined regulatory pathway

Topic 3: *Universal Platform for Living Adaptive Toxin-removal (UNI-PLAT)*	
Anticipated Awards	2
Anticipated Budget	$600k (Phase I), $3.5M (Phase II)
Anticipated Timeline	6-16 months (Phase I), 24-36 months (Phase II)
Type	SBIR and STTR
Eligible Phases	Fast-Track

Background / Introduction

This SBIR and STTR topic seeks to establish microbial platforms for effective removal of toxins present in food and water, aiming to advance American health. Such platforms would mitigate the chronic health burden associated with these exposures.

Engineered microbes have shown promise as living tools to convert, neutralize, or remove toxins present in the environment or in foods (such as ultra-processed foods), which contribute to the increasing prevalence of chronic diseases and metabolic disorders. Some single-strain bacteria, such as *Escherichia coli and* strains of *Bacillus*, have previously been engineered to remove individual toxins by converting acetaldehyde or plastics to healthier byproducts, or sequestering chemicals to mitigate potential ingestion. While current single-strain approaches benefit from regulatory simplicity and consistent performance in controlled settings, they are inherently limited in expanding their toxin removal capabilities for multiplex applications without imposing significant burdens on cell viability and metabolism. Thus, addressing new toxin targets or applications typically requires engineering additional strains or designing multi-strain or multi-species microbial consortia (MSMCs).

MSMCs are being explored for live bacterial therapeutics, utilizing individual strains that are either engineered or selected to perform distinct or complementary functions. However, the development of MSMC formulations face several significant technical barriers, including competitive resource use, ecological instability, and unpredictable inter-strain relationships, which can severely hinder reliability and make it difficult to balance host colonization without triggering dysbiosis. Additionally, batch-to-batch variation and multi-strain assembly challenges pose major barriers to manufacturing and regulatory requirements.

Both single-strain or multi-strain approaches present significant drawbacks that prevent efficient scalability or easy adaptability for addressing the diversity of toxins that contribute to chronic disease. This gap is critical, as chronic low-level exposure to dietary and water-borne toxins contribute to inflammation, metabolic dysfunction, cardiovascular disease, cancer, and neurodegenerative disorders. Although potential policy changes may eventually redefine toxin classifications and permissible levels in food and water, their impact will be delayed due necessary industry and supply chain adjustments. Consequently, there remains an urgent, unmet need for innovative technologies that mitigate the health risks associated with these substances.

Purpose and Goals

Given the critical and growing role of biomanufacturing, live microbial therapeutics, and holistic "food as medicine" interventions, the timing is optimal for small innovative companies to spearhead breakthroughs in universal synthetic biology platforms. ARPA-H seeks bold, high-impact solutions that have the potential to transform human health and adjacent sectors by introducing new, programmable functionality in engineered microbes.

The purpose of this topic area is to catalyze the development of a universal, "plug-and-play" synthetic biology platform that enables next-generation microbial chassis capable of performing a broad array of programmable functions. While this solicitation primarily uses toxin removal as a proof-of-concept in relation to chronic disease management, the platform is intended to be adaptable to a range of challenges across industries such as environmental remediation, biomanufacturing, agriculture, holistic medicine, and therapeutic discovery. The broader goal is to create a stable, reliable, and easily reprogrammable microbial platform that demonstrates potential for cross-sector impact beyond the initial use case.

Despite growing evidence supporting the potential of engineered microbes in these roles, current solutions often lack scalability, modularity, and the ability to perform multiple, complex functionalities simultaneously. Small businesses, with their agility and capacity to rapidly integrate disruptive technological advances, are uniquely suited to bridge this innovation gap and validate the feasibility of a universal, programmable, co-expression-capable microbial chassis.

Projects may leverage previously established microbial functionalities for relevant targets, provided that the approach demonstrates a significant advancement towards a universal, multifunctional platform as described in the deliverable requirements.

Requirements Supported (In-Scope)

Platforms must focus on two of the three categories below, propose two toxins to focus on per selected category, and be supported by evidence for chronic disease relevance in the proposals:

- Category 1 Food-based: selection of specific toxic metabolites or food additives (e.g. oxalate, nitrates, or nitrites).
- Category 2 Heavy metals: must select arsenic, lead, cadmium, or mercury with no off-target effects to metals such as (sodium, potassium, magnesium, and calcium).
- Category 3 Chemical contaminants: selection of specific plastics, pesticides, or chemical aerosols (e.g. benzene or formaldehyde).

- Selected topics and proposed targets should be focused on toxin removal at relevant United States Food and Drug Administration (FDA) action levels, toxicological references or clinically relevant values.
- Engineered microbial strains must convert, sequester, or secrete molecules to detoxify, neutralize, or transform the target compounds, making them inert or yielding positive health benefits.
- Solutions must demonstrate simultaneous removal of at least two independent targets within a single engineered strain (in Phase II), without imposing a metabolic burden that decreases productivity or growth rate per target below the baseline for single-function strains. Offerors

must also provide a plan to assess the biosafety of the developed strains and kill switch mechanisms both during human use and outside the human body.

- Solutions that utilize an existing engineered parental strain, chassis, or bacterial system that has previously demonstrated the removal of a toxin(s) aligned with any of the categories above may count that function as fulfilling a corresponding target requirement for this topic. For example, a strain already engineered to remove a specific metabolic toxin satisfies one of the four toxin requirements. However, proposals must clearly articulate how the platform builds upon, adapts, or substantially advances beyond prior work to achieve the universality, modularity, and programmability goals outlined herein. The intent is to enable offerors with strong foundations to accelerate platform development, while avoiding incremental improvements or repackaging of established capabilities as the primary innovation.

Out-of-Scope Requirements

- Solutions that do not focus on human use applications such as probiotics or live bacterial therapeutics.
- Incremental improvements to existing platforms and strains, or minor modifications to commercially available solutions will not be considered responsive.
- Solutions targeting pathogens (e.g., bacteria, fungi, parasites, viruses) or not aligned with the mitigation of toxins per the three categories.
- Concepts that do not advance the universality or modularity of the plug-and-play platform by solely focusing on one category rather than two (see first bullet of *Requirements Supported*).

Metrics and Milestones

Phase I Activities: Deliverables will vary by approach, targets and type of data being collected. Offerors must propose both qualitative and quantitative success metrics aligned with their platforms. Minimum metrics and deliverables include:

- Selection of a specific single-strain chassis with a simpler metabolic network, designed for universal reprogramming and tailored to the proposed application areas.
- Documentation of platform design, including strain characterization, modularity, scalability, programmability, biosynthetic pathway engineering, and relevance to the proposed proof-of-concept health applications (as outlined in *Requirements Supported*).
- In both standard and simulated fluids (e.g., simulated gastric/intestinal fluid, food/water matrices), demonstrate the following in three independent biological preparations (i.e., three separate transformation and culture batches):
    - For each toxin (targeted individually in two separate engineered strains), demonstrate ≥75% removal within 3 hours at regulatory or clinically relevant concentrations. Include appropriate controls (parental strain, comparators).
    - For each toxin, show ≥20% higher toxin removal rate and ≤10% reduction in growth rate compared to the engineered parental strain, with ≤15% variation across replicates.
    - Demonstrate plug-and-play gene integration for toxin removal, achieving ≥90% transformation efficiency per batch.

    - Assess genetic stability by serially passaging each engineered strain for 20 days and show that ≥80% of cells retain the engineered function and detoxification activity at the end of the period.
- Submission of Phase II plan based on insights and technology development from Phase I activities.
- Note: A critical deliverable for Phase I is a microbial chassis with a simplified metabolic network, demonstrated to remove two toxins (in two separate strains, each targeting a single toxin) using a plug-and-play design. The remaining two toxin targets may be demonstrated for microbial removal using modifications of a parental strain.

Phase II Activities: These are deliverables that are expected in a follow-on Phase II. These are included solely to guide proposal development for Phase I by providing greater context into potential activities in a future Phase II.

- Demonstration of a universal, single-strain chassis with a simplified metabolic network, capable of multiplexed reprogramming and tailored to the proposed application areas.
- Comprehensive documentation of platform advancement, including updated strain characterization, modularity, scalability, programmability, biosynthetic pathway engineering, and expanded relevance to health and environmental applications (as outlined in Requirements Supported).
- In both standard and simulated fluids (e.g., simulated gastric/intestinal fluid, food/water matrices), demonstrate the following in three independent biological preparations (i.e., three separate transformation and culture batches):
    - For each toxin (single-plex, tested individually), demonstrate ≥90% removal within 3 hours at regulatory or clinically relevant concentrations. Include appropriate controls (parental strain, comparators).
    - In simulated fluids, confirm ≤10% change in non-target molecules (off-target effects) using liquid chromatography-mass spectrometry (LC-MS) or equivalent analytical methods.
    - For two-plex (multiplexed) strains, demonstrate ≥85% simultaneous removal of two selected toxins within 3 hours at regulatory or clinically relevant concentrations, with ≤15% variation across replicates compared to single-plex strains.
    - For two-plex strains, show ≤10% reduction in growth rate compared to single-plex strains in simulated fluids.
    - Demonstrate plug-and-play, multiplex gene integration for simultaneous two-toxin removal, achieving ≥90% transformation efficiency per batch, for each toxin category addressed.
    - Assess genetic stability by serially passaging each engineered strain for 20 days and show that ≥80% of cells retain the engineered function and detoxification activity at the end of the period.
- Submission of a commercialization and scale-up plan based on insights and technology development from Phase II activities.
- Note: A critical deliverable for Phase II is a universal microbial chassis with a simplified metabolic network, demonstrated to achieve robust, simultaneous removal of two toxins in a single strain using a plug-and-play, multiplexed design. Offerors may include additional metrics and deliverables that will advance their technologies to achieve their commercialization goals. Examples are not limited to expanded safety and efficacy testing

in small animal models, expansion of multiplexable capabilities, or additional two-plex toxin removal capabilities beyond the four initial toxins.

Topic 4: *Breaking Ground: The First Curative, Durable, Non-Surgical Therapy for Endometriosis*	
Anticipated Awards	2
Anticipated Budget	$600k (Phase I), $3.5M (Phase II)
Anticipated Timeline	12 months (Phase I), 24-36 months (Phase II)
Type	SBIR and STTR
Eligible Phases	Phase I, Direct-to-Phase II, or Fast-Track

Background / Introduction

The SBIR topic is designed to identify solutions that can commercialize the first-of-its-kind, non-surgical, and curative therapy for endometriosis. Endometriosis (endo) is one of the most significant women's health crises of our time, affecting 10-15% of women globally with an estimated 200 million cases worldwide, including more than 10 million in the U.S. alone. Endometriosis is an incurable, inflammatory, and life-disrupting chronic disease that causes lesions across 11 body systems, leading to organ adhesion, pain, infertility, disability, and damage to organ function. Unfortunately, the average woman waits 8-10 years before receiving an initial diagnosis and treatment of symptoms, and no cures are currently available. Endometriosis is also a causative factor in 30-50% of infertility cases and contributes significantly to the reality that 1 in 6 individuals struggle to conceive.

Despite its high prevalence, endometriosis is notoriously difficult to treat because it mimics other medical conditions and impacts a broad array of organ systems. A lack of provider awareness and training means that endometriosis symptoms are often missed thus preventing patients from receiving even symptomatic relief through prescription drugs or excision surgery. Currently, there are no treatments that can slow, shrink, stop, or prevent endometriosis progression. Hormonal medications (e.g., birth control, Lupron, Orilissa, Myfembree) only briefly address symptoms in the limited number of patients who are responsive but often cause substantial side effects. Many of these drugs cannot be taken for longer than 1-2 years due to the effects of hormonal suppression on the rest of the body (e.g., osteoporosis, chemically induced menopause, etc.) causing a poor safety profile.

Surgical excision of endometriosis is the gold standard yet there are few properly trained experts, and lesions can be difficult to distinguish from other tissues. Further, reimbursement for lengthy and complex surgery is insufficient making it difficult to justify.

There is an urgent, unmet need for effective and lasting endometriosis therapeutics as current disease management focuses exclusively on symptom relief. Through this topic, ARPA-H strives to break down the therapeutic barriers for endometriosis by identifying and advancing a curative, non-surgical therapy that is effective, accessible, and ready for successful commercialization.

Purpose and Goals

The SBIR topic aims to advance progress in the endometriosis field by identifying and commercializing therapeutics that address the root cause of the disease. Proposers are expected to develop a first-of-its-kind, non-surgical therapy capable of reducing the size of endometriosis lesions, deactivating endometriosis tissue, and/or preventing regrowth thereby ideally achieving curative outcomes. Additionally, the treatment must be specific, meaning it accurately locates and addresses endometriosis lesions without causing adverse effects elsewhere in the body.

Proposers must include quantitative metrics detailing the targeted reduction in lesion size along with a qualitative explanation of how this approach is expected to deliver a lasting therapeutic benefit. For instance, proposers can consider measuring the size of endometriomas, which are readily identifiable on ultrasound or MRI, prior to and post treatment. Proposers must clearly specify the route of therapy administration and required number of doses to ensure efficacy without imposing an unnecessary patient burden. Lastly, proposers need to outline the regulatory pathway, including defined steps to reach key regulatory milestones and a comprehensive plan for reimbursement strategies to ensure broad patient access.

Requirements Supported (In-Scope)

Solutions that are in scope include therapy that does not require surgery and can be administered non-invasively to the body (e.g., oral, topical, intravenous, subcutaneous, etc.). In scope solutions may include but are not limited to novel nanoparticles that target only lesions, medications that specifically suppress estrogen production in a targeted manner exclusively in endometriosis lesions, therapeutics that shrink lesions, etc. Some examples of treatments may include inserting (subcutaneously, via insulin-like pump, etc.) or ingesting endo-suppressing, drug-embedded seeds that localize to and act directly on endometriosis lesions. Since endometriosis is also characterized by formation of dense fibrosis, therapeutics may involve reducing inflammation caused by the dynamic fibrotic process or physiologically reshaping this tissue remodeling caused by fibrosis to ameliorate impacts of the disease and deactivate endometriosis lesions.

Out-of-Scope Requirements

ARPA-H will consider the following solutions to be out of scope for this topic: any invasive surgical procedures; general hormonal treatments (including GnRH agonists, GnRH antagonists, and birth control) that put women into premature menopause or negatively impact the body's function; drugs that can only be taken for a limited time (e.g., due to causing irreversible systemic damage); or treatments that do not address the root cause of this disease. The ideal solution will solve the underlying disease process of endometriosis by blocking, deactivating, or shrinking endometriosis lesions. ARPA-H is not interested in solutions that only address symptoms.

Metrics and Milestones

Phase I Activities

1. Demonstrating proof-of-concept *in vitro* (e.g., cell lines, organoids, *ex vivo* endometriosis lesions through surgical dissection and culturing of endometriosis lesions, etc.) or *in vivo* (e.g., rodent model, etc.) for endometriosis lesion dismantling technology with a report outlining these findings. The primary metric should be the percentage reduction in

endometriotic lesion mass or area, supported by additional measures such as selectivity index, cell viability or toxicity, and biomarker release assays. Examples of what performers should showcase include the following:

a. For *in vitro* or *in vivo*:
    i. At least a 50% reduction in endometriosis lesions
    ii. Quantitative assay of biomarker release for measurement of breakdown products that are specific to endo-affected tissues
b. For *in vitro:*
    i. At least >80% cell viability by live/dead assay or MTT cell viability assay
c. For *in vivo*:
    i. Toxicity study showing 100% survival, body weight maintenance, and no observable clinical or behavioral changes

2. Validation of delivery method reaching appropriate endometriosis targets with a report showing data and results. Examples of what performers should showcase include the following:
    a. Target site concentration/localization as seen by percentage of administered dose found in target tissue
    b. Specificity/selectivity index on ratio of getting in target tissue vs. affected-target tissues, indicating minimal off target distribution
3. Regulatory pathway chosen and initial collection of data to support a regulatory submission.

Phase II Activities

At a minimum, the solution must meet the requirements from Phase I and accomplish Phase II as detailed below. The primary metrics should be demonstration of efficacy, safety, and toxicology with the expectation of submitting the therapeutic for regulatory authorization. Phase II should fulfill the following:

1. Demonstration of efficacy in an advanced *in vivo* model to support a regulatory submission with a report on the innovation that shows data and results including:
    a. *In vivo* efficacy in a disease-relevant advanced animal model suitable for an FDA submission (at least a 60% or more reduction in lesions)
    b. Durability of effect that includes sustained reduction of lesions (i.e., no increase in size from a visualized decrease over a specified time) and symptom improvement
    c. Confirmation of precise delivery to endometriosis lesions and therapeutic effect on disease progression with no off-target consequences
2. Demonstration of safety and toxicology in advanced *in vivo* models with a report showing data and results including:
    a. Expanded safety studies with more comprehensive toxicity and safety data with GLP-combination studies if planning an IND submission
    b. Pharmacokinetics/pharmacodynamics (PK/PD) to understand dosing, systemic exposure, and mechanism of action
3. Submission to FDA for regulatory authorization (e.g., IND or IDE) or FDA clearance at the end of Phase II with documentation of regulatory submissions and authorizations.

4. If FDA authorization (e.g., IND or IDE) is obtained, provide a first-in-human safety demonstration of the innovation with a report showing data and results.

Topic 5: *ARPA-H Lineage Topic*	
Anticipated Awards	2
Anticipated Budget	$3.5M (Phase II)
Anticipated Timeline	24-36 months (Phase II)
Type	SBIR and STTR
Eligible Phases	Direct-to-Phase II

Background / Introduction

ARPA-H seeks to ensure the technologies developed through its R&D efforts are put into practice and develop into products that improve the health of all Americans. ARPA-H's programs, however, are focused on developing and demonstrating moonshot technologies and may end before a commercially viable product is complete. Additionally, they do not necessarily support performers using the technology for secondary or intermediate applications.

This topic advances the ARPA-H's mission by helping small businesses that are developing ARPA-H funded technologies to cross the gap between early demonstration and real-world deployment. Selected companies will receive funding and access to commercialization support services to transition their R&D into viable products, bring them to market, navigate regulatory challenges, and become financially self-sufficient post-government funding.

Purpose and Goals

This topic supports the advancement, commercialization, and translation of technologies that originated from ARPA-H funded efforts. It is intended to help small businesses and startups develop viable products based on these technologies. ARPA-H's goal is to give small businesses an off-ramp to finish developing their technology/product, explore secondary or interim applications of the technology, and time to achieve self-sufficiency.

In addition to being eligible small businesses, proposers must be previous or current performers or sub-contractors on an ARPA-H funded R&D effort. Proposers may also be finalists in ARPA-H funded or sponsored challenges, spin-outs from a performer/sub-contractor (e.g. a startup created by an academic lab) or a small business partnering with a performer team to commercialize their technology. In all cases, the product being developed must be based on a technology created during an ARPA-H R&D effort.

These Direct-to-Phase II projects should mature promising solutions that already demonstrated initial technical feasibility during an ARPA-H R&D effort. Projects may also develop products for secondary applications of the technology that were not the primary focus of the original funded effort, or that offer interim applications for the technology or a portion of the technology being developed. The scope of projects must be non-duplicative with existing ARPA-H funded efforts.

Requirements Supported (In-Scope)

Proposed work is considered in-scope when it directly builds on prior ARPA-H-funded research (including technologies advanced through ARPA-H funded or sponsored challenges), and focuses

on further developing, adapting, scaling, or commercializing technologies that have already demonstrated initial feasibility. In-scope efforts should leverage the foundational work created through an ARPA-H program/project and clearly describe (1) their commercialization/transition strategy, (2) the additional research and development needed for the intended healthcare applications, and (3) how the research enables their commercialization strategy..

In-Scope efforts include clinical studies to generate evidence for regulatory submissions or clinical adoption, pilots with potential users or commercial partners, prototype refinement, or other R&D tasks that also address significant commercialization challenges.

Activities below are considered in-scope for this topic:

- Intermediate applications of technology (e.g., using technology to solve near-term problems before the final form is complete)
- Secondary applications of technology (e.g., not the primary focus of the program)
- Products for the primary intended application of the technology
- Pilots to improve design, test user acceptance, or generate data for commercial adoption
- Finalization of prototype design and related manufacturing tasks
- Clinical/Pre-Clinical studies to generate evidence for regulatory submissions
- Address technical challenges necessary for product viability

Out-of-Scope Requirements

Work is considered out of scope if it:

- Does not build on an ARPA-H funded technology/effort
- Is not done by an ARPA-H funded performer, sub-contractor, spin-out, or transition partner without a licensing agreement for the ARPA-H funded IP
- Does not involve meaningful progress towards a viable product
- Does not have an initial proof-of-concept
- Is an incremental improvement over state-of-the-art
- Does not address a specific need or problem
- Has no viable path to market
- Does not address barriers to commercialization/transition

Metrics and Milestones

Phase II activities must show clear progress toward transitioning the technology from an early prototype to a version that is ready for commercial deployment. All activities should be structured around measurable milestones that demonstrate technical progress, regulatory readiness, manufacturing capability, and/or commercial potential. Because each project and technology is unique, companies should propose their own milestones with clear metrics to measure progress. This should include the final end-state and intermediate milestones.

Topic 6: *Rapid Comprehensive Diagnostic Test for Multi-System Autoimmune Disease*	
Anticipated Awards	2
Anticipated Budget	$3.5M (Phase II)
Anticipated Timeline	24-36 months (Phase II)
Type	SBIR and STTR
Eligible Phases	Phase I, Direct-to-Phase II , or Fast-Track

Background / Introduction

The goal of this SBIR topic is to drive the development of new diagnostic assays that would help physicians assess the multi-system nature of autoimmune disease and thus better guide care for these patients.

Autoimmune disease is a major public health problem, with >24 million Americans impacted and $100-125 billion annual cost to the healthcare system. Approximately 65% of these patients have one autoimmune disease, 24% have two autoimmune diseases, 8% have three autoimmune diseases, and 2% have four or more autoimmune diseases. Autoimmune disease is often a systems process whose tissue-specific manifestations in certain patient populations can be difficult and time-consuming to diagnose. Specifically, patients that experience diverse and seemingly unpredictable multi-organ autoimmune disease experience long delays in obtaining appropriate treatment planning and care delivery, with current diagnostic tests being focused on assessing the presence of autoantibodies or defining general patterns of immune activation. These existing diagnostic modalities are by their nature often inconclusive, lag behind disease manifestations, and expensive.

Given this state of diagnostic technology for autoimmune diseases, this topic will likely either support a quick tech-to-market win or provide an investigational new device (IND)-enabling technology for a new program.

Purpose and Goals

The overall purpose of this SBIR topic is to spur the development of novel, rapid diagnostic assays for multi-system autoimmune disease, which represents an unmet healthcare need. Moreover, in its ideal embodiment this diagnostic test might allow typical primary care physicians to diagnose and predict tissue-specific autoimmune disease manifestations, thereby streamlining referral of the patient to a specialist. This goal is made more feasible by recent technological developments including the ability to detect tissue-specific signatures of immune-mediated stress by assessing circulating cells and/or tissue-specific molecular products.

Requirements Supported (In-Scope)

Specific requirements that would be supported under this topic area include:

1) Tissue specificity and ease of use: ability to define emerging immune/inflammatory activation in specific tissues/organs based on easy to obtain patient samples or data from wearable sensors
2) Speed: ability to obtain diagnostic/prognostic data within a week of sampling, ideally more quickly (i.e., point of care)
3) Low cost: diagnostic test should be at most 50% of the cost of current comprehensive autoantibody tests and inflammatory mediator panels, which can cost up to $3000

Out-of-Scope

The following would be considered not responsive under this topic area:

1. Exploratory studies on autoimmune disease
2. Work focused on the development of diagnostic tests lacking the ability to suggest specific affected tissues/organs
3. Diagnostic approaches that would be too complex to be performed in typical physician office/diagnostic laboratory settings and/or that could not realistically reach the cost target within program timeframes
4. Therapeutic approaches to autoimmune disease
5. Work targeting diseases associated with immune deficiencies

Metrics and Milestones

Phase I (18 months)

- Detect and differentiate between immune/inflammatory stress signatures in at least 2 tissues/organs of relevance to multi-system autoimmune disease
- Detect time to actionable diagnostic results within 4 weeks of sample acquisition
- Cost for prototype assay at $3000 or less
- Draft regulatory and reimbursement plan

Phase II (18 months)

- Detect and differentiate between immune/inflammatory stress signatures in at least 4 tissues of relevance to multi-system autoimmune disease, or differentiate between at least 2 distinct manifestations of autoimmune disease in 2 tissues/organs
- Time to actionable diagnostic test results within 2 weeks at midpoint of funding and within 1 week or less by completion
- Cost for prototype assay $1500 or less
- Pre-IND submission
- Regulatory and reimbursement plan
- Market survey and stakeholder engagement

Topic 7: *Virtual Human Brain for the Development of Neurosurgical Robotics*	
Anticipated Awards	2
Anticipated Budget	$600k (Phase I), $3.5M (Phase II)
Anticipated Timeline	3-5 years
Type	SBIR and STTR
Eligible Phases	Phase I, Direct-to-Phase II, or Fast-Track

Background / Introduction

There is insufficient access to neurosurgeons and neurosurgical facilities to meet the needs of Americans in a timely manner. Studies have shown that pre-operative wait time for elective neurosurgeries are negatively correlated with survival and/or positive outcomes. Surgical treatment options for traumatic brain injury often have very short therapeutic windows due to rapid fibrosis, necrosis, and neuron die back, making it logistically challenging to get patients to often distant specialized neurosurgical centers in time. In addition, even when neurosurgical treatments are available and performed in a timely manner, a relatively high level of adverse events from surgery still occur in part due to insufficiently high resolution or difficulty interpreting pre-operative and real-time information at the surgical scene. Finally, becoming a skilled neurosurgeon takes many years of training. As regenerative medicine matures and demographics shift toward an aging population continue, both the demand for and the number of neurosurgical treatment options will grow in proportion to the available surgeons. AI-assisted intracranial microsurgery could solve all these problems.

The goal of this SBIR is to take a step toward derisking future automated neurosurgery platforms. Namely, this SBIR aims to develop a simulated human brain that accurately reflects the anatomical, physical, and imaging properties of a real brain.

The virtual brain would provide a platform with many uses. These include widespread access to brain surgery (when combined with autonomous surgical platforms), training in neurosurgical procedures (existing and new), and, most significantly, intraoperative real-time AI-assistance to enhance neurosurgeons' perception, dexterity, and augmented cognitive abilities. These advances would in the future increase accessibility and mitigate risks for any brain-related surgical procedures.

For all indications, there would be a decrease in:

- invasiveness
- surgery times
- risk of complications
- patient convalescence times

Overall, development of a virtual brain would be an important technical achievement on the path to improving the accessibility, precision, and scalability of neurosurgery – alleviating current and future bottlenecks and enabling better outcomes for patients.

Purpose and Goals

This topic area aims to take a first step toward AI-assisted intracranial microsurgery, which will ameliorate patient outcomes as described in point 5 above, by creating a high-resolution, physically and anatomically accurate virtual human brain.

While robotic assistance has become commonplace in neurosurgery, these systems predominantly function as stereotactic guidance tools, essentially serving as robotic versions of traditional frame-based methods like the Leksell frame. No existing neurosurgical robot currently offers surgeons enhanced visual perception, refined dexterity, and augmented cognitive capabilities.

The unique challenges of neurosurgery such as sparing delicate neural structures, handling deformable brain tissue, and adapting to dynamic intraoperative conditions highlight a critical unmet need for advanced robotic systems that can integrate real-time imaging, precision manipulation, and autonomous cognitive assistance. Addressing this gap holds significant promise for revolutionizing neurosurgical outcomes and advancing the broader field of robotic-assisted surgery.

Additionally, the recent device-based ENRICH study has shown that surgical management of intracerebral hemorrhage (ICH), if delivered in a timely manner, can offer significantly better outcomes than medical management alone. However, much of rural America lacks adequate neurosurgical care, leaving many patients without timely treatment options. Due to latency issues across long distances, teleoperation of robotic systems is infeasible. Therefore, surgical automation presents an opportunity to provide critical care to underserved populations who would otherwise have no viable treatment options.

The absence of platforms, tools, and datasets hinders progress toward automated micro-neurosurgery. To develop these, we need the ability to train machine learning models on large numbers of simulations, which requires a virtual brain with meninges and skull along with virtual tools, performing procedures that can incorporate adverse events such as bleeding and pressure changes. This first training stage would be followed by further training in the real world on pre-clinical models of similar size, and finally in neurosurgeon-supervised clinical trials.

The landmark ENRICH clinical trial, which is a device-assisted minimally invasive procedure for intracerebral hemorrhage applied to a first cohort of 300 patients, is driven by NICO Corp, a small business, providing precedence for innovation in this space by small enterprises. In addition, given the tight foci of mid-to-large surgery-related businesses, and their fear of regulatory restrictions, innovation is currently unlikely to take place anywhere but in small businesses.

Requirements Supported (In-Scope)

- Accurately simulate anatomical, physical, and imaging properties of a real human brain down to the micro level (50-micron scale). All proposals should aim to include, but need not be limited to, all the following properties:
    - anatomical (e.g. cell/area/tissue structures, fiber tracts, vasculature);

    - physical (elastic modulus, viscoelasticity, density, hydraulic permeability, surface tension, compressibility, anisotropy, thermal conductivity);
    - imaging (light, OCT, ultrasound, MRI).
- Along with the virtual brain, develop algorithms for virtual tools and procedures
- Achieve a platform for training AI on surgical interventions
- Simulate intracranial surgical procedures that require a craniotomy, keyhole craniotomy, or burr hole craniotomy

Out-of-Scope

- A focus on other parts of the body
- Simulation of any endovascular procedures
- A virtual brain that does not embody the physical, anatomical, and imaging properties of a real human brain
- Other types of robotics (non-surgical, non-relevant to brain surgery because of size, degrees of freedom, etc.)
- Macro whole brain simulation (with resolutions >50 microns)

Metrics and Milestones

Tentative deliverables by phase (for FastTrack):

The simulated brain, along with simulated tools, would be the initial MVP for this SBIR, and would be developed in a FastTrack Phase 1. Translation of AI-driven procedures to real-world testing would occur in Phase 2, using pre-clinical models with adjustments and validation, prior to commercialization.

Phase 1:

- Simulation of vessels, circulating blood itself, tissue types (soft, fibrous, etc.), skull, and meninges.
    - Deformation error (RMSE) compared to 3D segmentation from stereo camera of a large mammal cadaver brain: < 0.05 mm
    - Simulation of adverse events: bleeds (location accuracy: ≤ 0.05 mm RMSE. Bleeding Rate accuracy: <10% error. Bleed Onset Timing error: < 1 sec.)
    - Human surgeon evaluation: Perceived realism: > 4.0 out of 5.0 on Likert
    - Realtime simulation of 30 fps.
- Simulation of camera, stereo camera and ultrasound.
    - Pixel accuracy: SSIM > 0.9, PSNR > 30 dB
    - Stereo Camera Depth Map Accuracy (RMSE): < 0.05 mm
    - Ultrasound/OCT segmentation Anatomical Accuracy: dice coefficient ≥ 0.85
- Simulation of an existing robot
    - Control over parameters such as joint friction
    - Kinematic accuracy: End-effector RMSE: < 0.05 mm, Orientation Error: < 0.5°
- Autonomous Tumor Resection/ICH evac with robotic policy in simulation
    - Task completion success rate: > 99%

- Faster than human
- Force control precision: Especially in soft tissue manipulation (< ±0.1 N)
- Adverse event rate: e.g., simulated hemorrhage rate < 1%

Phase 2:

- Validation that an existing tool, simulated in Phase 1, can perform a real-world procedure based on policies learned in the virtual human brain (real world models can be live postmortem human brains, human brain tissue, or animal models). The real-world procedures can include but are not limited to: tumor resection, clipping or coiling blood vessels for aneurysms, clot removal and pressure relief in TBI, resections for drug-resistant epilepsy, hydrocephalus shunting, vascular malformations, deep brain stimulation, infections or abscesses that require surgical intervention, ischemic or hemorrhagic strokes.
  - Performance should be on par with that of human surgeons (precision, speed, complication rate, and can depend on the real-world model used).
- Design and simulate a novel robot prototype
  - With an expected production cost: < $100,000
  - Setup time: OR-ready (target: < 30 minutes)
  - Footprint of system in OR (target: < 1.5 m^2)
  - Portability: Weight and ease of transport (target: fits in one OR cart)
  - components in the sterile field are sterilizable: > 80%
  - must outperform existing robots in precision and task versatility
- Policies that are capable of autonomous tumor resection (priority) or ICH evac:
- Tumor Resection
  - < 1mm margin of removed tissue with <.2 mm margin of error vs planned resection
  - <1% major bleed rate
  - > 90% Extent of resection
  - Anatomical structure preservation: % of surrounding tissue preserved (> 95%)
  - Faster than human
- ICH evac
  - Ex-vivo demonstration of automated ICH evac (large mammal cadaver)
- Task completion success rate: > 90%
- Faster than human
- Anatomical structure preservation: % of surrounding tissue preserved (> 95%)
- > 80% evacuated
- < 1mm target accuracy
  - In-vivo demonstration on animal model
- Success rate: >90%
- Recovery rate: > 90%
- Faster than human
- < 5% rebleed rate
- Simulation generation AI framework
  - From image/video to simulation
- Time: < 24 hours
- GPU inference cost: < $1,000

- Simulation accuracy metrics on par with Phase 1 goals
  - Time taken to update a new simulation
- Time: < 1 minute
- GPU inference cost: < $10
- Simulation accuracy metrics on par with Phase 1 goals
- Novel surgical robot generation AI
  - From text + simulation to a novel robot design
- Time: < 24 hours
- Robot performance in simulation exceeds metrics for other robots
- Plan to distribute and commercialize the platform, as well as consideration for how and when the FDA will become engaged.