[DRAFT] PROGRAM SOLICITATION
Sections 1, 3, 9

47QFCA24R0036

SBIR/STTR Phase I and II

in support of:

ADVANCED RESEARCH PROJECTS AGENCY FOR HEALTH (ARPA-H)

This is a Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) Solicitation in accordance with SBIR/STTR Policy Directive (May 3, 2023).

Issued by:
U.S General Services Administration (GSA)
Federal Acquisition Service (FAS)
Assisted Acquisition Services (AAS) Innovation

(June X, 2024)

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IMPORTANT

Please read the entire solicitation carefully prior to submitting questions and/or a proposal.

Only Procurement contracts will be awarded resulting from this solicitation; Grants will not be awarded.

ARPA-H Webinar: All potential offerors are encouraged to attend the APRA-H Webinar for this solicitation. The webinar will highlight important aspects of the SBIR/STTR Program, ARPA-H's mission, Topic Areas, and important elements of this solicitation. The Webinar is being held on **TBD.** Please see the webinar specific announcement for more details.

Deadline for Questions: Solicitation questions must be received by **TBD .** All questions shall be submitted via email to GSA-ARPA-H-SBIR@gsa.gov and in accordance with Section **X** of this Solicitation.

Deadline for Receipt: All written proposals shall be received by **TBD**. The offeror shall submit its written proposal via email to GSA-ARPA-H-SBIR@gsa.gov in accordance with Section **X** of this Solicitation. **Hard copies/Paper proposals will not be accepted.**

All potential offerors, new to the Small Business Administration's SBIR/STTR program, are highly encouraged to read the SBIR/STTR Policy Directive issued by the Small Business Administration with **special attention directed to the inclusion of a new proposal requirements found in Section X – Disclosure of Foreign Relationships.** The SBIR/STTR Policy Directive can be found here: https://www.sbir.gov/sites/default/files/SBA%20SBIR_STTR_POLICY_DIRECTIVE_May2023.pdf

1 Program Description

1.1 Introduction

The U.S. General Services Administration (GSA), Federal Acquisition Service (FAS), Assisted Acquisition Service - Innovation (AAS) in direct support of The Advanced Research Projects Agency for Health (ARPA-H) invites small business concerns (SBCs) to submit innovative research proposals under this Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) Contract Solicitation. The Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs are highly competitive programs that encourage domestic small businesses to engage in Federal Research/Research and Development (R/R&D) with the potential for commercialization. Through a competitive awards-based program, SBIR and STTR enable small businesses to explore their technological potential and provide the incentive to profit from its commercialization. By including qualified small businesses in the nation's R&D arena, high-tech innovation is stimulated, and the United States gains entrepreneurial spirit as it meets its specific research and development needs. Firms with the capability to conduct research and development (R&D) in any of the health-related topic areas described in Section X, and to commercialize the results of that innovative R&D, are encouraged to participate.

This solicitation contains opportunities to submit a proposal under a variety of different Topics, which are summarized in Section X below. AAS in direct support of ARPA-H is under no obligation to fund any proposals or any specific number of proposals in a given topic. It may also elect to fund several or none of the proposed approaches to a given topic. All awards are subject to the availability of funds. The Government is not responsible for any monies expended by the offeror before award of any contract. Only Procurement contracts will be awarded resulting from this solicitation; Grants will not be awarded.

The mission of ARPA-H is to accelerate better health outcomes for everyone by supporting the development of high-impact solutions to society's most challenging health problems. Awardees will develop groundbreaking new ways to tackle health-related challenges through high potential, high-impact biomedical and health research. With a scope spanning the molecular to the societal, ARPA-H seeks SBIR/STTR proposals that aim to rapidly achieve better health outcomes across patient populations, communities, disease, and health conditions, including in support of the Cancer Moonshot. Proposals are expected to use innovative approaches to enable revolutionary advances in science, technology, or systems. Specifically excluded are proposals that represent an evolutionary or incremental advance in the current state of the art. Additionally, proposals directed towards policy changes, traditional education and

training, or center coordination and construction of physical infrastructure are outside the scope of the ARPA-H mission.

1.2 Program Background

The basic design of the ARPA-H SBIR/STTR program is in accordance with the Small Business Administration (SBA) SBIR/STTR Program Policy Directive dated May 3, 2023. This SBIR/STTR solicitation strives to encourage scientific and technical innovation in areas specifically identified by ARPA-H. The potential contributions of the proposed effort are relevant to health outcomes for all Americans. Specifically, ARPA-H's mission is to benefit the health of all Americans by catalyzing health breakthroughs that cannot readily be accomplished through traditional research or commercial activity. The guidelines presented in this solicitation reflect the flexibility provided in the SBIR/STTR Policy Directive to encourage proposals based on scientific and technical approaches most likely to yield results important to ARPA-H and to the private sector.

1.3 Phased Program

1.3.1 SBIR/STTR Phased Program

The SBIR/STTR program consists of three separate phases as detailed below. Note: This solicitation is not accepting Phase III proposals. Please refer to the individual topics above as to which phase is being considered.

Phase I: Feasibility

The objective of Phase I is to determine the scientific or technical feasibility and commercial merit of the proposed research or R&D efforts.

Phase II: Full R/R&D Effort

The objective of Phase II is to further develop the research or R&D efforts initiated in Phase I. If your project has already demonstrated feasibility, you may prepare a Direct-to-Phase II proposal and begin your Federal SBIR/STTR award at Phase II.

Phase III: Commercialization stage without SBIR/STTR funds

Phase III refers to work that derives from, extends, or completes an effort made under prior SBIR/STTR Funding Agreements, but is funded by sources other than the SBIR/STTR programs. Each of the following types of activity constitutes SBIR/STTR Phase III work:

(i) Commercial application of SBIR/STTR funded R/R&D that is financed by non-Federal sources of capital.

(ii) SBIR/STTR derived products or services intended for use by the Federal Government, funded by non-
SBIR/STTR sources of Federal funding.

(iii) Continuation of SBIR/STTR work, funded by non-SBIR/STTR sources of Federal funding including R/R&D. For HHS SBIR/STTR projects, Phase III is primary financed by non-Federal sources of capital.

The competition for SBIR Phase I and Phase II awards satisfies the competition requirements of the Competition in Contracting Act. Therefore, an agency that wishes to fund an SBIR project beyond the Phase II and the project is derived from, extends, or logically concludes efforts performed under prior SBIR funding agreements may award a Phase III contract on a sole source basis.

1.4 ARPA-H Phased Approach

For purposes of this solicitation , the following phased approaches will be used:

1) Phase I Proposals

As part of this solicitation, the Government may award a Phase I contract to an offeror that believes it has a concept that might provide a solution to one of the Topics listed in section X, but has not built a prototype and tested its technical feasibility. The purpose of the Phase I contract will be to determine the scientific or technical feasibility and commercial merit of the proposed research or R&D effort.

2) Direct to Phase II Proposals

As part of this solicitation, the Government may award a Direct to Phase II contract to an offeror whose project has already demonstrated feasibility, but the offeror has not received a Phase I SBIR or STTR award. The offeror can apply for a Direct to Phase II award and bypass Phase I. Offerors applying for Direct to Phase II awards must have **already built a technology prototype and tested its technical feasibility**. The purpose of the Phase II R&D contract will be to test the functional viability of the prototype according to scientific methods and potential for commercial development. Refer to Section X List of Topics for notation of Topics allowing Direct to Phase II proposals.

3) Fast Track Proposals

As part of this solicitation, the Government may award a Fast Track contract to an offeror whose Fast Track proposal may result in an initial award for a Phase I contract with a contractual option that the Government may exercise to continue the effort into Phase II without the need to re-solicit the topic. This mechanism allows for streamlined processes that have the potential to significantly minimize the funding gap between

Phase I and Phase II. However, it shall be noted the Government is not obligated to fund the Phase II contractual option. The awardee may only start performing the Phase II effort unless and until the Government exercises that option.

If a Topic notes that Fast Track proposals will be accepted, a Phase I proposal and a Phase II proposal may be submitted simultaneously. As described in Section X "Proposal Instructions," a Fast Track submission consists of one complete Phase I proposal and one complete Phase II proposal, separately paginated. The Phase I proposal and Phase II proposal will be separately evaluated as set forth in Section X "Technical Evaluation Criteria."

2 CERTIFICATIONS [Placeholder]

3 PROPOSAL PREPARATION AND INSTRUCTIONS

3.1 Introduction

It is important to read and follow the proposal preparation instructions carefully, which are outlined below. Pay special attention to the requirements concerning Human Subjects and use of Vertebrate Animals if your project will encompass either of item.

3.2 Proposal Instructions

A complete Phase I proposal consists of a Technical Proposal (Appendix A) and a Business Proposal (Appendix B).

A complete Phase II proposal consists of a Technical Proposal (Appendix C) and a Business Proposal (Appendix D). Each proposal will be submitted via the application template in the corresponding Appendix.

A complete Fast-Track proposal consists of both a complete Phase I proposal and a separate, complete Phase II proposal. To identify the submission as a Fast Track proposal, check the box marked "Yes," next to the words "Fast Track Proposal" shown on the Phase I and Phase II applications. The Phase I proposal and the Phase II proposal in a Fast Track submission will be evaluated and scored individually. However, if a Phase I proposal is evaluated and found to be unacceptable, the corresponding Phase II Fast Track proposal will not be evaluated.

Please see below for additional proposal submission instructions.

3.3 Human Subjects and Clinical Trials Information Form and Attachments

Appendix A.1. is required for every proposal submission. If your proposal does not involve Human Subjects or Clinical Trials, you must still note this on the form and submit the form. If applicable, Appendix A.2. – Study Record must be attached to Appendix A.1.

- **APPENDIX A.1 — HUMAN SUBJECTS AND CLINICAL TRIALS INFORMATION FORM**

  Instructions to complete this form can be found at:
  https://grants.nih.gov/grants/funding/SBIRContract/ContractAppendixH.1.pdf

- **APPENDIX A.2. — STUDY RECORD, ATTACHMENT TO HUMAN SUBJECTS AND CLINICAL TRIALS INFORMATION FORM**

For SBIR or STTR Phase I and II Technical Proposals, the Human Subjects and Clinical Trials Information form and its attachments (Appendix A.1., and, if applicable, Appendix A.2.) are excluded from Appendix A and are to be submitted as a separate document from the Technical Proposal. Ensure proposal submission specifically identifies the Human Subjects and Clinical Trials Information Form and its attachments, separate from the Technical Proposal.

3.4 Business Proposal

The award will result in a Firm-Fixed Price (FFP) contract type. The offeror shall fully support all proposed costs/prices. The offeror's proposal is presumed to represent the offeror's best efforts in response to the solicitation. Any inconsistency, whether real or apparent, between promised performance and cost/price, shall be explained in the proposal. The Business Proposal includes the Pricing Proposal and Summary of Related Activities, as well as the following:

1. SBIR Application VCOC Certification, if applicable. See SECTION X – PROPOSAL FUNDAMENTALS to determine if this applies to your organization. If applicable, please complete this form in Appendix B - Business Proposal.

2. Proof of Registration in the SBA Company Registry is required at proposal submission. Refer to SECTION X – PROPOSAL FUNDAMENTALS for directions. All applicants to the SBIR and STTR programs are required to register at the SBA Company Registry prior to proposal submission and attach proof of registration to the Business Proposal.

3. The offeror shall provide a statement that it has been registered in ASSIST and that all information in ASSIST is up to date (assist.gsa.gov/assist-web/registration/contractor/search).

3.4.1 Content of the Business Proposal (Item Two)

Complete the Pricing Item in the format shown in the Pricing Proposal. Some items in the Pricing Proposal may not apply to the proposed project. If that is the case, there is no need to provide information on each and every item. What matters is that enough information be provided to allow us to understand how you plan to use the requested funds if a contract is awarded.

- List all key personnel by name as well as by number of hours dedicated to the project as direct labor.
- While special tooling and test equipment and material cost may be included under Phase I, the inclusion of equipment and material will be carefully reviewed relative to need and appropriateness for the work proposed. The purchase of special tooling and test equipment must, in the opinion of the AAS Contracting Officer, be advantageous to the Government and should be related directly to the specific topic. These may include such items as innovative instrumentation or automatic test equipment. Title to property furnished by the Government or acquired with Government funds will be vested with the HHS Component; unless it is determined that transfer of title to the contractor would be more cost effective than recovery of the equipment by the HHS Component.
- Cost for travel funds must be justified and related to the needs of the project. Describe reason for travel, location of travel, number of travelers, and number of nights of lodging in the Description fields in Appendix C.
- Cost sharing is permitted for proposals under this solicitation; however, cost sharing is not required, nor will it be an evaluation factor in the consideration of a Phase I proposal.
- All subcontractor costs and consultant costs must be detailed at the same level as prime contractor costs in regard to labor, travel, equipment, etc. Provide detailed substantiation of subcontractor costs in your cost proposal. Enter this information in the Explanatory Material section of the on-line cost proposal form.
- **Policy on Threshold for Negotiation of General and Administrative (G&A)/Indirect Costs (IDC) Rates for SBIR proposals** – SBIR offerors who propose a G&A/IDC rate of 40 percent of total direct costs or less will not be required to negotiate Final Indirect Rates with the NIH Division of Financial Advisory Services (DFAS), or other cognizant auditing agency. However, awarding AAS Contracting Officers may require offerors to document how they calculated their IDC rate(s) in order to determine that these costs are fair and reasonable. Furthermore, the

Division of Financial Advisory Services (DFAS) will retain the authority to require well-documented proposals for G&A/IDC rates on an *ad hoc* basis. If the SBC has a currently effective negotiated indirect cost rate(s) with a Federal agency, such rate(s) shall be used when calculating proposed G&A/IDC costs for a proposal. (However, the rate(s) must be adjusted for IR&D expenses, which are not allowable under HHS awards.)

SBCs are reminded that only actual G&A/IDC costs may be charged to projects. If awarded at a rate of 40 percent or less of total direct costs, the rate used to charge actual G&A/ID costs to projects cannot exceed the awarded rate unless the SBC negotiates an indirect cost rate(s) with DFAS.

- Offerors submitting proposals may include the amount of up to $6,500 per year for a Phase I and up to $50,000 per Phase II project (across all years) for technical assistance as discussed and outlined in Section X State Assistance and Technical Assistance of SECTION X – PROPOSAL FUNDAMENTALS of the solicitation. Include a detailed description of the technical or business assistance that your vendor/s will provide, including the name of the vendor/s and the expected benefits and results of the technical or business assistance provided. A letter of support from the vendor describing their qualifications and services to be provided is recommended.

- **Prior, Current, or Pending Support of Similar Proposals or Awards**.

  If a proposal submitted in response to this solicitation is for **essentially equivalent work** (as defined in this solicitation) as another proposal that was funded, is now being funded, or is pending with a federal agency, you must make the appropriate certification in Appendix A, as well as provide the following information in Appendix C:

  1) Name and address of the Federal Agency(s) or HHS Component, to which a proposal was submitted, will be submitted, or from which an award is expected or has been received.
  2) Date of proposal submission or date of award.
  3) Title of proposal.
  4) Name and title of principal investigator for each proposal submitted or award received.
  5) Title, number, and date of solicitation(s) under which the proposal was submitted, will be submitted, or under which award is expected or has been received.
  6) If award was received, state contract number.
  7) Specify the applicable topics for each SBIR/STTR proposal submitted or award received.

4. Method of Selection and Evaluation [Placeholder]
5. Considerations [Placeholder]
6. Submissions of Proposal [Placeholder]
7. Scientific and Technical Information [Placeholder]
8. Submission Forms [Placeholder]

9. SBIR/STTR Research Topics

This solicitation invites proposals in the following areas. The detailed project descriptions can be found on the following pages. Each topic description contains "exams" meant to signal metrics and expectations for each topic area, and to assist offerors in developing a proposal for the topic area.

- ARPA-H 01 Ambulatory Edema Monitor
- ARPA-H 02 Predictive Language Models for Cognitive Disability Adaptive Communication Tools
- ARPA-H 03 Cell and Gene Therapy Process Analytical Technology and Quality Control Testing
- ARPA-H 04 Wearable Cell sorting and Gene Delivery Systems
- ARPA-H 05 Precision Brain Targeting: non-invasive delivery at the right place and time
- ARPA-H 06 NutriTech: Revolutionizing Personalized Food as Medicine
- ARPA-H 07 Clinic-ready Imaging Devices and Protocols for Visualizing the Inner Ear with High Accuracy
- ARPA-H 08 Advanced Continuously Wearable Blood Pressure Monitoring Technologies

ARPA-H 01: Ambulatory Edema Monitor

Only Direct to Phase II proposals will be accepted. This topic is open to SBIR or STTR.

Number of anticipated awards: 2-3

Budget (total costs, per award): Direct to Phase II: up to $3,500,000.00 for 1 to 3 years. It is strongly suggested that proposals adhere to the above budget amounts and project periods. Proposals with budgets exceeding the above amounts and project periods will not be funded.

Background/Introduction:

The human heart pumps five liters of blood daily throughout the body, delivering oxygen and nutrients to cells and tissues. Approximately 90% returns through our veins and back to the heart, while 10% leaks out into our tissues via small blood capillaries into a space between our cells known as the interstitial space. It is here in interstitial space that our lymphatic system comes into play. The leaked fluid must be collected by the lymphatic system, a one-way system of vessels starting with terminal lymphatics and progressing through to larger lymphatic vessels to lymph nodes where protein-rich fluid is filtered to remove waste and pathogens. The remaining lymph moves up and into the thoracic duct, emptying back into the venous circulation.

The key here is that the lymphatic system is the ONLY body system that removes fluid from our tissues. If our lymphatic system is not working properly, then fluid will accumulate, causing edema — a swelling that occurs when too much fluid is trapped in the body's tissues and is unable to drain back into circulation.

Edema can affect any part of the body. Any insult to our lymphatic system, be it a medication, pregnancy (mechanical or hormonal), or a disease such as congestive heart failure (CHF), kidney disease, venous insufficiency, or cirrhosis of the liver, can cause edema.

There is no current means of quantitatively monitoring edema. Despite all our technical marvels, the only tool providers use to measure and monitor edema is literally a tape measure and/or pressing a finger into the skin of a patient's extremity looking for "pitting".

Early detection of edema will improve rapid diagnosis and early treatment of CHF and other edematous states like kidney disease, venous insufficiency, liver failure and lymphedema.
The topic is for wearable technology and on-skin interfaces (i.e., stocking, patch) to monitor peripheral edema enabling continuous assessment of the fluid status of patients with congestive heart failure or other fluid overload conditions (e.g., lymphedema).

The Small Business Program (SBP) mechanism will support the development of a prototype that can serve as an initial milestone for what is envisioned as a larger ARPA-H program non-invasive lymphatic diagnostics. A wearable system that enables a patient in an outpatient, with a strong focus on at-home, setting to monitor peripheral edema with minimal effort and with no expertise necessary.

Purpose & Goals:

Purpose and unmet need: The purpose of this overall topic area is to fill a huge and neglected gap in the field of lymphatic medicine – that of the inability to detect subclinical edema and, importantly, to do this in a scalable and equitable way.

The goal: Develop a wearable tool that can be used at home or in an outpatient setting even in rural areas around the country to detect early subclinical edema.

Why is this important? Early diagnosis = preventable complications. If patients, for example, in rural locations, could be identified early with edema, they could be triaged to appropriate facilities to address the edema before it causes serious health consequences and the condition is irreversible.

Why this is doable? Wearable sensors are not a new concept and several prototypes for other health conditions are currently successfully used (example: (1) ring sensor that monitors heart rate and oxygen in the blood , (2) a smart wristband for real-time perspiration analysis, (3) And SwellFit – a prototype of a wearable edema monitor.

References:
1. Asada, H. Harry, Phillip Shaltis, Andrew Reisner, Sokwoo Rhee, and Reginald C. Hutchinson. "Mobile monitoring with wearable photoplethysmographic biosensors." IEEE engineering in medicine and biology magazine 22, no. 3 (2003): 28-40.
2. Gao, Wei, Sam Emaminejad, Hnin Yin Yin Nyein, Samyuktha Challa, Kevin Chen, Austin Peck, Hossain M. Fahad et al. "Fully integrated wearable sensor arrays for multiplexed in situ perspiration analysis." Nature 529, no. 7587 (2016): 509-514.
3. Kim, Sunyoung, Yasha Iravantchi, and Krzysztof Gajos. SwellFit: developing a wearable sensor for monitoring peripheral edema. Proceedings of the 52nd Hawaii International Conference on System Sciences | 2019.

List Technical Deliverables and Success Metrics below:

The deliverable will be a prototype of a flexible wearable sensor which is: (1) comfortable and tolerable to wear, (2) mechanically feasible for human use, (3) wireless power and ability to transfer data to a personal device, and (4) capable of measuring fluid accumulation. Solutions should clearly address the three technical areas (TAs) listed below:

TA 1. Hardware sensing platform – several metrics to consider include bioimpedance, temperature changes, pressure sensing, accelerometer/gyroscope (movement patterns), infrared imaging, electrodermal activity, ultrasonography, heart rate variability (as swelling increases), machine learning algorithms.

TA 2. Mobile application (for data visualization) –(i.e., smartphones, tablets, laptop computers, smart watches, e-readers)

TA 3. Web server with database for processing and storing data

Initial exam:

1. Provide a detailed document outlining the specifications for the wearable sensor's design and functionality.

2. Provide a computer aided design (CAD), schematic and a functional prototype of the edema detection wearable sensor.

3. Document detailing the data collection process, including ethical considerations.

Midterm exams

1. Beta testing for comfort and wearability with patient ambassadors demonstrates 85% satisfaction.

2. Provide a statistical analysis and validation report.

3. No edema detected in a normal control patient > 99% accuracy

4. Subclinical edema detection minimal result >75% accuracy

Final exams

1. Optimized design of wearable sensor with >85% user satisfaction

2. Subclinical edema detection minimal result/ideal results ->85% accuracy/> 95% accuracy

- Ex. Detection threshold for patient with history of congestive heart failure over 24-hour period of time (allowing for timely intervention):

    Volume Change: 50 to 200 ml

    Percentage Change: 1 to 2% of body weight

3. Provide a plan for continuous improvement and updates to the device

4. Upon submission provide a Target Product Profile (TPP) for your solution with measurable minimal and ideal results.

ARPA-H 02 Predictive Language Models for Cognitive Disability Adaptive Communication Tools

Only Fast-Track proposals will be accepted. This topic is open to SBIR or STTR.

Number of anticipated awards: 2-3

Budget (total costs, per award): Phase I: up to $600,000.00 for 6 months to 2 years. Phase II: up to $3,500,000.00 for 1 to 3 years. It is strongly suggested that proposals adhere to the above budget amounts and project periods. Proposals with budgets exceeding the above amounts and project periods Will not be funded.

Background/Introduction:

Speech or language impairment impacts millions in the US, including those associated with Autism Spectrum Disorder and cognitive disabilities. Up to 1 in 36 children and 1 in 34 adults in the US have been diagnosed with an Autism Spectrum Disorder, with a total of ~5.5 million affected. Cognitive disabilities, including Down's Syndrome, account for up to a million more. Many of these people will require lifelong care and support.

Recent research has shown that alternative and augmentative communication tools (AAC) dramatically improve the quality of life of people with cognitive and intellectual disabilities. Early introduction of AACs in education mainly shows dramatic outcomes with improved language acquisition, social cognition, and prospects for lifelong autonomy and independence.

Yet, AAC tools are in their infancy. Far from Stephen Hawking's custom-built communication device, the tools currently available in the community are, at best, primitive due to limitations on-screen interaction and interface complexity. They are often limited to pragmatic requests and incapable of helping their users communicate their emotions, be expressive with their language, or grow with the user's growing command of language. Large Language Models provide an opportunity to give AAC users such an expressive tool.

As more families from ethnic minority groups seek special education and autism services, the need for a multilingual tool also increases. In the past, families were recommended to pursue a monolingual approach to language learning in special education. However, recent studies show that a bilingual learning approach does not impede language acquisition and results in a significantly lower burden to families whose primary language is not English. As large language models are capable of multilingual operation and translation, a desired outcome would be a multimodal AAC tool that enables multilingual language learning and adaptive communication capabilities.

The overarching mission of this topic, in both content and program design, is to advance inclusion and autonomy for individuals with autism and neurocognitive disabilities.

Purpose & Goals:

The goal of this topic is to stimulate the development of intelligent, learning and adaptive AAC tools that will enable users with speech or language impairment to communicate expressively in education, social, and workplace environments. These tools should be aimed to foster language acquisition in the zone of proximal development, with the ultimate goal of communication-driven autonomy for the individual users.

As a "stretch goal" for the topic, we suggest developing a brand-new, full-duplex Cognitive AAC tool. Utilizing cameras, microphones, and AR/mixed reality devices, this tool would use AI to interpret what the user is seeing and hearing, offer prompts, and suggest responses, thus closing the comprehension/response loop. Such a tool has never been developed before.

Current AAC tools are severely limited, with a conceptual vocabulary of 200-300 words and no ability to express complex thoughts or emotions. In comparison, a typically developing 5-year-old has a command of ~2000 words, growing to 25,000-50,000 by high school. This limitation is due to the users' limited command of language and the user interface constraints for severe cognitive disabilities. Multiple reports suggest that AAC tools lose relevance as users acquire language and may hold them back in their development through their inherent limitations.

The proposed AAC tool must be able to:

• Run on commodity hardware (smartphone or tablet) without requiring custom sensors

• Employ an intelligent predictive model to enhance the users' ability to communicate pragmatic needs, thoughts, and emotions to help users fully use expressive language capabilities.

• The tool should "meet the users where they are" in terms of vocabulary size and complexity and assist them with language acquisition and growth of conceptual vocabulary.

• The tool should be able to learn and accept user input through continuous online or offline retraining.

The tool should be capable of bilingual or multilingual operation, enabling improved communication with educators, family members, and caregivers whose first language is not English.

The tool should encapsulate typical interactions in the Special Education setting and enable the users to learn and communicate in varied settings and scenarios (e.g., taking a bus, grocery shopping, managing money, asking for help and accommodations, applying for a job, etc.). The tool should allow the introduction of concepts and vocabulary on an as-needed basis, with a focus on growth.

AAC tools specific to one setting or scenario (e.g., education, or simple pragmatics) will NOT be responsive to this solicitation.

Teams responding to this topic should include a special education specialist or a disability advocate and one or more persons with diagnosed autism or a cognitive disability associated with speech or language impairment as part of the core team. This requirement is intended not only to provide valuable first-person feedback during the development process but also to advance this program's mission of inclusion and autonomy for individuals with autism and neuro-cognitive disabilities through employment in work that benefits the community.

List Technical Deliverables and Success Metrics below:

Initial Exam:

1) User-centered design for novel AAC's. Must include people with disabilities, education specialists and disability advocates.

2)Initial prototype of the AAC model, shown to adapt to the locus of development.

3) Pilot test showing that the AAC system performs in at least two settings, with at least 10 participants.

4)Vocabulary > 2000 words.

5) Quantitative metrics for pilot:

a. Pre-and post-trial data via Vineland-3, FCP-R or equivalent metrics.

b. Discrete trial classroom metrics of classroom performance, language acquisition and use, social pragmatics, and rates of problematic behaviors during duration of the pilot test.

c. User, teacher and family feedback questionnaire.

Mid-term Exam:

1) Demonstration in at least four settings.

2) Demonstration of the ability to adapt with the users' language acquisition.

3) Vocabulary > 10,000 words; ability to use LLM/machine translation for bilingual operation.

4) Ability to work with non-pragmatic topics, communicate emotional states and provide means of expressive language use.

5) Quantitative metrics of system usage in multiple defined settings as well as outside defined settings.

6) Initial public beta deployment of the AAC.

7) At least 500 active users.

Final Exam:

1) AAC tool fully deployed and available to everyone.

2) Full predictive capabilities allowing users to utilize the AAC tool in a variety of settings, including potential for unlimited expressive usage utilizing the LLM capabilities.

3) Vocabulary > 25,000 words/concepts; multilingual operations.

4) Demonstrated ability to respond to user feedback with model changes.

5) Deployment to both children and adults with cognitive disabilities.

6) At least 1000 active users and healthy growth rate.

7) Commercialization Plan

ARPA-H 03: Cell and Gene Therapy Process Analytical Technology (PAT) and Quality Control (QC) Testing

Phase I or Direct to Phase II proposals will only be accepted. This topic is open to SBIR only.

Number of anticipated awards: 2-3

Budget (total costs, per award): Phase I: up to $600,000.00 for 6 months to 2 years. Direct to Phase II: up to $3,500,000.00 for 1 to 3 years. It is strongly suggested that proposals adhere to the above budget amounts and project periods. Proposals with budgets exceeding the above amounts and project periods may not be funded.

Background/Introduction:

High manufacturing costs, drug shortages, expired/unstable intermediates or products, and regional treatment silos limit the ability to provide quality and economical health care for all. The one-product, one-facility design contributes to high patient costs, slow development times, and regional access limitations. Decentralized manufacturing is an advanced manufacturing concept that seeks to replace centralized facilities with multiple "like-for-like" distributed manufacturing (DM) facilities deployed regionally or near patient care (POC). Proof-of-concept DM/POC strategies are emerging in real-time for several modalities, including, but not necessarily limited to, autologous cell therapies (i.e., CAR-T) and oligonucleotide-based therapies (i.e., mRNA vaccines and personalized cancer treatments). The DM/POC paradigm has yet to be demonstrated in sufficient technical, quality, and operational readiness to minimize risk to drug manufacturers for broad implementation.

Decentralized manufacturing systems producing "small batch" drug products on demand will require additional innovation regarding process analytical and/or quality control testing to release drug products rapidly without further risk to safety or efficacy. Scalable solutions are needed to enable advanced in-line or at-line process analytical technologies informing on critical process parameters and/or rapid, automated product quality testing.

Successful development of process analytical technology and/or rapid, automated, walk-up lot release testing equipment would enable a quick tech-to-market win as these same technologies would be valuable to the centralized manufacturing paradigm of today. More importantly, these are enabling technologies that will integrate into a holistic solution for the decentralized manufacturing paradigms of the future.

Technical solutions will likely impact a broad array of cell and gene therapies, vaccines, and other biologics modalities, enabling faster release of high-quality products for cancer, infectious disease, and other indications.

Purpose & Goals:

Goal Area 1: Advanced in-line or at-line process analytical technologies informing on critical process parameters.

Potential measurements include but are not necessarily limited to:

- Cell – soft sensors enabling attribute-relevant chemometric models, cell density, cell viability, cell biophysical properties, -omics data, vector concentration, phenotypic markers, or other relevant biomarkers.

- Oligonucleotide - Critical reagent monitoring (i.e., enzymes, nucleotide triphosphates, capping reagent, plasmid DNA, process intermediates (i.e., RNA, dsRNA, etc.), or soft sensors enabling attribute-relevant chemometric models.

Current process analytical technology (i.e., pH, dissolved oxygen, temperature) will not be considered.

Goal Area 2: Rapid, automated, walk-up-enabled product quality testing.

Ideal lot release assays in a distributed manufacturing paradigm would require minimal hands-on sample processing. The instrument user interface would be intuitive, utilize pre-developed methods, and not require expert knowledge of the underlying principles of the measurement (walk-up enabled). Analytical methods should be completed in no less than 24 hours from sample acquisition to results. The software enabled with clear pass/fail metrics according to pre-programmed, product-specific lot release criteria is required.

Proposed systems may target product quality attributes, purity, or sterility testing. Proposed systems may be novel or significantly improve existing measurements via automation, integration, small footprint, or ease of operation. Representative measurements may include, but are not necessarily limited to:

- Cell therapies – cell viability, transgene expression, endotoxin, microorganism, mycoplasma, replication-competent virus, and other product quality attributes.

- Oligonucleotide-based therapies – identity, size and polydispersity, encapsulation efficiency, gene delivery vehicle composition, oligonucleotide integrity, endotoxin, sterility, and potency.

List Technical Deliverables and Success Metrics below:

Deliverables depend highly on the technology type identified, analyte, and complexity of the matrix (dependent on the process step to be utilized). The offeror will be required to propose analytical metric targets (i.e., LOD, LOQ, repeatability, reproducibility, sample needs, and time to data). The offeror shall also propose prototype samples to be used, including forced degradation samples and/or intentionally altered samples to demonstrate feasibility. Minimal metrics are listed below, noting the TRL at project initiation may heighten stage-gated metrics.

Initial Exam:

1) Proof of concept deliverables will include differential analysis of known positive and control samples. A high degree of assurance that the proposed analytical target is being monitored and a quantitative response is observable. Data acquisition and processing software must be developed.

Mid-term Exam:

1)Additional analytical performance metrics must be demonstrated to indicate sensitivity, dynamic range, and selectivity appropriate for the intended use case. Qualification shall be performed to demonstrate suitability for intended use.

Final Exam:

1) Integration of hardware and software components meets desired deliverables (i.e., automation, integration, walk-up status, etc.). Validation shall be performed to demonstrate utility for intended use.

ARPA-H 04: Wearable Cell sorting and Gene Delivery Systems

Phase I or Direct to Phase II proposals will only be accepted. This topic is open to SBIR only.

Number of anticipated awards: 2-3

Budget (total costs, per award): Phase I: up to $600,000.00 for 6 months to 2 years. Direct to Phase II: up to $3,500,000.00 for 1 to 3 years. It is strongly suggested that proposals adhere to the above budget amounts and project periods. Proposals with budgets exceeding the above amounts and project periods will not be funded.

Background/Introduction:

The cost, manufacturing challenges, and logistics of centralized manufacturing of autologous cell therapies such as chimeric antigen T-cell receptor therapy (CAR-T) have spurred interest in alternative solutions for gene delivery. One approach has been the development of closed, automated, single use manufacturing systems that, in theory, can be moved closer to the point of care. The technical and operations readiness of these systems shows great promise. However, additional advancements in digital architecture, quality control, and logistics are still necessary. An additional alternative route being pursued is in vivo cell therapy, which shares the common operating principle of gene therapy, targeting genetic modification to a specific cell type in vivo. Several advances are being made in this space, however, the need to target specific tissues for gene delivery and the potential for unwanted incorporation continues to be technical hurdles

An alternative approach is the in-situ delivery of genetic material with minimal ex vivo manipulation of cells. In this paradigm, the gene delivery system must be mechanically introduced to the desired cells or tissue that have been sufficiently isolated to enable targeted gene delivery. Such an approach may eliminate the need for time-consuming offline manufacturing and enable administration of the gene delivery in a hospital setting. Such a strategy would revolutionize the delivery of certain genetic medicines and enable more widespread uptake of life-altering medicines.

Purpose & Goals:

The purpose of this topic is to develop an entirely new format for cell and gene therapy delivery that maximizes the attributes of both ex vivo and in vivo cell therapy technologies. This SBIR would attempt to spur innovators that find the middle ground between fully ex vivo and in vivo by leveraging materials/device science AND biology to target cells more efficiently. Potential embodiments could include but are not necessarily limited to, engrafted scaffolds with functionalized gene delivery systems, mechanical delivery of a therapeutic expressing gene delivery system (topical, patch, electroporation), or miniaturized cell sorting and isolation devices that simultaneously perform CAR-T transformation, activation, and reintroduction. Devices of this nature would surpass the unmet needs of ex vivo cell therapy (long wait time and complex manufacturing logistics) as well as unmet needs of in vivo cell therapy (inadequate tissue targeting leading to potential unwanted off-target effects). Literature examples of this type of technology are sparse, with few academic examples of initial proof of concept. This field is ripe for small business spin-off companies to accelerate innovation into a new realm of cell therapy manufacturing. The lack of historical experience and regulatory pathway for such delivery platforms make them less likely for large companies to undertake and thus is a perfect ground for ARPA-H to catalyze further development.

List Technical Deliverables and Success Metrics below:

Deliverables will be highly dependent on the technology type identified, gene delivery system, and target cell line. The offeror shall also propose prototype samples to be used. Minimal metrics are listed below, noting the degree of TRL at project initiation may heighten stage-gated metrics.

Initial Exam:

1)Proof of concept deliverables will include fabrication of the desired device to specifications.

Mid-term Exam:

1)Demonstrated ability to isolate the cells of interest to >70% from a complex mixture (i.e., whole blood or serum). The ability to incorporate the desired genetic medicine into the cell line will be evaluated using offline methods (PCR, NGS, flow cytometry, etc.).

Final Exam (Phase II only)

1)Demonstration of the ability to perform cell isolation and gene incorporation in an animal model or mimetic organoid system. Therapeutic effect will not be a requirement, however gene incorporation must be demonstrated with offline methods.

ARPA-H 05: Precision Brain Targeting: non-invasive delivery at the right place and time

Phase I, Direct to Phase II, or Fast-track proposals will only be accepted. This topic is open to SBIR or STTR.

Number of anticipated awards: 2-3

Budget (total costs, per award): Phase I: up to $600,000.00 for 6 months to 2 years. Direct to Phase II: up to $3,500,000.00 for 1 to 3 years. It is strongly suggested that proposals adhere to the above budget amounts and project periods. Proposals with budgets exceeding the above amounts and project periods may not be funded.

Background/Introduction:

In recent years, recognition has grown for the potential of noninvasive methods to precisely target the brain for diagnostic, monitoring, and therapeutic purposes. Traditional invasive procedures (e.g., those that require direct injection into the peripheral or central nervous system) carry inherent risks and limitations, prompting a surge in research efforts towards safer and more precise alternatives. This topic aims to catalyze innovation in neuroscience by fostering the development of novel non-peripheral or central nervous system (P/CNS) invasive techniques that can deliver diagnostics, monitoring devices, and therapeutic interventions to the brain with unprecedented precision and timing.

The health problem at hand is the need for effective treatments for brain disorders, ranging from neurodegenerative diseases to psychiatric disorders. These conditions pose significant challenges to public health, impacting millions of individuals worldwide. Current treatment options often involve invasive surgeries, direct injection into the P/CNS, or systemic drug administration, which can be imprecise, inefficient, imperfectly timed and associated with undesirable side effects. Diagnostic tools are largely limited to self-report/subjective tools and costly imaging techniques for many of the most common neurological and psychiatric disorders, which prevents earlier and accurate diagnosis needed for more effective treatment.

Purpose & Goals:

The overarching purpose of this topic area is to spur the development of innovative non-P/CNS invasive approaches (i.e., those that do not require injection into the P/CNS) for precise and timely brain targeting to treat brain-specific diseases such as glioblastoma, neurological, or psychiatric disorders. Currently, there are no available technologies that can be administered outside the P/CNS capable of targeting the brain, while providing a platform to modulate and turn off therapeutic delivery. By leveraging the unique capabilities of small businesses, we aim to address the unmet need for safer and more effective *in vivo* diagnostics, monitoring, and treatments for neurological and psychiatric

disorders. Small businesses possess agility, creativity, and a strong entrepreneurial spirit, making them well-suited to tackle complex challenges in health care innovation.

Specific requirements supported under this topic area may include the development of novel non-C/PNS administered brain-targeting technologies, such as advanced imaging techniques, nanotechnology-based delivery systems, novel small molecule, and viral-based innovations. Non-invasive technologies should include delivery options outside the central AND peripheral nervous systems, as well as cerebrospinal fluid (CSF). Proposals focused on integrating these technologies with data analytics, artificial intelligence, or personalized medicine approaches are encouraged. Offerors should articulate a proof of concept of how the delivery will precisely reach a brain region and cell type of interest and express the delivered agent for a nominal amount of time that correlates with a diagnosis or therapeutic effect. Further the proposer should determine how the proposed agent will be able to be turned off. The offerors should target an inflection point for their delivery by the end of funding (for example: IND or IDE approval, first in-human demonstration, etc.)

Notably, proposals solely focused on incremental improvements to existing technologies (such as focused ultrasound) or those lacking clear potential for transformative impact will not be considered responsive under this topic area. We seek bold, high-risk, high-reward projects that have the potential to revolutionize the field of brain-targeted therapeutics. Interdisciplinary research teams with expertise across neuroscience and vascular biology are encouraged.

List Technical Deliverables and Success Metrics below:

Initial Exam:

· Outline the data collection and analysis plan in a report that includes ethical considerations (including how technology will be accessible to different populations).

Midterm Exam:

1) Demonstration of proof of concept for brain-targeting technology with a report outlining proof of concept.

2) Validation of delivery method reaching specific brain regions or cell types with accurate timing (time of delivery and/or duration of time, ability to up/downregulate therapy, and an “on/off switch”) to deliver the appropriate result with a report showing data and results. For example, offerors should demonstrate accurate time of delivery for maximum therapeutic effect, or duration (e.g., 1 min or 3 hours) and the ability to turn off the therapeutic.

3) Initial assessment of safety and efficacy *in vitro* (cell lines, organoids, etc.) and/or in animal models with a report showing data and results to support a regulatory submission of choice.

Final Exam:

1) Approval for regulatory authorization (e.g., IND or IDE) or FDA clearance to move to clinical trials or beyond with documentation of the regulatory submissions and authorizations.

2) First demonstration in animals or human subjects of brain region and cell type specificity with accurate timing (time of delivery and/or duration of time) and accurate off switch to deliver appropriate results with a report showing data and results.

3)Confirmation of targeted delivery and therapeutic effect with a report showing data and results.

4) Plan to integrate technology with clinical practice or personalized medicine strategies (striation of patients using biomarkers for clinical trials or treatment, etc.)

ARPA-H 06: NutriTech: Revolutionizing Personalized Food as Medicine

Only Phase I proposals will be accepted. This topic is open to SBIR or STTR.

Number of anticipated awards: 2-3

Budget (total costs, per award): Phase I: up to $600,000.00 for 6 months to 2 years. It is strongly suggested that proposals adhere to the above budget amounts and project periods. Proposals with budgets exceeding the above amounts and project periods may not be funded.

Background/Introduction:

We have long known that nutritious food improves health and, in contrast, poor nutrition can exacerbate health outcomes. Unfortunately, 60% of Americans have a diet-related chronic health condition, 20% of young people aged two to 19 and 42% of adults have obesity, which in some cases increases risk for chronic health conditions like heart disease, hypertension, type 2 diabetes, and certain cancers, as well as stroke and cognitive impairment. Current techniques to assess nutritional intake are limited to unreliable self-report, non-biologically informative/arbitrary measurements (BMI, etc.), and metabolic blood tests that only broadly assess physical health. As a result, health concerns of those not classified as high risk based on BMI and other measures are missed and clinicians often make general dietary recommendations without targeting an individual's specific

needs. This topic aims to develop new digital health tools and diagnostics to help determine a patient's nutritional status to better inform development of targeted nutritional interventions or food as medicine to improve health outcomes.,

References:

National Academies of Sciences, Engineering, and Medicine. 2024. *The Role of Advanced Computation, Predictive Technologies, and Big Data Analytics in Food and Nutrition Research*: *Proceedings of a Workshop*. Washington, DC: The National Academies Press. https://doi.org/10.17226/27478.

National Academies of Sciences, Engineering, and Medicine. 2024. *Exploring the Science on Measures of Body Composition, Body Fat Distribution, and Obesity*: *Proceedings of a Workshop Series*. Washington, DC: The National Academies Press. https://doi.org/10.17226/27461.

Purpose & Goals:

The purpose of this topic area is to develop digital health tools and diagnostics that use information such as dietary habits, health data and genetic/other biological data to inform on personalized food as medicine recommendations, including specific meal plans, grocery lists, suggested portion sizes and recommended nutrient intake to improve health outcomes. Small businesses can address unmet needs of specific populations, including children, older adults and low-income communities; stimulate technology innovation and capitalize on unique approaches to collect information from patients. Advances in data analytics, artificial intelligence and metabolomics have opened opportunities that could make small businesses successful in addressing this area at this time.

Some specific requirements that would be supported under this topic include demonstration of technology feasibility for a digital health tool or diagnostic to evaluate specific nutritional needs of a patient, including the intersection of environmental and biological (genetics, epigenetics, gut microbiome, endocrinology, etc.) factors that impact metabolism, as well as combined with social factors (social determinants of health, dietary habits, lifestyle habits, cultural connections to food) and other health data. The proposed concept can inform on malnutrition (including both undernutrition and overnutrition), micronutrient (vitamins and minerals) deficiency or excess, as well as innovative new ways of understanding factors that lead to diet-related health conditions (e.g. beyond weight/BMI), such as type 2 diabetes, cardiovascular disorders, high blood pressure, etc. for precision nutritional interventions. Additionally, the digital health tool or diagnostic can be clinician or patient-facing.

It is important to note that proposals with a one-size-fits-all approach and/or those that only inform the promotion of a healthy lifestyle (e.g. general wellness products, including

nutrition intake and/or fitness-only trackers) are out of scope. It is anticipated that the proposed technology would eventually be regulated by the Food and Drug Administration (FDA). ARPA-H specifically seeks bold, high-risk, high-reward projects with the potential to revolutionize personalized nutritional interventions for clear health outcomes. Incremental improvements over current state-of-the-art will be considered non-responsive. Additional considerations, such as socio-economic backgrounds, cultural differences, and specific population considerations, as well as integration into the US health system are highly encouraged to help guide nutritional intervention recommendations.

List Technical Deliverables and Success Metrics below:

Deliverables are highly variable based on the type of technology proposed, population and type of data being collected. Minimal metrics listed below:

Initial Exam:

· Document outlining specifications for digital health or diagnostic design including the data collection plan and how potential AI/ML or other advanced data analytic tools will improve individual nutrition recommendations or outcomes.

Midterm Exam:

1) Demonstration and full outline of proof-of-concept

·2) Report outlining the demonstration of the technical feasibility of proposed innovation to provide personalized nutrition recommendations to an indicated population including the following:

a. Biomarker development and validation studies including context of use and/or diagnostic, predictive, prognostic ability to inform on nutrition status in appropriate clinical population
b. Demonstrated correlation of nutrition status data with precision nutrition intervention in appropriate clinical population

Final Exam:

1) For Digital Health: Development of a technology platform that can assess nutrition status for individuals of a particular population cohort and feasibility to provide a precision nutritional intervention

2) For Diagnostics: Development of a diagnostic assay to assess individual nutrition status and feasibility to correlate with a nutritional intervention including completion of analytical validation studies to include sensitivity, specificity, accuracy, precision and other relevant performance metrics

3) Clear path to advance the innovation toward commercialization including identifying clear health outcomes that the nutrition status will inform on associated population

4) Partnership established with relevant population

ARPA-H 07: Clinic-ready Imaging Devices and Protocols for Visualizing the Inner Ear with High Accuracy

Only Direct to Phase II and Fast-Track proposals will be accepted. This topic is open to SBIR or STTR.

Number of anticipated awards: 2-3

Budget (total costs, per award): Phase I: up to $600,000.00 for 6 months to 2 years. Phase II and Direct to Phase II: up to $3,500,000.00 for 1 to 3 years. It is strongly suggested that proposals adhere to the above budget amounts and project periods. Proposals with budgets exceeding the above amounts and project periods may not be funded.

Background/Introduction:

The senses of hearing and balance are critical to daily human function; when damaged due to disease, injury, or aging, the individual and societal costs are immense. Hearing loss affects some 60 million Americans over the age of 12. Physical falls, many of which can result from balance issues and damage in the vestibular system, are the leading cause of injury and death due to injury in people over 65. In addition, other related disorders and diseases are associated with hearing and balance loss. For example, hearing loss is associated with increased cognitive decline in Alzheimer's disease, and restoring hearing can mitigate this decline. Other hearing and balance impairments can lead to social isolation, communication issues, depression, language disorders, tinnitus, vertigo, etc. Current clinical practice to diagnose these impairments relies mostly on behavioral tests, far-field electrophysiology records and rudimentary imaging that only reveals gross structural abnormalities. Clinicians are often unable to accurately identify the underlying pathophysiology for hearing loss and balance dysfunction and therefore are limited to imprecise treatment options.

Understanding the root causes of hearing loss and balance dysfunction often hinges on the ability to closely examine the anatomy and physiology of the inner ear. To date, structural information about this system comes mostly from post-mortem examinations. The tiny inner ear is comprised of the cochlea, which is the main sensory organ for hearing, and the vestibular end organs for balance. It is surrounded and protected by the densest bone in the body – which can be up to half an inch thick. Despite this heavy protection, the inner ear is often damaged. Precise treatments, including novel gene therapies, require

accurate data to pinpoint which minute structure or function is present or impaired. Unfortunately, however, obtaining this information is currently not possible. Non-invasive techniques like CT or MRI do not presently provide images with sufficient detail for fine-grade distinctions of inner ear cellular components in living human tissue. Invasive techniques can damage the delicate membranous labyrinth that houses the sensory inner-ear hair cells and the supporting structures, readily causing loss of function.

Purpose & Goals:

To address the challenging clinical problem of visualizing the inner ear's anatomy and function, this announcement requests the development of novel, non-destructive technologies to image the anatomy and function of the delicate system with high detail, in human patients. Noninvasive, 3D imaging approaches capable of cellular resolution through dense bone will be strongly preferred. Understanding the difficulties of this specific ask, two alternative solutions will be considered:

1) Invasive (e.g., endoscopic) approaches capable of subcellular resolution (i.e., less than 2μm isotropic resolution).
2) Non-invasive, volumetric, 3D imaging with in-plane spatial resolution no less than 100 μm x 100 μm x 100 μm.

For submissions proposing invasive devices, sufficient detail must be presented detailing how the endoscope will navigate the cochlear labyrinth and how potential damage to the inner cochlea will be mitigated.

Technologies supported in response to this funding opportunity are expected to clear the way for visualization of auditory and vestibular components at the patient's bedside. In contrast to other RFAs, this call requests specific device metrics (e.g., resolution, total acquisition time, etc.) and has specific performance expectations/milestones – including supply chain strategy and regulatory plans by the end of Phase I. This funding call is not meant to be interpreted as a research opportunity – a clinic-ready device and imaging protocol are expected by the program's end.

List Technical Deliverables and Success Metrics:

Phase I activities and deliverables:

1) Development of technology that enables non-destructive visualization of the anatomy and function of the human inner ear (cochlea and/or vestibular end organ). Contrary to other RFAs, the total acquisition time must remain under 1 hour.
    a) Noninvasive approaches must achieve visualization of human inner ear structures at a spatial resolution better than 100 μm x 100 μm x 100 μm.

b) Alternatively, invasive approaches must achieve detailed visualization at a spatial resolution of at least 2 μm x 2 μm x 2 μm.

2) Additional potential areas of focus could include, though are not restricted to, the examples provided below:

a) Discerning bone from surrounding media in the inner ear

b) Capturing stereocilia motion and other dynamic movements of inner ear machinery

c) Detailed assessment of inner ear physiology

d) Identification and localization of otoconia in the vestibular system

3) Histological verification of cellular, structural, and/or functional imaging capabilities of proposed technology using intact human temporal bones.

4) Development of a report detailing the source(s) of necessary equipment or components, possible costs, and a flexible supply chain strategy required to support potential for scalability and eventual commercialization.

5) A coherent plan for undertaking device validation in human subjects in Phase II.

6) Interviews with relevant clinical staff to ensure the acceptability of the proposed solution.

Phase II activities and deliverables:

1) Further advancement of the initially developed imaging technology. Imaging must include the ability, even if in a stop and shoot approach, to see most of the human cochlea and/or vestibular end organs.

2) Validation of the *in vivo* imaging results with post-mortem analysis in large animal models.

3) Testing of the developed imaging approaches in awake normal volunteers and patients suffering from hearing loss.

4) Evaluation of device safety in large animal models.

5) Development of an action plan for FDA approval.

6) Collection of clinician and patient feedback and implementation of quality improvement initiatives based on the findings.

7) Regulatory submissions in preparation for a Food and Drug Administration (FDA) Premarket Notification 510(k).

ARPA-H 08: Advanced Continuously Wearable Blood Pressure Monitoring Technologies

Only Phase I proposals will be accepted. This topic is open to SBIR or STTR.

Number of anticipated awards: 2-3

Budget (total costs, per award): Phase I: up to $600,000.00 for 6 months to 2 years. It is strongly suggested that proposals adhere to the above budget amounts and project periods. Proposals with budgets exceeding the above amounts and project periods may not be funded.

Background/Introduction:

- Background: current blood pressure (BP) measurement approaches that are integrated with commercial wellness devices (e.g., watch type fitness devices) provide relative change BP measurements only, requiring periodic re-baselining from external absolute measurements as frequently as every 28 days. Therefore, the user experience and the quality of the data is not equivalent to the other measurements from these devices (e.g., heart rate, blood oxygen, etc.).
- Goal: Accelerate prototype technology development of a miniaturized, low power, high frequency, blood pressure monitoring technique capable of accurate absolute BP measurement that would be suitable for future integration with fitness form factor wearable devices (watches, rings, patches) for continuous home use. Initial target is FDA Wellness applications, desired end state is as part of medical device applications.
- Many chronic health conditions can be detected and monitored via home blood pressure monitoring (HBPM) and Ambulatory Blood Pressure Monitoring (ABPM) to include hypertension, organ damage, and cardiovascular disease. Additional applications will be possible once high-quality BP data is widely available as an integral data element along with respiratory rate, heart rate and its derivatives, blood oxygen saturation, and body temperature measurements that are available in current wellness and medical devices.

Purpose & Goals:

- The overall purpose of this topic to develop a new technology for HBPM that will better support all future applications of wearable physiological monitoring (WPM) and close the capability gap between current WPM systems and HBPM/ABPM using traditional

means. This may yield a technology that can be licensed and integrated into multi-capability WPMs or an easier to use stand-alone HBPM/APBM device.

- The unmet need is a blood pressure measurement technique that 1) does not require periodic re-baselining via a user manually entering the results of a blood pressure measurement taken with a traditional inflatable cuff or a single purpose home or ambulatory blood pressure monitoring medical device, and 2) may be suitable for future integration into a single, multi-function wellness device/system. Wrist and finger monitors are currently not recommended by the American Heart Association because they yield less reliable readings than inflatable cuff type systems. Closing this gap would provide an individually wearable quality data source a basis for many future wellness and regulated medical applications, including software as a medical device applications.
- The overall purpose of this topic to develop a new technology for HBPM that will better support all future applications of wearable physiological monitoring (WPM) and close the capability gap between current WPM systems and HBPM/ABPM using traditional means. This may yield a technology that can be licensed and integrated into multi-capability WPMs or an easier to use stand-alone HBPM/APBM device.
- The unmet need is a blood pressure measurement technique that 1) does not require periodic re-baselining via a user manually entering the results of a blood pressure measurement taken with a traditional inflatable cuff or a single purpose home or ambulatory blood pressure monitoring medical device, and 2) may be suitable for future integration into a single, multi-function wellness device/system. Wrist and finger monitors are currently not recommended by the American Heart Association because they yield less reliable readings than inflatable cuff type systems. Closing this gap would provide an individually wearable quality data source a basis for many future wellness and regulated medical applications, including software as a medical device applications.
- Target Product Profile (TTP) of end state Wearable Physiological Monitoring device
    - Measures systolic pressure and diastolic pressure in millimeters of mercury (mm HG)
    - Suitable for continuous wear
    - Provides sufficient accuracy regardless of skin color variation or age, weight, or body mass index of wearer
    - Self-powered and/or open standard charging (USB-C)
    - If charged, 7-day battery life from full charge
    - Secure supply chain

- Zero trust cybersecurity architecture
- Open standard data schema
- Open standard wired/wireless communication interfaces
- Section 508 compliant interfaces
- Water resistant
- Cost of goods sold (COGS) <$20
- Able to be transported via U.S. mail to all U.S. states and territories.

List Technical Deliverables and Success Metrics below:

Initial Exam

1) Technical report detailing laboratory proof of concept of miniaturized form factor home blood pressure monitor capable of absolute BP measurements
2) Feasibility analyses for size, power, cost, demographic compatibility, and licenses / intellectual property that would pertain to this technology.

Mid-term Exam

1) Feasibility analyses for size, power, cost, demographic compatibility, and licenses / intellectual property that would pertain to this technology.
2) Regulatory pathway and risk assessment

Final Exam

1) Technical report detailing laboratory proof of concept of miniaturized form factor HBPM/ABPM capable of absolute BP measurements
2) Market assessment & commercialization strategy
3) Potential teaming strategy, if applicable, for subsequent SBIR phases, if approved.