THE ADVANCED RESEARCH PROJECTS AGENCY FOR HEALTH (ARPA-H) SMALL BUSINESS INNOVATION RESEARCH (SBIR) PROGRAM SOLICITATION

IMPORTANT

Deadline for Questions: Solicitation questions must be received by **June 12, 2023, 5:00 PM EDT.** Please send questions to the ARPA-H SBIR/STTR Program mailbox (sbir@arpa-h.gov).

Deadline for Receipt: Proposals must be received by **July 3, 2023, 5:00 PM EDT.**

Please read the entire solicitation carefully prior to submitting your proposal.

IMPORTANT: All proposals must be submitted using the electronic contract proposal submission (eCPS) website. **Paper proposals will not be accepted.**

Please go to the following link to read the SBIR/STTR Policy Directive issued by the Small Business Administration for further information:
https://www.sbir.gov/sites/default/files/SBA_SBIR_STTR_POLICY_DIRECTIVE_OCT_2020_v2.pdf

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***If doing Human or Animal Research, please refer to Appendix F**

1 INTRODUCTION

The Advanced Research Projects Agency for Health (ARPA-H) invites small business concerns (SBCs) to submit research proposals under this Small Business Innovation Research (SBIR) Contract Solicitation. Firms with the capability to conduct research and development (R&D) in any of the health-related topic areas described in Section 1.1, and to commercialize the results of that R&D, are encouraged to participate.

This solicitation contains opportunities to submit a proposal under a variety of different Topics, which are summarized below. Some Topics will only accept Direct-to-Phase II proposals, and some Topics will accept either Direct-to-Phase II proposals *or* Fast Track proposals. **Submission of proposals that only address Phase I are not permitted at this time, and if submitted, may be rejected without evaluation**. For more information on the SBIR program, including descriptions of Direct-to-Phase II and Fast Track proposal requirements, refer to Section 2.

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. HHS is not responsible for any monies expended by the offeror before award of any contract.

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 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.

1.1 List of Topics

This solicitation invites proposals in the following areas:

- ARPA-H 01 – Novel telehealth instruments for assessing pediatric well-being.
- ARPA-H 02 – Microneedle-based patches and digital patch interfaces for remote and real-time transdermal drug delivery and chronic disease management.
- ARPA-H 03 – Robotics for autonomous soft tissue surgery.
- ARPA-H 04 – Intra-operative contrast agents.
- ARPA-H 05 – Scale-Up: Transition disruptive technologies from proof-of-concept prototypes to commercially scalable and deployable technologies.

The detailed project descriptions can be found on the following pages.

ARPA-H 01 – Novel telehealth instruments for assessing pediatric well-being

Only Direct to Phase II proposals will be accepted.

Number of anticipated awards: 1-2

Budget (total costs, per award): 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.

Objective: Develop novel telehealth instruments for assessing pediatric well-being

Summary:

Three of the six most common reasons for pediatrician visits include ear infections, common colds, and sore throats; an estimated 30 million visits a year are solely due to ear infections. Office visits usually involve the doctor directly interacting with the child (by checking his/her ear, throat or listening to his/her lungs). These visits represent a particular burden to socioeconomically disadvantaged families and underserved rural populations, where clinics may be far from home and time away from work or transportation means may not be guaranteed. Prompted by the recent pandemic, telehealth has emerged as a critical tool in healthcare delivery, providing remote access to healthcare services for children and their families. Visits requiring specific tests not available at home (e.g. strep throat tests), or direct physician-patient interaction (for ear checks or lung auscultation), however, have lagged behind in transitioning to telehealth.

The objective of this topic is to advance the implementation and utilization of pediatric telehealth services specifically focused on the management of colds, sore throats, and ear infections. The goal is to improve access to high-quality care, reduce unnecessary office and emergency department visits, and enhance overall healthcare outcomes for pediatric patients. Other conditions that currently require office visits will be considered as well, and proposals aiming to help diagnose more than one condition (e.g. ear and throat checks, or ear, throat and lung checks) will be given priority. The proposed approaches should rely solely on cell phone capabilities (such as photo or video recording), with minimal or no attachments. Example of acceptable attachment may be inexpensive otoscopes, magnifying lenses or microphones, which could be provided by the pediatrician at an initial well-check visit and used for the ensuing year(s). It is envisioned that most of the proposed research would focus on developing detection algorithms using audio, video or photo recordings taken by parents as input; these algorithms would output the probability for the child to have strep throat, an ear infection or a lung infection, which may require antibiotic treatment, or trigger a request for an office visit for the more serious cases. Partnering with broad providers of retail clinic services (such as CVS/Target/Walmart) is encouraged, as it would speed up testing. A plan for recruitment of study subjects from diverse ethnic, racial and socio-economic backgrounds is required.

Phase II activities and deliverables:

- Identification of clinical/pharmacy partners who will collect the required data for algorithm development, optimization and validation
- Interviews with pediatricians and parents to ensure the acceptability of the proposed solutions
- IRB submission and approval (pilot study in adult population)
- Finalization of algorithms/phone attachment choices (if necessary) for the detection of intended conditions
- Feasibility testing of algorithms in the adult population
- Comparison with standard of care determination through office visits
- Collect patient feedback, implement quality improvement initiatives based on the findings
- IRB submission and approval (pediatric population)
- Validation and testing of algorithms in the pediatric population
- Algorithm adjustment, if necessary, to account for potential adult/child differences
- Regulatory submissions (pre-submission, Q-submission, IDE, 510k, etc)
- Note that an adult feasibility study is suggested prior to a pediatric study, with the intent of allowing for faster data collection. If sound arguments can be made as to why effective recruitment of pediatric patients is practical, the adult pilot study is not required.

ARPA-H 02 - Microneedle-based patches and digital patch interfaces for remote and real-time transdermal drug delivery and chronic disease management

Direct to Phase II proposals will only be accepted.

Number of anticipated awards: 1-2

Budget (total costs, per award): 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

Over the past decade, the use of microneedle drug delivery modalities has become a topic of significant interest, particularly in the management of chronic diseases via drug infusions. One chronic autoimmune disease, Systemic Lupus Erythematosus (SLE), can affect almost any organ system and can cause a litany of clinical manifestations from malar rashes and fever to seizures and hemolytic anemia. According to the CDC there are approximately 1.05 million people with SLE in the US and approximately 16,000 new cases diagnosed each year. The standard of care for SLE is often frequent, monitored intravenous (IV) drug infusions in a hospital and/or outpatient setting.

One IV treatment, Benlysta, costs $35,000 per year and can carry a number of adverse side effects outside of the poor quality of life that results from frequent, clinic-based care and drug infusions. However, in more

recent and promising peer-reviewed studies, SLE can be treated with daily, low-dose, subcutaneous infusions of interleukin-2 (IL-2) over a series of two-week courses. This finding, coupled with breakthroughs in microneedle capabilities by large medical technology and pharmacology companies, suggests that chronic diseases like SLE could be successfully treated remotely through the combined use of subcutaneous drugs and microneedle patches. To that end, the FDA approves approximately one transdermal drug every 2.2 years, and they currently have a portfolio of over 200 approved drugs for transdermal delivery, suggesting we could treat a range of diseases through a minimally invasive, transdermal approach.

The global transdermal skin patch market is projected to grow to $9.6B by 2026, with a CAGR of 4.78% according to a Mordor Intelligence Consulting report. It should be noted, however, that this transdermal skin patch market primarily consists of simplistic devices (e.g., single-layer drug-in-adhesive and multi-layer drug-in-adhesive devices). These devices rely on simple diffusion mechanisms and do not provide a reliable mechanism through which providers can repeatedly and precisely deliver medications. There is, however, a newer focus on reproducibly of transdermal drug delivery using additional modalities such as iontophoresis and sonophoresis.

This initiative seeks to combine all the technologies into one elegant approach: a removable microneedle patch that can be used for controlled, reliable, repeatable transdermal drug delivery (using the ever-growing list of FDA-approved drugs for chronic diseases) and can have its operation controlled electronically by a patient's Primary Care team through their Electronic Health Record application. This, in turn, would drastically improve patients' quality of life while still allowing providers to interface directly with a patient's remote healthcare. Importantly, this device would require a drug "cartridge" port that would allow patients to insert the specific container and/or volume of the intended therapeutic into the unit to then be infused by their provider in real-time from anywhere in the country. With a surge in telehealth and wearables, a remotely controlled microneedle patch, that will likely also integrate electronic circuitry for modalities like iontophoresis and sonophoresis, could be yet another tool for a more remote healthcare future. To minimize healthcare waste, this device would need to allow patients to insert a new drug "cartridge" for each infusion into the device and would also need to have a way to replace the microneedles in an affordable fashion when they become dull, clogged, or faulty after repeated use. This device must also be removable, as it is not intended to be perpetually affixed to a patient's body but should instead be attached for the therapeutic infusion and then removed after/between use.

It is critical to note that the goal of this product is to use all FDA-approved transdermal drugs, including those in the pipeline. This product is intended to provide real-time transdermal infusions of drugs for a range of conditions, not just SLE. By integrating this device into EHRs and an existing wearable sensor network, the quality of life for patients suffering from a range of comorbidities that used to keep them confined to hospitals and outpatient clinics could drastically improve.

Project Goals and Specific Objectives:
The purpose of this project is to create a new, multi-purpose device for controlled, reliable, long-term, repeated transdermal drug delivery with remote and digital interfaces for real-time chronic disease management from virtual Primary Care teams through their Electronic Health Record application. Additionally, this device needs to provide a reliable distribution of drugs across the transdermal barrier regardless of age, weight, race, or gender. The device must also be removable between uses so patients aren't wearing them

continuously like an insulin pump. This product must be affordable for any patient. Finally, the drug reservoir must be easy to replace per infusion and the microneedle array must be reproducibly fabricated in case of malfunction or degradation.

The preliminary goal of this project is to show finalized product development and to then transition towards scalability and commercialization. The final product will be an instrument or set of instruments that are accessible to as many civilian Americans as possible as well as to active-duty military and veterans for accelerated and multiplexed point of care, data analysis, and personalized treatments. The long-term goal of this project is to disrupt the current standards of care for treatment of numerous chronic diseases, including SLE, diabetes, and cancer, via a patch and digital interface for transdermal drug delivery, real-time diagnosis, and disease management. The future of this project should aim to mimic the simplicity of modern wound adhesives, such as Band-Aids, while integrating advanced drug delivery mechanisms, digital health monitoring, and disease management.

Phase II activities and expected deliverables may include:

- Develop software and methods.
- Establish in vitro success metrics.
- Finalized prototype with the following characteristics to demonstrate durability and repeatability of the final product:
    - Replaceable drug reservoir for transdermal drugs of varying volumes.
    - Replaceable, precise, pain-free, low-cost microneedles that provide reproducible transdermal infusion.
    - Electrical circuitry for infusion technology allows consistent drug delivery.
    - Adhesive mechanism to stay connect to patient through daily activity.
    - Bluetooth and/or Wi-Fi technology to connect to local devices and HER.
- Demonstrate consistent, safe, reproducible transdermal delivery of TWO (2) different FDA approved transdermal drugs using the product.
- Identify GMP and GLP manufacturing partners.
- Determine and demonstrate that performance, including durability and repeatability, of the final product outperforms or matches the standard of care using in vitro success metrics.
- Establish in vivo success metrics.
- Complete animal study that demonstrates abilities for remote transdermal drug delivery, real-time measurement and reporting, and disease management over time.
- Integration of secure Wi-Fi connection between device and EHR for HIPAA-compliant drug infusion
- Scale up and production for multi-site testing using clinical samples.
- Report summarizing progress bi-weekly, including both raw and summary data.

ARPA-H 03 – Robotics for autonomous soft tissue surgery

Fast-Track or Direct to Phase II proposals will only be accepted.

Number of anticipated awards: 1-2

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 may not be funded.

Objective: Develop a robotic system capable of autonomously performing a complex surgical task

Background:

Autonomous surgery has the potential to improve patient outcomes by providing a surgical option where an experienced surgeon is not available, increasing access to high-quality healthcare in an inequitable landscape, performing repetitive operations consistently, increasing the quality of care, and freeing up manpower and performing operations where human performance is limited by the visual interface and robotic tools.

Autonomy in surgical robots is traditionally described on a 6-point scale, where 0 denotes a robot entirely driven by the surgeon's motions or direct commands, and 5 indicates a robot that can perform an entire procedure with no human supervision. The end goal of this proposal is for performers to develop a surgical robot capable of operating with autonomy level 3: conditional autonomy. A level 3 autonomous robot generates task plans but requires a human to select among plans. The robot then executes the surgical task independently. Examples include a robot that can identify complex wound boundaries and plan and execute sutures, a robot that can recognize luminal polyps, navigate to the polyps, and perform a laparoscopic biopsy, or a robot that can plan and execute an intestinal anastomosis.

Project Goals:

Phase I: Design and develop a prototype level 2 autonomous surgical robot and demonstrate a successful surgical task in tissue-mimicking phantoms. The level 2 autonomous robot will accomplish a specific surgical task based on parameters established by the surgeon, e.g., suturing or cutting between two surgeon-specified fiducial markers. The robot should accomplish the task with a $>75\%$ success rate, where success is measured in terms of the mechanical performance of the task (e.g., all tissue cut within 2 mm of the surgeon's guiding line and no tissue is cut outside that).

Performers may use a combination of commercial off-the-shelf (COTS) robotics and software and custom-built and designed elements. Proposals should address the following requirements for the robot:

Imaging and computer vision

• Create a representation of the topology of the instrument's local context, whether by use of human-designated fiducial markers, local distance sensing, or full 3D reconstruction. This may be achieved through active or passive sensors on the surgical implement, on auxiliary manipulators, or on a separate platform that feeds information to the main robot.

• Update the representation of the local context in real time, accounting for positional changes and deformation of tissue from the task.

• Accurately represent the position of the surgical implement relative to the local surgical context. This may involve range finding, establishment of non-traditional fiducial markers or modes of reference, or external sensing of surgical tip location.

Manipulation and motion

- Access the surgical area.
- Dexterously execute the task with fine manipulation, including use multiple arms or attachments if it is required to e.g., stretch tissue in order to cut it.

Planning and control

- Plan a path between or along surgeon-designated fiducial markers.
- Control the execution of the surgical task at the specified location. May involve force sensing to determine tension, friction, etc.

Phase II: design and develop a level 3 autonomous surgical robot and demonstrate a successful surgical task in soft tissue in a large animal model. Examples of potential tasks to be completed independently include complex wound suture, intestinal anastomosis, or wound/burn/infection debridement. Metrics to characterize task success will vary dependent on task and should be specified by the performer. These should not just include speed of surgery, survival rate, complication rate, and healing times, but should include specific characteristics of mechanical performance (e.g., a measure of accuracy of suture placement and tightness of wound closure).

Performers should describe a vision for the robot's use in clinical practice. A suturing robot may be designed as a standalone device to be deployed in a medical but non-OR setting, whereas a laparoscopic tumor excision robot may be a software addon to and minor mechanical modification of an existing robotic surgery platform.

Proposals should address the capability requirements listed under Phase I, as well as the following additional requirements:

Imaging and computer vision

- Create a representation of the topology of the surgical context, whether by full 3D reconstruction or local distance sensing. This may be achieved through active or passive sensors on the surgical implement, on

auxiliary manipulators, or on a separate platform that feeds information to the main robot. This may not rely on human-placed fiducial markers.
- Accurately represent the position of the surgical implement relative to the 3D context. This may involve range finding, establishment of non-traditional fiducial markers or modes of reference, or external sensing of surgical tip location.
- Update the representation of the 3D context in real time, accounting for positional changes, breathing movements, and deformation of tissue from the task.
- Provide a way for a monitoring human to assess the progress of the ongoing task.

Planning and control

- Plan a path to navigate the 3D spatial context to autonomously approach the relevant area. The robot can start in the general proximity of the task (e.g., a laparoscopic robot does not have to perform the initial navigation from exterior to the organ or structure of interest).
- Plan the task execution, potentially presenting multiple options for the surgeon to choose from.
- Detect if the chosen task plan has been deviated from and raise the issue to the operator. Preferably the robot will automatically generate a new task plan based on the current status.

References:

1. Attanasio et al. Autonomy in Surgical Robotics. Annu. Rev. Control Robot. Auton. Syst. 2021. 4:651–79
2. Saeidi et al. Autonomous Robotic Laparoscopic Surgery for Intestinal Anastomosis. Sci Robot. 2022 January 26; 7(62)

ARPA-H 04 – Intra-operative contrast agents

Fast-Track or Direct to Phase II proposals will only be accepted.

Number of anticipated awards: 2-3

Budget (total per award): Phase I: up to $600,000.00for 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 may not be funded.

Objective: Advance intra-operative contrast agents towards clinical practice

Summary:

Interventional procedures are currently ambiguous and only qualitatively supported, have no decision support and no error prediction or detection. Nerves and cancerous tissue appear similar to normal tissue, making them difficult to distinguish during surgeries. Consequently, nerves are accidentally cut during procedures, leading to high patient morbidity (up to 35% of the patients, e.g., have cavernous nerve injury during prostatectomies). Cancers are also accidentally left behind, resulting in high reoperation rates and increased healthcare system costs. For example, breast cancer lumpectomies alone have reoperation rates of ~23%, at a total annual cost in the United States of about >0.5 billion dollars.

The goal of this topic is to accelerate the transition of promising intraoperative contrast agents towards commercialization, enabling clinicians to better visualize the relevant structures of interest such as nerves and cancer during surgery. Due to the urgency of this public health need, projects supporting a lead compound with a robust body of background data will be prioritized. Background data may include rigorous preclinical testing, sufficient bioactivity and in vivo efficacy and/or target engagement. Applications focusing solely on basic science research are not considered responsive, such as: novel target identification/validation, generation of new animal models, development/testing of new human laboratory models, assay development, new biomarkers, or mechanistic studies.

Projects aiming to modify an existing contrast agent, such as enabling it to fluoresce in a different spectral range, will be considered as part of a FastTrack approach. By the end of the funding period, projects are expected to achieve milestones that significantly move the compound towards the next phase of drug development (Investigational New Drug (IND) application and/or early clinical trials- depending on the starting point). Contrast agents highlighting nerves for prostatectomies and musculo-skeletal procedures, as well as those highlighting breast, colorectal and head and neck cancers will be prioritized, although others will be considered responsive.

Phase I activities and deliverables:

- Changes of agent structure (if needed), such as replacing its dye molecule for fluorescence in a different spectral domain.
- Chemistry, Manufacturing, and Control (CMC) activities, CMC analytical development, formulation development.
- Pharmacokinetic evaluations in species relevant for toxicology or human dose-prediction.
- Preliminary safety such as safety pharmacology and/or dose-range finding toxicology.
- Optimizing and/or validation of appropriate assays for pharmacokinetics, bioactivity (potency), target engagement markers or other assays to monitor safety to be used in human trials.
- Evaluation of compound safety/efficacy in established animal models.
- IND-enabling studies.

Phase II activities and deliverables:

- IND-enabling toxicology, with toxicokinetics.
- Immunogenicity evaluations, if applicable.
- Biodistribution and stability studies.
- Large animal study to assess biocompatibility of means of clinical delivery of the candidate.
- Validation of appropriate assays such as for target engagement markers to enable human use.
- IND and other regulatory submissions.
- IRB submissions.
- Phase I/Phase II clinical studies (depending on the starting point).

ARPA-H 05 – Scale-Up: Transition disruptive technologies from proof-of-concept prototypes to commercially scalable and deployable technologies

Direct to Phase II proposals will only be accepted.

Number of anticipated awards: 2

Budget (total per award): 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.

Summary

The Scale-up program builds on ARPA-H's primary research and development mission to support the scaling and transition of prototypes from the lab (proof of concept) to the market. The goal of the program is to help disruptive technologies transition from proof-of-concept prototypes to commercially scalable and deployable versions of the technology that are well-positioned for investment and adoption by the private sector. Scale-Up specifically targets cost-intensive activities to reduce the risk, optimize regulatory approval potential (when applicable), and increase technology, investment, manufacturing, and adoption readiness levels. The Scale-up program will be managed by the ARPA-H Project Accelerator Transition Innovation Office (PATIO), which will provide a variety of services to support performers, including:

- Testing of minimum viable products (MVPs)
- Growth acceleration
- Regulatory support
- Entrepreneurship education

Program Objectives

The purpose of this program is to increase the probability of scaling high-risk and potentially disruptive new technologies and solutions across the full spectrum of health-related applications. Projects will focus on scaling and transition challenges associated with the underlying technology. These can be related to technology integration, manufacturing, clinical trials and proving efficacy, and building capacity. The specific objectives of the program are to develop proven demonstrations of efficacy, receive regulatory approvals, eliminate barriers to manufacturing or distribution, secure key partnerships with commercial partners, user-groups, and stakeholders, and to attract outside investment.

The purpose of the program is to advance the candidate technologies and accelerate the path to widespread commercial adoption by funding the elimination of the primary challenges to widespread scaling. Scale-up candidate projects will reduce these commercialization friction points for pharma (medications), biotech (immunizations and therapies), medtech devices (user devices, provider devices, diagnostics), and/or healthcare IT (inclusive of data and bioinformatics).

Because of the breadth of health-related solutions addressed by ARPA-H, technical and project targets are not specified but rather should align with the ARPA-H mission and one or more ARPA-H Focus Areas (Health Science Futures, Scalable Solutions, Proactive Health, Resilient Systems). We are particularly interested in projects that focus on women's health, maternal health, mental health, and pediatrics. Two additional specific topics of interest that may be conducted under this scale-up program are described in more detail below.

Technology for Mental Health Recovery

This scale-up sub-topic seeks to develop the underlying science and technology for tests and treatments to support improved mental health and substance use disorder recovery. When appropriate, FDA approval should be included in the technical plan. Of particular interest are technology innovations that demonstrate a high correlation between application and improved patient recovery pace or recovery quality. Approaches of interest include intelligent chatbots, virtual telepresence, pervasive connectivity, local sensing of patient state (no patient information stored or transferred over a network), local testing (no patient information stored or transferred over network), and laboratory-based tests for new marker identification. This sub-topic is also open to other emerging technology approaches with the potential to deliver a high correlation between application and improved recovery.

A successful proposal should focus on developing a viable structure for observational trials to demonstrate the desired high correlation between use of a given technology and improved recovery. These trial designs should build toward implementation of the trials and the ultimate goal of a commercially viable FDA approved test or treatment.

Artificial Pancreas Technology

Of interest to this sub-topic are technologies and systems to support proposed closed-loop artificial pancreas systems. Enabling closed-loop functionality is important because it enables continuous monitoring of an individual's sugar levels and subsequent automatic dispensing of insulin without human input. Recent advances in component miniaturization, electronic control, and algorithms (including machine learning) may enable improved comfort, accuracy, performance, and portability while simultaneously reducing overall system cost as well as cost of care.

A successful proposal should outline a technical plan for completion of a prototype suitable for demonstration of the drug-delivery and sugar sensing functions of the artificial pancreas along with an appropriate programmable controller designed to iteratively test and evaluate closed-loop algorithms. The proposal should also outline a plan to develop, test, and evaluate a set of closed-loop algorithms with the ultimate goal being a commercially viable FDA approved device.

Proposers are to address how the proposed scale-up project will sufficiently:

1. Reduce transition friction points (including but not limited to team development, regulatory/approval requirements, technology risk, funding access, capital needs, challenges around scale-up/production/deployment, and diversity, among others).
2. Increase readiness levels.

3. Advance the technology/solution to enable a path to market and ultimately lead to realized impact.

We are NOT interested in incremental technologies, or technologies that are in early R&D stage.

Third-Party Commercialization Partnership Requirement

Competitive preference and funding priority is given to applications deemed likely to result in a commercial product, as indicated by the applicant's ability to secure substantial independent third-party investor funds (i.e., third-party funds that equal or exceed the requested ARPA-H funds) or commercialization partnerships.

Examples of third-party investors include, but are not limited to, another company, a venture capital firm, an angel investor, a foundation, a university, a research institution, a state or local government, or any combination of the above.

Other Commercialization Partners may include potential customers, end-users, suppliers, manufacturers, distributors, etc. It is preferable for Applicants to have at least one Commercialization Partner that represents the viewpoint and needs of the target customer to help ensure market adoption for the technology after the completion of the Scale-up project.

Commercialization Partners can make a contribution of cash, in-kind (e.g., a demonstration site, intellectual property, etc.), or via other justifiable means that will be integral to the success of the project. Identified and planned Commercialization Partners are expected to actively participate in the project. Commercialization Partners make contributions with the goal that the technology will be successfully proven and commercialized.

Applicants must provide a commercialization plan that describes the long-term commercialization strategy and details any independent third-party investor funding that has already been secured or will be provided during the Scale-Up Award project period.

Deliverables and Activities

- Active participation by Commercialization partners
- Gating steps to show progress towards market adaptability including progress to remove regulatory hurdles, manufacturing/distribution barriers, investment hurtles, etc.
- Demonstrate the proof-of-concept solution has been de-risked for market adaptability. For example, the solution could:
    - Receive regulatory approval.
    - Eliminate barriers to manufacturing or distribution.
    - Secure key partnerships commercial partners, user-groups, and stakeholders.
    - Attract outside investment.

2 PROGRAM DESCRIPTION

2.1 Background

The basic design of the ARPA-H SBIR program is in accordance with the Small Business Administration (SBA) SBIR Program Policy Directive dated October 1, 2020. This SBIR contract 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 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.

2.2 Phased Program

The SBIR program consists of separate phases. Note: At this time, ARPA-H is only accepting Direct to Phase II and Fast-Track proposals for this solicitation. Please refer to the individual topics above for more information.

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 award at Phase II.

Phase III: Commercialization stage without SBIR funds *(Not Accepting Proposals)*

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, for an agency that wishes to fund an SBIR project beyond the Phase II, it is sufficient to state for purposes of a Justification and Approval pursuant to FAR 6.302-5 that the project is derived from, extends, or logically concludes efforts performed under prior SBIR funding agreements and is authorized under 10 U.S.C. 2304(b)(2) or 41 U.S.C. 253(b)(2).

2.2 Direct to Phase II Proposals

If your project has already demonstrated feasibility, but you have not received a Phase I SBIR or STTR award, you can apply for a Direct to Phase II award and bypass Phase I. Small business concerns applying for Direct to Phase II awards must have **already built a technology prototype and tested its technical feasibility** (i.e., completed Phase I type R&D or another effort). Phase II type R&D tests the functional viability of the prototype according to scientific methods and potential for commercial development. Refer to Section 1.1 List of Topics for notation of Topics allowing Direct to Phase II proposals.

2.3 Fast Track Proposals

A Fast Track submission may result in an initial award for Phase I with a contractual option that the Government may exercise to continue the award on to Phase II. The Government is not obligated to fund the Phase II portion unless and until ARPA-H exercises that option. This mechanism allows for streamlined processes that have the potential to significantly minimize the funding gap between Phase I and Phase II.

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 4.2 “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 3.3 “Technical Evaluation Criteria.”

3 METHOD OF EVALUATION

All proposals will be evaluated on a competitive basis. Each proposal will be judged on its own merit. ARPA-H is under no obligation to fund any proposals or any specific number of proposals in each topic. It may also elect to fund several or none of the proposed approaches to a given topic.

3.1 Evaluation Process

ARPA-H will conduct a preliminary review of each proposal, followed by a scientific/technical review of conforming proposals. Conforming proposals must comply with all requirements detailed in this solicitation; proposals that fail to do so may be deemed non-conforming and may be removed from consideration.

Proposals will be evaluated based on their individual merits rather than against each other since they are not submitted in accordance with a common work statement. Award(s) will be made to proposers whose proposals are determined to be the most advantageous to the Government, consistent with instructions and 3.2 and 3.3 herein, and availability of funding.

The scientific/technical review members will determine whether each proposal is technically acceptable, meaning that it demonstrates sufficient technical understanding and capabilities to perform the technical objectives set forth in the solicitation.

3.2 Award Decisions

To receive an award, offerors must be eligible according to the requirements defined in APPENDIX E – PROPOSAL FUNDAMENTALS, Section 6.2 Offeror Eligibility and Performance Requirements. ARPA-H will make awards to the offerors who provide the best overall value to the Government, considering the below:

- Ratings resulting from the technical evaluation.
- Areas of high program relevance to the ARPA-H Mission. The ARPA-H mission is to accelerate better health outcomes for everyone by supporting the development of high-impact solutions to society's most challenging health problems. Therefore, an award decision will be made to the extent proposals align to and further ARPA-H's mission.
- Program balance (i.e., balance among areas of research).
- Availability of funds and cost/price reasonableness

3.3 Technical Evaluation Criteria

The technical evaluation criteria are of equal importance and will be adjectivally rated.

Non-price Factors:

1. The soundness and technical merit of the proposed approach. Identification of clear, measurable goals (i.e., milestones) that have a reasonable chance of meeting the topic objectives.

2. The potential of the proposed research for technological innovation – whether the end product or technology proposed would offer significant advantages over existing approaches, methodologies, instrumentation, or interventions currently utilized in research or clinical practice.

3. The potential of the proposed research for commercial application – whether the outcome of the proposed research activity will likely lead to a marketable product or process considering the offeror's proposed methods of overcoming potential barriers to entry in the competitive market landscape.

4. The qualifications of the proposed Principal Investigators, Project Directors, supporting staff and consultants, and the appropriateness of the leadership approach (including the designated roles and

responsibilities, governance, and organizational structure).

3.4 Price Factor

Price:

A price evaluation will be conducted to ensure that the proposed price is reasonable. The Government may use various price evaluation techniques and methodologies to ensure the proposed price is reasonable. An assessment that the proposal price is not reasonable may result in the proposal being non-selectable for award.

4 PROPOSAL PREPARATION AND INSTRUCTIONS

4.1 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 item.

4.2 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.

For Fast-Track submissions, both a complete Phase I proposal and a separate, complete Phase II proposal must be submitted. 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:

Human Subjects and Clinical Trials Information Form and Attachments

NOTE: For SBIR 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 separately from the rest of the Technical Proposal. There is a field in the eCPS proposal submission website that is specifically identified for upload of the Human Subjects and Clinical Trials Information Form and its attachments, separate from the Technical Proposal.

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**
  Fillable PDF (https://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/PHSHumanSubjectsAndClinicalTrialsInfo_2_0-V2.0.pdf)

  Due to large file size, Appendix A.1 and Appendix A.2. can only be opened in Internet Explorer. However, you may download them from any browser, then view them once you have saved them onto your computer.

  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**
  Fillable PDF (https://oamp.od.nih.gov/sites/default/files/DGS/contracting-forms/HumanSubjectStudy_2_0-V2.0.pdf)

  Due to large file size, Appendix A.1 and Appendix A.2. can only be opened in Internet Explorer. However, you may download them from any browser, then view them once you have saved them onto your computer.

Business Proposal

The award will result in a Firm-Fixed Price (FFP) contract type. 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 APPENDIX E – 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 APPENDIX E – 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.

5 PROPOSAL SUBMISSION

5.1 How-to-Submit

Offerors are responsible for submitting proposals to the electronic Contract Proposal Submission (eCPS) website at https://ecps.nih.gov/ by the date and time specified on the first page of this solicitation. **Offerors must use this electronic transmission method. No other method of proposal submission is permitted.**

Any proposal, modification, or revision, that is received after the exact time specified for receipt of proposals is "late" and will not be considered for award.

If an emergency or unanticipated event interrupts normal Government processes so that proposals cannot be received at the eCPS website by the exact time specified in the solicitation, and urgent Government requirements preclude amendment of the solicitation closing date, the time specified for receipt of proposals will be deemed to be extended to the same time of day specified in the solicitation on the first work day on which normal Government processes resume.

Proposals may be withdrawn by written notice at any time before award. A copy of withdrawn proposals will be retained in the contract file.

Instructions on how to submit a proposal into eCPS are available at https://ecps.nih.gov/howtosubmit. Offerors may also reference Frequently Asked Questions regarding online submissions at https://ecps.nih.gov/faq. **Be advised that registration is required to submit a proposal into eCPS and registration may take several business days to process.**

The proposal must be uploaded in 2 parts: Technical Proposal and Business Proposal. Each Proposal must consist of a single PDF file.

5.2 Questions

Offerors with questions regarding this solicitation must submit them in writing to the Contracting Officer point of contact identified on page 1 of this solicitation. To ensure that the Government has sufficient time to respond, questions should be submitted by **June 14, 2023.** The Government may issue an amendment to this solicitation which publishes its responses to questions submitted. The Government anticipates that responses would be published in sufficient time for interested offerors to consider them prior to submission of a proposal.

5.3 Proposal Naming Conventions

To aid the Government in the efficient receipt and organization of your proposal files, please follow the following file naming conventions:

a. The language entered into the 'Proposal Name' field in eCPS for your proposal submission should include, in order: (1) the Phase the proposal is for; (2) the name of the Offeror; (3) Agency name and (4) the Topic being proposed under. An example is provided below:

- Phase II_XYZ Company_ARPA-H_Topic_02

b. Files uploaded for your proposal submission should include, in order: (1) the name of the Offeror; (2) Agency name, (3) the Topic being proposed under; and, (4) the type of proposal (i.e., Technical, Business, or Excel Workbook). Use the format set forth in the examples below when naming your files, prior to uploading them into eCPS:

- Technical Proposal: XYZ Company_ARPA-H_TOPIC_02_Technical.pdf
- Human Subjects and Clinical Trials Information Form: XYZ Company_ARPA-H_TOPIC_02_HumanSubjectsForm.pdf
- Business Proposal: XYZ Company_ARPA-H_TOPIC_02_Business.pdf
- Excel Workbook (Optional): XYZ Company_ARPA-H_TOPIC_02_Business.xlsx