Innovative Solutions Opening (ISO)

Platform Optimizing SynBio for Early Intervention and Detection in Oncology (POSEIDON)

Health Science Futures (HSF) Office

ARPA-H-SOL-24-109

August 9, 2024

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1.0 Innovative Solutions Opening (ISO) Summary Information

Federal Agency: Advanced Research Projects Agency for Health (ARPA-H), Health Science Futures Office (HSF)

Program Title: Platform Optimizing SynBio for Early Intervention and Detection in Oncology (POSEIDON)

Announcement Type: Solicitation

ISO Solicitation Number: ARPA-H-SOL-24-109

Dates (all times listed are Eastern Time):

- *Proposer's Day:* 4 SEP 2024, 8:30am – 5pm
- *Questions & Answers (Q&A) Due*: 24 SEP 2024
- *Priority Submission Date* (Initial collection of Solution Summary Submissions)*: 16 OCT 2024
- *ISO Closing Date* (last day for Solution Summary submission)*: 6 NOV 2024
- Full Proposal Due Date*: estimated as no later than 8 JAN 2025

Anticipated awards: Multiple Other Transaction (OT) Agreements

Agency Contact: All inquiries shall be sent to POSEIDON@ARPA-H.GOV

*See ISO Sections 4, 5 and 6 for additional information about Solution Summary and Full Proposal Submissions (e.g., to be eligible to submit a Full Proposal, a Proposer must have submitted a timely Solution Summary and received feedback from the government).

1.1 ISO Purpose

ARPA-H seeks proposals from all eligible entities (see Section 3, *Eligibility Information*) to accomplish the POSEIDON program goals as described in this solicitation package. Ultimately, ARPA-H intends to negotiate multiple OT Agreements with Proposers whose proposals are most advantageous to the government.

1.2 ISO Questions and Answers

All questions regarding this ISO must be submitted to POSEIDON@arpa-h.gov. ARPA-H will post Q&As to the POSEIDON program website on an on-going basis and will not respond to questions directly. All questions must be submitted in English and must include the name, e-mail address, and telephone number of a point of contact. Proposers submitting questions to individual government team members (e.g., Program Manager) should not expect a response. ARPA-H will attempt to answer questions in a

timely manner; however, questions submitted after the Q&A due date may not be answered. Further, duplicative questions may be combined and rephrased to streamline responses.

1.3 Proposers' Day

ARPA-H will host a Proposers' Day on 04 September 2024 in support of the POSEIDON program as described in Special Notice ARPA-H-SN-24-110 (see SAM.gov). The purpose of the event is to provide potential Proposers with information on the POSEIDON program, promote discussion, and encourage team networking.

Interested Proposers are not required to attend; materials formally presented at the Proposers' Day will be posted to www.sam.gov.

ARPA-H will not reimburse potential Proposers for participation at the Proposers' Day (nor for time and effort related to the submission of Solution Summaries or full proposals).

2.0 The Program

2.1 POSEIDON Overview

2.1.1 Introduction. POSEIDON envisions a future in which all cancers are detected early (while they are still localized) and when curative treatment is far more likely. To achieve this goal, POSEIDON aims to develop first-in-class, at home, over the counter, synthetic-sensor based Multi-Cancer-Early Detection (MCED) tests for Stage I detection of 30+ solid tumors using only breath and/or urine samples. Detecting these 30+ tumors at Stage 1 would save millions of lives and eliminate the economic burden of late-stage cancer care. POSEIDON leverages extensive, human-centered design to create a program that combines:

(1) Cutting-edge synthetic biology approaches for sensor and reporter design (TA1),

(2) Innovative engineering solutions for at-home systemic sensor administration and detection (TA2), and

(3) Seamless integration into clinical practice with digitally enabled care and established paths for diagnostic resolution (TA2).

Through this revolutionary combination, POSEIDON seeks to deliver the most sensitive, accurate, cost-effective, and accessible 30+ MCED test to all

Americans.

2.1.2 Cancer Incidence. Cancer is the second leading cause of death in the United States (U.S.) and is the leading cause of death for those under 65 years old. The number of new cancer diagnoses in 2024 is estimated to be more than 2 million, and cancer deaths over 611,000, which is equivalent to about 5,500 new cases and 1,600 deaths every day. Further, early-onset cancer has been steadily increasing for the past several decades; the global incidence of early onset cancer increased by 79% in the past 35 years and the number of early-onset cancer deaths increased by 28%. In the U.S., cancer diagnoses for patients under 50 years old increased by 13% between 2000 and 2019. Currently available screening tests are not sufficient to address the healthcare need imposed by the changing demographics of cancer patients. POSEIDON aims to overcome this challenge by delivering low-cost, accessible, at-home cancer screening for 30+ solid tumors in a single test, including many rare cancers, to Americans of all ages.

2.1.3 Cancer Detection. Cancer is difficult to detect and diagnose early (when it is most curable) and before it progresses to late stages with metastasis. 75% of cancer-related deaths are from late stage-diagnoses. Based on data collected between 2016 and 2020, 1.5 million cancer deaths were estimated to be patients with late-stage diagnoses. Over the next 30 years, more than 40 million Americans are projected to be diagnosed with late-stage cancers, accounting for 44% of all new cancer diagnoses in the US. Late-stage diagnoses are estimated to result in over 29 million deaths in the US. If half of these late-stage diagnoses could be prevented by early detection, over 8 million lives would be saved over the next 30 years, far exceeding the Cancer Moonshot goal of preventing more than 4 million cancer deaths by 2047. POSEIDON aims to contribute to the first Cancer Moonshot goal of preventing those cancer deaths by developing the next-generation MCED tests for Stage 1 detection of 30+ solid tumors.

2.1.4 Economic Burden. The patient-related economic burden of cancer in 2019 was more than $21 billion in the US, which includes out-of-pocket and patient time costs. The estimated global economic cost of cancer for the next 30 years is expected to be $32.2 trillion, with the U.S. facing 21% of the global economic burden, second only to China. In high-income countries like the U.S., treatment costs have the greatest impact on total economic cancer costs. Critically, annual treatment costs associated with late-stage diagnoses are two-to three times higher than early-stage diagnoses. Drastically reducing late-stage diagnoses by detecting cancer at Stage I will not only increase the likelihood of curative treatment but also significantly reduce total cancer care costs, restoring up to $2.3 trillion to the U.S. economy. Thus, POSEIDON's MCED tests will also make

progress towards the second Cancer Moonshot goal of improving the experience of people who are touched by cancer.

2.1.5 Underserved Populations. Cancer imposes an excessive burden on underserved and vulnerable populations. For all cancers combined, non-Hispanic Black men have the highest rate of new cancer diagnoses and non-Hispanic Black men and women have the highest cancer death rates. Further, a higher incidence of cancer and a lower likelihood of survival have been observed in rural communities, underserved populations and/or those with lower socio-economic status. Access to a low-cost cancer screening test that does not require a doctor's visit or laboratory testing is key to preventing late-stage diagnoses, increasing survival rates, and reducing high treatment costs associated with late-stage diagnoses. POSEIDON's human-centered design prioritizes cost, accessibility, user experience, and preferences as key features of technology development, translation, and commercialization efforts to ensure that the program deliverables will be accessible to the most vulnerable and underserved populations in the U.S.

2.2 Technical Approach and Structure

2.2.1 Technical Areas (TAs)

(a) The POSEIDON program will develop at-home, affordable, Multi-Cancer Early Detection kits (breath and urine) for unmatched screening of 30+ cancers at Stage 1. POSEIDON aims to identify cancers at a stage when the tumors are more responsive and less costly to treat, thus saving lives and money for Americans. POSEIDON will develop sensors and synthetic reporters to be administered at home that can detect early-stage cancer with unmatched sensitivity and specificity. The synthetic reporters are shed in urine or breath and detected with a low-cost device that integrates telemedicine with user-friendly hardware and, if necessary, provides patients and clinicians a path forward follow-up diagnosis and care.

(b) To accomplish this, POSEIDON builds upon two key disciplines:

(1) Synthetic biology, which allows for engineering of cell-free and cell-based circuits with sophisticated sensing, signal analysis, and signal output functions, and

(2) Multi-omic tumor profiling efforts, which combine genomics, transcriptomics, epigenomics, proteomics, volatilomics, and metabolomics to decipher features of tumor molecular

landscapes.

The program seeks to functionalize tumor-specific and/or pan-cancer molecular signatures via synthetic biology circuits engineered to sense and respond by releasing synthetic reporters that distinguish between cancers. To build a revolutionary, 30+ cancer MCED test, these sensors will be combined into a single library for one-time patient administration and downstream clinical implementation. The stability, sensitivity, and half-life of synthetic reporters can be altered to improve performance and overcome key limitations of endogenous biomarkers currently used in MCED tests (i.e. low quantities and short half-life in blood, high noise due to background shedding from healthy cells etc.).

(c) Synthetic sensors can be based on cell-free or cell-based designs, each with their own advantages and disadvantages. Cell-free approaches allow direct interaction between the sensor and its target molecular input(s) without a requirement for transmembrane transport (e.g., extracellular proteases in the tumor microenvironment directly activating a sensor, releasing a reporter detectable in the breath or urine). Cell-based systems on the other hand allow sophisticated genetic circuits that can take advantage of internal cellular processes (transcription, translation, transport etc.) but may be more difficult to manufacture, transport, and administer (e.g., genetic circuits that require transcription and translation of transcription factors, transmembrane proteins, RNA and/or protein-based reporters to produce a positive signal detectable in breath or urine). POSEIDON will consider all these approaches to give Performers the opportunity to select the most appropriate sensor design approach for the specific tumor signatures they are targeting.

(d) Currently, there are no at-home tests that can detect a large number of diseases simultaneously. Further, there are no-at home tests that have a sensor administration and a synthetic reporter detection component. The level of multiplexed detection required to produce distinct, non-ambiguous outputs for 30+ cancers will likely require novel engineering approaches and/or materials. Importantly, as the MCED test kit (TA2) provides the framework in which the sensors and synthetic reporters (TA1) must function, and deliverables from TA1 and TA2 must coalesce as a single product before the end of Phase 1 of the program, ready for Investigational New Drug (IND)-enabling studies (Phase 2) and clinical testing (Phase 3), efforts across both TAs must be executed in parallel and closely coordinated. The interdependent nature of the innovations

required in the two TAs is also reflected in their respective metric tables (see Tables 1-4).

(e) To accomplish this vision, the POSEIDON program is focused on two TAs:

(1) Technical Area 1 (TA1): Sensors and synthetic reporters for Multi-Cancer Early Detection.

- ❖ Development and validation of sensors and synthetic reporters for one (1) breath- based and/or one (1) urine-based detection of each of the 25 cancers listed in this ISO and at least five (5) additional cancer types selected from the provided list (30+ cancers total) (see Figure 1). Performers must provide a clear justification for their selection of the remaining five+ (5+) cancer types. Selection criteria may include (but are not limited to) documented unmet need and/or excessive burden on underserved communities, the availability of representative experimental models for testing and/or cancer specific signatures for sensor design.
- ❖ Each sensor platform must meet the performance metrics for Stage 1 detection and tissue of origin prediction specified in Tables 1 and 2.
- ❖ Cell-free sensor technologies in this TA may include (but are not limited to) activity-based sensors with peptide, nucleic acid, other synthetic small molecule and/or macromolecule components, which may be coupled with biocompatible carriers to optimize safety, targeting, and/or biodistribution.
- ❖ Sensor designs may leverage innovative synthetic circuits, multi-layer logic gates, and positive and negative feedback loops to detect and respond to complex cancer-specific molecular signatures in the tumor micro-environment. They may also include signal amplification and multiplexed reporter detection strategies to improve sensitivity, specificity, and tissue of origin prediction.
- ❖ Sensor designs leveraging internal cellular processes including (but not limited to) transcription, translation, membrane transport, intracellular biosynthesis pathways, metabolite sensitive promoters and/or transcription factors and complex nucleic acid-based circuits that may not have

optimal stability and/or function in a cell-free setting are also appropriate for this TA. Cell-based sensor technologies may include any design that includes engineered live cells (prokaryotic or eukaryotic) and/or non-living artificial cells.

- ❖ Synthetic reporters may include (but are not limited to) synthetic or genetically encoded nucleic acids, proteins, other small molecules, metabolites and/or macromolecules that can produce distinct, non-ambiguous outputs in response to the presence of each cancer targeted by the test as well as negative (i.e. no cancer) and inconclusive results.
- ❖ Proposals for TA1 must also include TA2.
- ❖ Each Performer team must build one urine-based and/or one breath-based detection platform.
- ❖ Sensor and synthetic reporters must be designed to be compatible with TA2 metrics (Tables 3 and 4) and meet the accessibility and commercialization requirements of the program (Tables 5 and 6).
- ❖ As the sensor administration and reporter detection modalities developed in TA2 define the framework in which sensor designs must function, TA1 and TA2 metrics are highly interdependent. As a result, satisfactory progress in TA1 will require that sensors and reporters developed in TA1 also meet the performance metrics for sensor administration and reporter detection modalities described in TA2.

(2) Technical Area 2 (TA2): A cancer screening device kit for Multi-Cancer Early Detection.

- ❖ Development and validation of a low-cost, simple-to operate MCED test kit that integrates sensors and synthetic reporters from TA1. Each device kit must include hardware and software components for systemic sensor administration (e.g., intranasal, oral, intramuscular, intradermal), sample collection (breath or urine), biomarker detection (integrated smartphone reader/imaging), results transmission, and reporting.
- ❖ Teams may propose a plan to generate up to two kits in the following permutations: (A) one for urine-based detection,

(B) one for breath-based detection, or (C) both urine-based and breath-based kits.

- ❖ Multiplexed detection modalities should be low-cost at scale and may include (but are not limited to) paper-based lateral flow enzymatic assays, semi-conducting single-walled nanotube arrays, or bio-/chemi-luminescent readouts. Further, the kit must be designed for full interoperability with Electronic Health Record (EHR) systems and digitally enabled care.
- ❖ TA2 must establish smartphone connectivity through established EHR modalities for secure transmission of test results to a health care provider (HCP), and subsequent reporting of these results by an HCP to the patient through a telemedicine visit.
- ❖ All proposals must include TA2.

(f) Sensor administration and multiplexed reporter detection modalities must be designed in parallel with the sensors and synthetic reporters from TA1 and must meet performance metrics specified not only for TA2 but also for TA1. Iterative design, building, testing, and optimization of TA2 prototypes is expected to ensure that sensor function is not compromised and will accommodate any changes to sensor and reporter designs in TA1. As a result, satisfactory progress in TA2 will require that sensor administration and reporter detection modalities developed in TA2 also meet the *in vitro* and *in vivo* sensor performance metrics specified in TA1.

(g) Proposers can submit proposals that cover these two TAs in one of the following Technical Approaches:

(1) Technical Approach A: TA1 + TA2; urine-based test
(2) Technical Approach B: TA1 + TA2; breath-based test
(3) Technical Approach C: TA1 + TA2; breath-based test and urine-based test

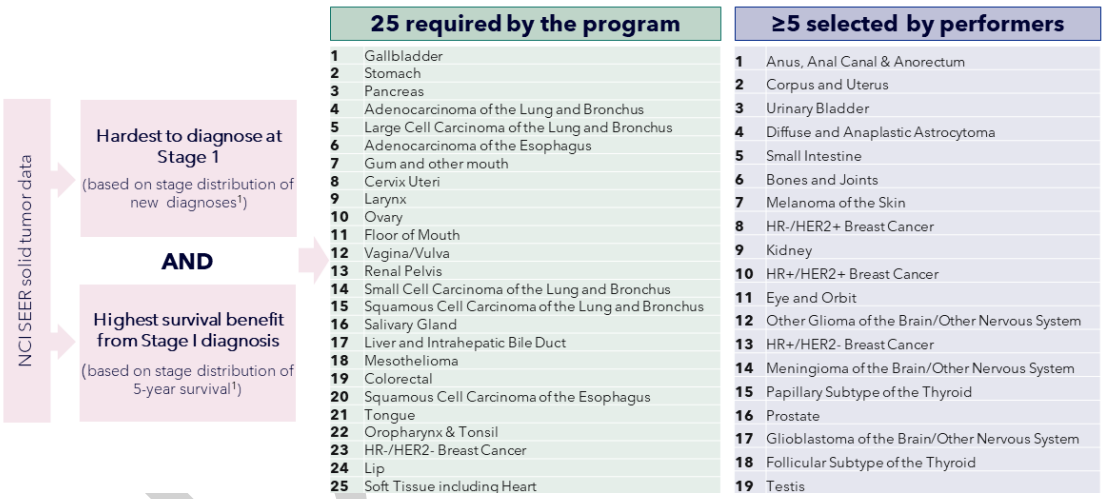
Proposals that fall outside of these three approaches or fail to propose all components required to build one breath-based and/or one-urine-based MCED, will be deemed non-conforming and rejected without further review. A successful proposal will account for all program requirements outlined in this ISO, both TA-specific and overall program metrics.

2.2.2 Cancer Selection Process:

(a) To meet POSEIDON's vision to transform cancer care with a simple at-home test for multi-cancer screening, all proposed tests must detect the 25 cancers in the list provided below and at least five additional cancers of the Performer's choice (Figure 1). These cancers are selected based on an analysis of cancer incidence counts, stage distribution of incidence cases, and five-year relative survival rates publicly available from the National Cancer Institute's (NCI) *Surveillance, Epidemiology and End Results* (SEER) program. To prioritize cancers most likely to benefit from an MCED test, each cancer type is scored using two independent selection categories:

(1) hardest to diagnose early, and
(2) greatest survival benefit from early detection.

Figure 1: 25 cancers and a description of how the list was generated



(b) To identify tumors that are hardest to diagnose early, the SEER dataset was sorted and ranked based on the percentage (%) distribution of new diagnoses at a localized stage from smallest to largest.

(c) To identify tumors with the largest increase in survival upon earlier diagnosis (i.e., an extended survival benefit from diagnosis at Stage 1), the difference in 5-year relative survival rates for patients diagnosed with regional and localized disease was calculated for each cancer type, and cancers were sorted from largest to smallest based on the survival differential.

(d) To select the final cancer list, cancer types were assigned priority scores for each category separately (i.e., hardest to diagnose early and largest

survival benefit upon earlier diagnosis). A cumulative priority score was calculated for each tumor type and used to identify the 25 cancers with the highest cumulative priority scores that are required by the program. Cancers with lower priority rankings make up the second list where Performers are required to select at least five cancers to include in their tests and include sufficient justification for their selections.

(e) We acknowledge that there are additional cancer types not represented in this list. The POSEIDON program's cancer selection process prioritizes cancers for which

(1) detailed stage distribution of cancer incidence and survival data are available, and
(2) well-established experimental models that will be necessary for preclinical validation studies exist and are broadly available.

Further, the POSEIDON Program only focuses on solid tumors as there is an urgent, unmet need for novel early detection technologies for solid tumors. Liquid biopsy-based cancer early detection tools currently in development are far more likely to be effective for blood cancers than Stage 1 detection of solid tumors. Despite these limitations, the 30+ solid tumors this program aims to detect will substantially reduce the death rate from cancer and the overall socio-economic burden of the disease for all Americans.

2.2.3 Technical Area 1 (TA1): Sensor and synthetic reporter development for Multi-Cancer Early Detection

(a) TA1 aims to develop sensors and synthetic reporters capable of detecting Stage 1 tumors. Technologies in this TA may include (but are not limited to) cell-free, activity-based sensors with peptide, nucleic acid, other synthetic small molecule and/or macromolecule components, which may be coupled with biocompatible carriers to optimize safety, targeting and/or biodistribution. Sensor designs may leverage innovative synthetic circuits, multi-layer logic gates, and positive and negative feedback loops to detect and respond to complex cancer-specific molecular signatures in the tumor microenvironment. Approaches may also include any design that includes engineered live cells (prokaryotic or eukaryotic) and/or non-living artificial cells. Cell-based sensor designs may include genetic circuits that leverage internal cellular processes including but not limited to transcription, translation, membrane transport and intracellular biosynthesis pathways for both sensing and reporting. They may also

include signal amplification and multiplexed reporter detection strategies to improve sensitivity, specificity and tissue of origin prediction. Collectively, the sensors that make up each MCED test must be capable of :

(1) Uniquely identifying each cancer type covered by the test upon systemic deployment into the body,
(2) Producing a synthetic reporter that can be detected in the urine and/or breath that indicates the presence of cancer, and
(3) Producing a distinct signal or a barcode that identifies the cancer type or the tissue of origin.

(b) Identifying the cancer specific signatures (i.e., molecular zip codes) that sensors will be designed to detect is a critical first step of this TA. Cell-free, activity-based sensor designs require inputs that are readily available and active in the tumor micro-environment. To this end, cancer metabolomic atlases, proteomic datasets that catalog extracellular enzyme activity profiles (e.g. transmembrane and/or extracellular proteases, glucosidases, nucleases, etc.), extracellular DNA and/or RNA atlases and secretomes could all be used to identify molecular signatures that will be used in sensor design and building. Further, transcriptomics datasets can be used to identify differentially expressed extracellular or transmembrane proteins to guide sensor designs. Cell-based sensors may include genetic circuits that leverage internal cellular processes including but not limited to transcription, translation, membrane transport and intracellular biosynthesis pathways for both sensing and reporting. As a result, cancer-specific signatures for cell-based sensors may leverage tumor microenvironment responsive promoters, enhancers and or transcription factors, tumor specific extracellular and/or transmembrane proteins, or antigens with no enzymatic activity. To this end, additional cancer-omics datasets, including (but not limited to) genomic, transcriptomic (mRNA, microRNA, non-coding RNA etc.) atlases, non-activity based proteomic datasets and/or cancer immunopeptidome data (i.e., cancer antigen atlases) could be used to identify molecular signatures for sensor design and -building. Performers may utilize publicly available datasets or may propose to build their own datasets during Phase I of the program, if consistent with program timelines. In either case, Performers will have to demonstrate, experimentally and/or computationally, that signatures selected for sensor building have high enough classification accuracy to be able to meet the *in vivo* performance metrics of the program in preclinical studies.

(c) Sensor designs must meet all technical and non-technical program requirements and performance metrics specified in this solicitation. Sensors that are not compatible with systemic self-administration (e.g. require IV injection or administration by a healthcare provider) or reporter detection in the urine and/or breath are not compliant with the program and will not be considered.

2.2.4 Technical Area 2 (TA2): A cancer screening kit for Multi-Cancer Early Detection

(a) TA2 aims to develop a low-cost, simple to operate test kit that integrates sensor and reporter designs from TA1 into a device designed for at home screening. All approaches will be considered if they allow:

(1) self-administration for systemic deployment of sensors,
(2) breath and/or urine sample collection and
(3) reporter detection without a requirement for a healthcare provider, hospital visit, or laboratory testing.

(b) Each kit must include all the hardware and software components necessary for

(1) at-home sensor administration and synthetic reporter detection,
(2) integration with EHR systems and telehealth capabilities to relay results to test-takers and healthcare providers for digitally enabled care, and
(3) pre-established paths for diagnostic resolution to recommend to patients with positive results that can also connect them with the nearest hospital for diagnostic work-up and care.

(c) Potential sensor delivery routes may include (but are not limited to) intramuscular, intranasal, oral, or transdermal. Multiplexed detection modalities should be low-cost at scale and may include (but are not limited to) paper-based lateral flow enzymatic assays, semi-conducting single-walled nanotube arrays, bio-/chemi-luminescent readouts, or photoionization/ ion mobility spectroscopy for detection of volatile compounds.

(d) As sensor administration and multiplexed detection modalities must be specifically tailored to the sensor and reporter designs proposed in TA1, the TA2 objectives are strongly tied to those of TA1. Therefore,

performers must carefully consider the requirements for TA1 in their TA2 designs. Given the interdependent nature of TA1 and TA2, Performers must coordinate sensor design, sensor administration, and multiplexed device-enabled detection modalities (e.g., smartphone or separate hardware for detection and EHR interoperability) to allow for home-based use to detect all 30+ cancers from the initiation of the program to ensure compatibility and optimization of test requirements. The user interface should provide easy-to-use test instructions and facilitate test administration. In addition, the test kit must be designed for full interoperability with EHR systems and digitally enabled care. TA2 must establish smartphone connectivity through established EHR modalities for secure transmission of test results to a health care provider (HCP), and subsequent reporting of these results by an HCP to the patient through a telemedicine visit with subsequent HCP recommendations to diagnostic resolution for positive tests. The device and software should optimize the test performance using the growing pool of real-world data generated as the program progresses.

(e) Both the hardware and software components of the kit design must meet all technical and non-technical program requirements and performance metrics specified in this solicitation. Kit designs that are not compatible with at-home screening and/or lack any of the aforementioned capabilities are not compliant with the program and will not be considered.

2.3 Program Structure

2.3.1 POSEIDON Phases. The POSEIDON program includes three sequential Phases that cover key steps of the preclinical and clinical technology development pipeline.

- POSEIDON Phase 1 is 36 months and includes sensor discovery, development and preclinical validation using animal models of cancer.
- POSEIDON Phase 2 is 15 months and includes IND-enabling non-clinical ADME/PK (Absorption, Distribution, Metabolism, Excretion/ Pharmacokinetic) studies to evaluate the safety and behavior of sensors.
- POSEIDON Phase 3 is 9 months and focuses on the first-in-human clinical testing of MCED kits for safety and efficacy in a Phase1b/2a clinical trial.

2.3.2 Performance Evaluations. To ensure program success, each POSEIDON phase will include regular performance evaluations, including (but not limited to) monthly, semi-annual, and annual progress reports. In addition to the technical

requirements associated with each TA and Phase, the POSEIDON program also includes additional metrics designed to guide and monitor each Performer's commercialization, regulatory engagement, and accessibility efforts, which are integral components of the overall program design.

2.3.3 Comprehensive Checkpoints. Further, there will be comprehensive check points at transitions between POSEIDON phases, which will evaluate both technical performance and readiness for the next phase. These include (but are not limited to) the establishment of Good Laboratory Practice (GLP) and current Good Manufacturing Practice (cGMP)-compliant manufacturing practices, Institutional Review Board (IRB) approval of clinical trial protocols, and demonstrated adherence to accessibility metrics and demographic requirements. Progression into each subsequent phase of the program will depend on the Performer's performance and the availability of funding.

2.3.4 Go/No-Go Determinations. The expectation is that Performers will develop plans that accommodate the rapid nature of the ARPA-H program schedule. We anticipate that innovative project management approaches by each team to achieve the fast timelines will be required. The iterations and experimental steps in Phase 1 require sufficient forecasting of risk and alternative methods to avoid delays in the programmatic schedule. Failure of a test to meet the metrics of Phase 1 will result in a "No-Go" for that test, or for that Performer team if only one test has been proposed. Therefore, the Performer's ability to iterate quickly will be required to eliminate the chance of a "No-Go" determination by ARPA-H. The specific goals, which align with the program metrics in Section 2.5, are described per TA and phase below. It is the Proposer's responsibility to propose methods to accomplish the goals and mitigate potential risks and delays in the POSEIDON program.

2.3.5 Technical Areas

(a) POSEIDON Phase 1 (36 months): Discovery & Development

(1) During the 36-month POSEIDON Phase 1, Performers will establish and validate sensors and synthetic reporters for breath-based and/or urine-based Stage 1 detection of 30+ solid tumors, which will include the 25 cancers specified previously and at least 5 selected by the Performer from the list provided in this solicitation. Each Performer team must pass three gated checkpoints that evaluate the *in silico*, *in vitro,* and *in vivo* performance of their designs (Table 2).

a. Identification of tumor-specific signatures that will be used as inputs for the "sensing modules" of proposed sensors and demonstration of their classification accuracy

b. *in vitro* validation of sensor performance, which may include evaluation of the specificity and kinetics of reporter release and demonstration of logic gate performance in logic truth table tests

c. *in vivo* validation of sensor performance in relevant experimental models of cancer. Performers must provide a justification for their cancer model selection and must demonstrate that cancer models capture the overall genetic complexity and diversity of cancers they represent.

(2) Simultaneously in POSEIDON Phase 1, the Performers will also develop the hardware and software components required to package, administer, and detect the sensors and reporters from TA1. Sensors and synthetic reporters must be designed for systemic distribution without the need for intravenous delivery. Delivery routes may include oral, nasal, transdermal, microneedle, or other minimally invasive procedures that a patient could perform on themselves. Each Performer team must pass two gated checkpoints for TA2 that demonstrate *in vitro* and *in vivo* performance of their MCED kit designs (Table 2).

a. *in vitro* demonstration that sensor formulation, sensor administration and multiplexed detection modalities do not reduce the sensor and synthetic reporter performance.

b. *in vivo* verification of the sensor administration and multiplexed reporter detection components of each kit.

(3) By the end of POSEIDON Phase 1, all Performers will establish and validate that their designed sensors and reporters

a. achieve systemic distribution without intravenous (IV) administration, and
b. require at most one sensor administration step for all ≥30 solid tumors.

The vision is that the test can be taken more than one time a year at the patient's and/or healthcare provider's discretion; however, each test must only require one administration step of the sensors.

(4) ARPA-H anticipates that teaming will be required to accomplish the discovery and development of TA1 and TA2 during POSEIDON Phase 1 with the potential for concurrent, collaborative teams of lab scientists (TA1) and hardware/software engineers (TA2). Teaming is highly encouraged to accomplish the timelines of POSEIDON Phase 1.

(b) POSEIDON Phase 2 (15 months): Non-Clinical Testing
During the 15-month POSEIDON Phase 2, Performers will validate the performance of their MCED kit(s) in IND-enabling studies, and manufacture kits in anticipation of clinical validation.

(c) POSEIDON Phase 3 (9 months): Clinical Testing
During the 9-month POSEIDON Phase 3, Performers will clinically validate their at-home screening test kits. A Phase 1b safety study will be conducted with 30 asymptomatic individuals, followed by a Phase 2a clinical study with 100 individuals who have been previously diagnosed with Stage 1 cancer.

2.3.6 Accessibility Requirements

ARPA-H has indicated it is committed to equitable healthcare access irrespective of race, ethnicity, gender/gender identity, sexual orientation, disability, geography, employment, insurance, and socio-economic status. It is also the goal of the program to negotiate full coverage through all health insurance via US government entities (Center for Medicare and Medicaid Innovation (CMMI), Centers for Medicare & Medicaid Services (CMS), Indian Health Service (IHS), and more) so that POSEIDON screening kits are accessible to all. To that end, POSEIDON will mandate that each Performer accounts for and actively engages with an Engagements Officer (EO) who will be dedicated to the project. The EO will also be responsible for onboarding at least one Outreach Coordinator (OC). Together, they will ensure that all Performers follow the FDA's guidance titled "*Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials*" and that clinical trial populations reflect the same US population proportions and severity as those affected by cancer through patient-centric design. The EO and OC will be approved by ARPA-H and will help perform key duties throughout all POSEIDON Phases, as described below.

2.3.7 POSEIDON EO and OC Metrics

The EO and OC will proactively work to ensure equitable demographic representation throughout the program, understand the unique barriers to healthcare access for different populations, and tailor all end-products for broad accessibility for all Americans. Further, some populations will be more difficult to reach due to historical disenfranchisement, lack of other government investments, and distrust of government programming. Significant work may be required to bring these Americans to the table, and it is ARPA-H's expectation that Performers and the EO and OC will do so. Performers and the EO and OC must seek out and establish mutually respectful relationships with community leaders and pre-existing communities of care.

2.3.8 POSEIDON Phase 1 Accessibility

Goals of POSEIDON Phase 1 for accessibility (metrics defined in Section 2.5)

- A dedicated Engagements Officer (EO)and at least one Outreach Coordinator (OC) on staff by Q1 FY1.
- >5 listening sessions targeting communities most vulnerable to cancer burden.
- Establish a Cancer Outreach Program (COP) for CX/UX design thinking, product optimization, community outreach, patient/provider buy-in.
- Generate an Affordability Plan to demonstrate how tests will be accessibly priced. Ideally, the final unit price should be ≤$100.
- Create the Insurance Action Plan, the Annual Road Map to Accessibility report, and provide annual progress updates.
- Generate the "*Race and Ethnicity Diversity Plan for Clinical Studies*" for submission to the FDA.

2.3.9 POSEIDON Phase 2 Accessibility

Goals of POSEIDON Phase 2 for accessibility (metrics defined in Section 2.3)

- Generate annual progress reports for the COP, Insurance Action Plan and the Road Map to Accessibility Plan
- Develop a plan for the nation-wide expansion of COP to promote screening uptake
- Demonstrate adherence to Phase 1 equity and accessibility metrics in the clinical study design

2.3.10 POSEIDON Phase 3 Accessibility

Goals of POSEIDON Phase 3 for accessibility (metrics defined in Section 2.5)

- Demonstrate continued adherence to equity and accessibility metrics from prior Phases and clinical study demographic requirements.

Additionally, any Performer across all TAs that does not meet the Accessibility Key Performance Indicators (KPIs) set by the EO may also be given a "No-Go" determination.

2.3.11 Commercialization and Regulatory Engagement

(a) The ARPA-H mission is to improve health outcomes for all Americans, and a significant part of improving outcomes is bringing innovations to market. To this end, POSEIDON has a series of commercial development- and government regulatory agency engagement milestones that Performers are required to meet. These milestones will help ensure that preclinical and clinical development of POSEIDON tests follow regulatory requirements and ideally position the Performers for commercial success after clinical validation. The teams will be required to submit 1 overall Commercialization Plan (CP) that combines 5 areas of focus for commercialization of POSEIDON-developed technologies. Within the CP for each Performer team, the Performer will be required to document sufficient progress based on their efforts toward the commercialization metrics of the program.

(b) The 5 areas of focus in the CP are:

1. Corporate Structure and Commercialization,
2. Intellectual Property (IP) Success Framework (IPSF), which includes the IP Development and Management (IPDM),
3. Regulatory,
4. Pricing Model, and
5. Market, Customer, and Competition Analysis (which includes Porter's *5 forces analysis*).

These reports should include sufficient detail to ensure that POSEIDON-funded technologies will be commercialized and successfully stay in the market to help all Americans. Thus, these deliverables should also include, at a minimum:

- risk assessments,
- risk mitigation plans,
- alternative strategies,
- quality management systems approach,
- manufacturing plans,
- corporate structure,
- IP protection,
- non-disclosure (NDA) strategy, and

- financing plans.

(c) The first CP report will be due at the end of Q1 FY1. The cadence of subsequent CP reports will be determined at ARPA-H's discretion and may range from quarterly to semi-annually. The Performers will incorporate all components of the commercialization metrics into the appropriate portions of the overall CP. The CP will serve as the actionable steps necessary to ensure the maximum number of POSEIDON technologies are successful. The template for the CP will be provided to enable the Performers to plan accordingly for necessary tasks.

(d) Within the CP, the Performers will be required to develop an overarching infographic that overlays the timelines for start and end periods of each step in Research & Development (R&D):

- regulatory (as defined by the metrics),
- commercialization,
- IP filings,
- pricing,
- market analysis, and
- accessibility.

This infographic should include significant detail regarding each required step that extends beyond the general goals of the POSEIDON metrics. Additionally, the timelines should make logical sense in terms of the sequence of events based on known timelines for each process (e.g., Intellectual Property filing, Food and Drug Administration (FDA) interactions, etc.). For example, the overlayed timelines should include:

- the time for R&D of the first sensor,
- when invention disclosures will be filed,
- when a provisional patent will be issued,
- when a potential commercialization advisory board (CAB) will be hired,
- when a 60- or 75-day request for meeting with the FDA will be initiated,
- when or if multiple informational meetings with the FDA will be requested, etc.

Notably, this is an example to support the Performers when developing this infographic timeline. Therefore, the Performers should develop their

own bespoke CP and overarching infographic based on their team's proposed technologies and the additional considerations, such as areas to truncate timelines where appropriate, within their institutions.

(e) The POSEIDON program will require state-of-the-art experimental testing that utilizes current Good Manufacturing Practices (cGMP) and Good Laboratory Practice (GLP)-compliant manufacturing. The timelines from discovery and development in POSEIDON Phase 1 will likely require partnerships to accomplish the metrics. The CP and the infographic will be utilized to streamline the processes from lab experiments to protocol tradeoff to GLP and cGMP partnership. The timelines and scale for manufacturing are critical to the success of the program and the program metrics will require manufacturers with the ability to accomplish the metrics of the program. Each Phase of the program requires manufacturing success; for example, the transition to IND-enabling studies requires GLP manufactured products. The ability to accomplish these manufacturing metrics within the timelines must be demonstrated within the infographic and Commercialization Plan.

(f) The regulatory timelines for this project are defined in the metrics as well; however, the government understands that conversations with the FDA and the timelines of R&D may justify changes to the regulatory timelines. ARPA-H aims to accelerate timelines for regulatory approvals through dedicated metrics and emphasis on commercialization and regulatory milestones without compromising product safety or efficacy to proceed with Phase 1 clinical trials. Given that, ARPA-H and the POSEIDON Program Manager may provide additional resources and efforts to assist the Performers in accomplishing these challenging metrics in the spirit of the ARPA-H mission to improve health outcomes for all Americans.

(g) As described above and defined in the metrics tables below, POSEIDON Performers will meet rigorous metrics and milestones that ensure future translational success into the clinic. Performers may routinely interface with U.S. government stakeholders (e.g., NCI and FDA) at portfolio reviews and through CDRH *Q-Submissions, Breakthrough Device Designation* and CBER *INitial Targeted Engagement for Regulatory Advice on CBER ProducTs* (INTERACT) meetings, as appropriate. Performers will be expected to stay on a strict regulatory timeline so that they can file for a "Breakthrough Designation" and ideally, qualify for CMS *Parallel Review with Transitional Coverage for Emerging Technologies* (TCET) designation as well. Through a partnership between the POSEIDON Program Manager (PM) and NCI CSRN leadership, the

POSEIDON Program has established a Memorandum of Understanding (MOU) with NCI's CSRN to ensure these technologies are on a consistent path to the CSRN for continued, post-program clinical trial. This NCI CSRN/POSEIDON collaboration will allow teams that successfully complete the program to have a linear path to large-scale clinical trials with established networks that are assembled by the NCI for cancer screening trials.

(h) Ultimately, success in POSEIDON doesn't only mean the creation of revolutionary technologies; it also means meeting regulatory, accessibility, and commercial milestones that will ensure these technologies successfully enter the CSRN pipeline and have a clear, accessible path to all patients regardless of their socioeconomic status. As such, POSEIDON Performers will create an Affordability Plan to demonstrate how tests will be accessibly priced, with the ideal unit price of the final product at ≤$100 (see metrics table in Section 2.5). The price was set based on the near-unanimous selection of the price threshold in an anonymous, IRB-approved pre-survey across thousands of Americans that was employed for the human-centered development of the POSEIDON program. The Government anticipates the assessment of unit prices will vary based on the technological approach to accomplish the metrics for TA1 and TA2. Success for POSEIDON ideally entails accessible and revolutionary technology for the greatest impact for all Americans and those afflicted by the continuing cancer burden.

2.3.12 POSEIDON Phase 1 Commercial and Regulatory Engagement

Goals of POSEIDON Phase 1 for commercialization and regulatory engagements (metrics defined in Section 2.5):

- All teams must have a commercial entity (ideally the Prime) on contract by kick-off that will house or have a pre-existing licensing agreement to use all IP generated within POSEIDON from day 0 to month 60.
- IP Development and Management (IPDM) & Commercialization and Regulatory Engagement (CaRE) teams on staff by Q1FY1.
- Generate annual IPDM and CaRE Reports, and updated Phase 2/3 plans.
- Submit Pre-RFD/RFD (Request for Designation) (if necessary), Pre-Sub/Q-Sub, Breakthrough Device, and INTERACT Applications.
- Submit a draft Target Product Profile (TPP) by end of Q9 and an Updated TPP at the end of Q12 that integrates features of Minimum Viable Product (MVP).

2.3.13 POSEIDON Phase 2 Commercial and Regulatory Engagement

Goals of POSEIDON Phase 2 for commercialization and regulatory engagements (metrics are defined in Section 2.5):

- Generate annual IPDM and CaRE Reports
- Submit Pre-IND and IND/IDE applications at times specified in the ISO
- Obtain IRB approval for clinical study protocols and consent forms
- Submit Revised TPP, Draft Go-to-Market (GTM) Strategy, & optimized MVP design

2.3.14 POSEIDON Phase 3 Commercial and Regulatory Engagement

Goals of POSEIDON Phase 3 for commercialization and regulatory engagement (metrics are defined in Section 2.5):

- Produce a Comprehensive Commercial Viability Assessment Report
- Submit Final TPP & Finalized GTM Strategy

2.4 Program Team Requirements

2.4.1 Teams must present a plan to have a qualified team of expert advisors with adequate level of effort and subject matter expertise to ensure translation and commercialization of the downstream tests. These team members should include personnel with expertise in (but not limited to) regulatory, reimbursement, commercialization, manufacturing, software development, and medical device development.

2.4.2 Program teams must also include a Project Manager, Engagements Officer, and at least one Outreach Coordinator . The Project Manager must be full-time. Unless sufficiently justified otherwise, the government's assumption is the other key personnel will be proposed for at least a minimum of a 0.5 full time equivalent and cannot be the same person.

2.5 Program Metrics

2.5.1 Objects and Metrics Categories

To evaluate how effectively a proposed solution will achieve the stated program objectives, the government hereby promulgates the following program metrics that may serve as the basis for determination of satisfactory progress to warrant continued funding. Performance will be assessed against program objectives and metrics that fall into the following broad categories:

- technical/scientific
- commercialization
- regulatory engagement and

- accessibility

2.5.2 Monthly Status Reports

Monthly status reports that describe progress in each category, as well as the financial status of each POSEIDON project, will be required from the Performer and will be evaluated by the ARPA-H Program Manager Team and discussed at monthly meetings. ARPA-H may alter the cadence of such reports and meetings and may request additional Performer data as deemed necessary to evaluate technical and non-technical progress as deemed necessary. Other U.S. government stakeholders (including the FDA and the NCI) may participate at Performer portfolio reviews to provide feedback to ARPA-H Program Manager Team. The expected metrics and objectives for each TA and phase as well as overall program metrics that are not TA-specific are defined below (Tables 1-6)

2.5.3 Proposal Requirements

Although the program metrics are specified below, Proposers should note that the government has identified these goals with the intention of bounding the scope of effort while affording maximum flexibility, creativity, and innovation of proposed solutions to the stated problem. Proposals should cite the quantitative and qualitative success criteria that the effort will achieve by each Phase's program milestone and intermediary metric measurement.

2.5.4 TA1 Metrics and Objectives

The overall program goals for TA1 are listed in Table 1. The expected metrics per phase in TA1 are listed in Table 2. In addition to frequent performance reviews throughout the phases, Performers must provide an end-of-phase final report that summarizes all efforts and data for each completed POSEIDON Phase. TA1 metrics and objectives are closely linked with metrics and objectives of TA2, which are listed in Tables 3 and 4. Satisfactory progress in TA1 will require successful completion of several TA2 objectives, therefore, all TA1 efforts must be coordinated with those of TA2.

Table 1. TA1 Overall Program Goals

Metrics	Specifications
# of Tests	Up to 2
Detection Method(s)	1 urine-based and/or 1 breath-based method for stage I detection of the ≥30 solid tumors listed in the ISO and identification of their tissue of origin.
Sensor Design	Synthetic sensors and reporters for stage 1 detection of the ≥30 solid tumors listed in the ISO and identification of their tissue of origin.
Performance Metrics	≥90% sensitivity, ≥99.9% specificity, ≥95% Tissue of Origin (TOO) prediction accuracy.
Gated Checkpoints	Each team must pass the three gated checkpoints outlined in Table 2 that evaluate the *in silico*, *in vitro* and *in vivo* performance of their design
Manufacturing	GLP-compliant manufacturing of sensor and synthetic reporter libraries for non-clinical IND-enabling studies (n≥15)

Table 2. TA1 Metrics for Each Phase and Sub-Phase

Metrics	Specifications
[Q1-Q12]	Phase 1: Discovery and Development
End Products	1 breath-based and/or 1 urine-based Multi-Cancer Early Detection assay
Sensor Design	Cell free and/or cell-based synthetic sensors and reporters for stage 1 detection of the ≥30 solid tumors listed in the ISO (25 solid tumors required by the ISO and ≥5 additional cancers from the provided list).
Performance Metrics	*In silico:* By the end of Q3, demonstrate, experimentally and/or computationally, ≥80% cancer type classification accuracy of signatures selected for sensor development. *In vitro*: By the end of Q5: 1. Demonstrate >5-fold increase in reporter release, and >2 signal-to-noise ratio in relevant *in vitro* tests, including tests with spiked urine and/or breath. Additional assays and performance criteria may be required depending on the nature of the sensors and synthetic reporters. 2. Meet TA2 Phase 1 *in vitro* performance metrics for sensor administration and multiplexed reporter detection (Table 4) *In vivo*: By the end of Q9, achieve ≥90% sensitivity, ≥99.9% specificity, ≥95% Tissue of Origin (TOO) prediction accuracy of each test in at least 2 genetically distinct experimental models representative of the genomic landscape of each tumor type. *In vitro* and/or *in vivo* tests of optimized sensor libraries may continue until the end of phase 1, when the features of a minimum viable product (MVP) are established.
Preliminary safety/ efficacy correlation	Using *in vivo* safety/efficacy correlation data from *in vivo* validation studies, select up to 5 sensor doses for nonclinical testing (phase 2)
Minimum Viable Product (MVP) Features	Integrate the finalized sensor and synthetic reporter libraries (TA1) with hardware and software components of each MCED test kit (TA2) to define and lock in the features of the MVP
Manufacturing	GLP compliant manufacturing of sensor and synthetic reporter libraries for nonclinical IND-enabling studies (n≥15)

Note: By the end of phase I of the Program, Performers are expected to combine deliverables from TA1 (Tables 1,2) and TA2 (Tables 3,4) to establish an integrated product for IND-enabling studies (Phase 2) and clinical testing (Phase 3). As a result, Phase 2 and Phase 3 metrics and objectives are not TA specific and are listed in the section 2.5.6, *Additional Program Metrics and Objectives*, which covers program goals that are not TA-specific (see Tables 5 and 6)

2.5.5 TA2 Metrics and Objectives

The overall program goals for TA2 are listed in Table 3. The expected metrics per Phase in TA2 are listed in Table 4. In addition to frequent performance reviews throughout the Phases, Performers must provide an end-of-phase final report that summarizes all efforts and data for each completed POSEIDON Phase. TA2 metrics and objectives are closely linked with metrics and objectives of TA1, which are listed in Tables 1,2. Satisfactory progress in TA2 will require successful completion of several TA1 objectives, therefore, all TA2 efforts must be coordinated with those of TA1.

Table 3. TA2 Overall Program Goals

Metrics	Specifications
POSEIDON Kit	Create up to 2 low-cost, simple-to-operate test kits (one urine-based test, one breath-based test, or one of each), for at-home screening of sensors from TA1. Teams must generate hardware and software components to administer sensors for multiplexed detection of 30+ cancers for each test. Should a Performer team elect to generate two tests, breath and urine, they may use the same kit components. Design should follow guidance set forth in FDA-2012-D-1161 for devices intended for home use and industry best practices.
Gated Checkpoints	Each team must pass the two gated checkpoints outlined in Table 4 that evaluate the *in vitro* and *in vivo* performance of their design
Sensor Administration	Create 1 systemic sensor administration modality for each test kit. Must also meet the sensor performance metrics specified in TA1. Sensors must be delivered via a self-administration modality that is less invasive than intravenous injection (e.g., intramuscular, intranasal, oral, intra-/transdermal, etc.). Must not require a healthcare provider or a hospital visit. For successful completion, design, building and testing must be coordinated with TA1 efforts.
Sample Collection	Produce one receptacle for at-home collection of each sample type (unprocessed urine and exhaled breath)
Sample Testing and Multiplexed Detection	Produce all hardware components required for sample testing and multiplexed synthetic reporter detection at home. 1. Must produce distinct, non-ambiguous outputs unique to each of the 30+ cancers, for the absence of cancer and for inconclusive tests. 2. Must meet test performance metrics specified in TA1. 3. Must include positive and negative controls. 4. Must be designed for seamless integration with the software components to deliver results to the test taker through EHR integration.

	For successful completion, design, building and testing must be coordinated with TA1 efforts.
Digital App	Produce 1 telemedicine-enabled and EHR system-integrated companion digital app for the test(s). Must be compliant with all relevant FDA guidelines for medical software development and should follow industry best practices (e.g., International Electrotechnical (IEC) and International Organization for Standardization's ISO guidelines)
Patient UI/UX	Produce 1 interactive interface that provides test instructions and additional educational resources to test-takers.
Patient/HCP Interaction	Produce 1 secure telemedicine interface to deliver test results through a HCP within 96 hours, facilitate subsequent patient-provider communications and EHR system integration of test results.
Path to Diagnostic Resolution	Cancer-type specific diagnostic paths to follow-up positive test results for each cancer type covered by the test, to be delivered to test takers as customized recommendations through a HCP.
Kit Performance & Compliance	1. Meets or exceeds relevant FDA guidelines for GLP Quality System requirements. 2. Meets or exceeds relevant FDA guidelines for Bench Performance Testing for device.
Minimum Viable Product (MVP) Features	Integrate the finalized synthetic sensor and reporter libraries (TA1) with hardware and software components of each MCED test kit (TA2) to define and lock in the features of the MVP

Table 4. TA2 Metrics for Each Phase and Sub-Phase

Metrics	Specifications
[Q1-Q1]	Phase1: Discovery and Development
Kit Hardware	1 urine-based MCED test and/or 1 breath-based MCED test with validated hardware components for sensor administration, sample collection and detection. If two tests are being generated, they may use the same kit components. Design should follow guidance set forth in FDA-2012-D-1161 for devices intended for home use and industry best practices.
Sensor Administration	≥1 FDA-compliant systemic sensor delivery method that allows self-administration. Must not require a healthcare provider or a hospital visit.
Sample Collection	Produce sample collection receptacles for unprocessed urine and/or exhaled breath at home.
Multiplexed Sensor Detection	1. ≥1 multiplexed synthetic reporter detection modality that can produce distinct, non-ambiguous outputs for each of the 30+ cancers, the absence of cancer and in response to inconclusive tests. Must include positive and negative controls. 2. Produce all hardware components required for sample testing at home. Must be designed for seamless integration with the software components to deliver results to the test taker through EHR integration.
Performance Metrics	*In vitro*: By the end of Q5, demonstrate: 1. Sensor formulation and/or administration modality developed for the test(s) (breath and/or urine) does not reduce the *in vitro* performance of sensors 25% more than what is observed in TA1 using the same assays (See the TA1 *in vitro* performance metric #1 in Table 2)

	2. Demonstrate that the multiplexed reporter detection modality meets the TA1 *in vitro* performance metrics using the same assays (See *in vitro* performance metric #1 in Table 2) *In vivo:* by the end of Q9, independently verify the performance of the sensor administration and multiplexed reporter detection modalities of each kit (breath and/or urine) using animals and/or samples from *in vivo* studies performed in TA1 (See TA1 *in vivo* performance metric in Table 2). *In vitro* and/or *in vivo* tests of optimized sensor libraries may continue until the end of phase 1, when the features of a minimum viable product (MVP) are established.
Minimum Viable Product (MVP) Features	Integrate the finalized sensor and synthetic reporter libraries (TA1) with hardware and software components of each MCED test kit (TA2) to define and lock in the features of the MVP
Manufacturing	GLP compliant manufacturing of ≥15 tests for nonclinical safety testing. Must meet or exceed GLP quality requirements for device/ kit and demonstrate compliance with FDA-2018-D-1329 for non-clinical bench testing
Software Development	Biannual reports to document compliance with the proposed Design and Development Plan (DDP) and FDA standards for Software as Medical Device, IEC 62304, and other relevant regulatory guidelines
Patient Interface	An interactive interface that provides instructions on sensor administration, sample collection, testing and relevant educational resources to test takers
Provider Interface	An interface that allows provider access to test results, relevant educational resources for medical professionals and diagnostic paths specific to each cancer type covered by the test to deliver to test takers as customized recommendations.
Telemedicine Interface	A secure interface that facilitates patient-provider communications
EHR Integration	A secure, HIPAA compliant interface to integrate test results and subsequent follow-up tests into patient electronic health records
Software Validation and Verification	Biannual reports summarizing verification and validation activities for each software module.

By the end of Phase I of the Program, Performers are expected to combine deliverables from TA1 (Tables 1,2) and TA2 (Tables 3,4) to establish an integrated product for IND-enabling studies (Phase 2) and clinical testing (Phase 3). As a result, Phase 2 and Phase 3 metrics and objectives are not TA specific and are listed in section 2.5.6, *Additional Program Metrics and Objectives*, which covers program goals that are not TA specific (see Tables 5 and 6).

2.5.6 Additional Program Metrics and Objectives

Additional overall program goals that are not TA-specific are listed in Table 5. The expected metrics per Phase are listed in Table 6. In addition to frequent performance reviews throughout the Phases, Performers must provide an end-of-phase final report that summarizes all efforts and data for each completed POSEIDON Phase.

Table 5. Additional Overall Program Goals (not TA specific)

Metrics	Specifications
Nonclinical Testing	IND-enabling study to determine acute, chronic, local and systemic toxicities, immunogenicity and ADPA/PK (*Absorption, Distribution, Metabolism, Excretion and Pharmacokinetic*) profiles of the sensor/reporter libraries.
Clinical Testing	A First-in-Human (FIH) Phase 1b/2a clinical study to obtain safety, dosing, and preliminary clinical validation data
Commercialization and Regulatory Engagement	1. Have a commercial entity, ideally the Prime, that will house or have a pre-existing agreement to use all IP generated by POSEIDON-funded work from day 0 to month 60 on contract by kick-off. 2. Generate annual *IP Asset Development and Management* (IPDM) Reports. 3. Generate annual *Commercialization and Regulatory Engagement* (CaRE) Reports 4. Generate a Target Product Profile (TPP) for each test that integrates features of Minimum Viable Product (MVP) 5. Generate a *Go-To-Market* (GTM) strategy 6. Submit Pre-RFD (Request for Designation) (if necessary), RFD, Pre-IND/Pre-Sub, Breakthrough Device, INTERACT and IND/IDE Applications to the FDA as appropriate. Proposals must include an overall regulatory submission timeline with target dates for each submission and a justification
Equity and Accessibility	1. Generate annual Community Outreach and Engagement Summary Reports. 2. Generate *Annual Road Map to Equity* Reports 3. Build and define accessibility Key Performance Indicators (KPIs) to evaluate program success 4. Establish a companion Cancer Outreach Program (COP) for CX/UX design, product optimization, community outreach and patient/provider buy-in. 5. Establish the *Insurance Action Plan*. 6. Generate the *Race and Ethnicity Diversity Plan* for clinical studies.

Table 6. Additional Metrics for Each Phase and Sub-Phase (not TA specific)

Metrics	Specifications
[Q1-Q12]	Phase 1: Discovery and Development
Commercialization and Regulatory Engagement	1. *IP Asset Development and Management* (IPDM) team on staff by Q1 of FY1. 2. *Commercialization and Regulatory Engagement* (CaRE) team on staff by Q1 of FY1. 3. Submit Pre-RFD (if necessary), RFD, Breakthrough Device, INTERACT and pre-IND/pre-Sub applications to the FDA as appropriate. Proposals must include an overall regulatory submission timeline with target dates for each submission and a justification. 4. Generate annual IPDM and CaRE Reports, and updated Phase 2/3 plans. 5. Submit draft *Target Product Profile* (TPP) by the end of Q9 and an updated TPP at the end of Q12 that integrates features of *Minimum Viable Product* (MVP)
Equity and Accessibility	1. An EO on staff by Q1 FY1 (minimum 0.5 FTE). 2. An Outreach Coordinator on staff by Q1 FY1 (minimum 0.5 FTE). 3. Build and define accessibility *Key Performance Indicators* (KPIs) to evaluate program success

	4. >5 listening sessions targeting communities most vulnerable to cancer burden. 5. Establish a companion *Cancer Outreach Program* (COP) designed to promote patient and provider buy-in within the catchment area of clinical trial site(s) and produce annual reports documenting progress. 6. Create an *Affordability Plan* to demonstrate how tests will be accessibly priced. Ideally the final unit price should be ≤$100. 7. Create the *Insurance Action Plan* and provide annual progress reports 8. Generate annual *Road Map to Equity* and *Community Outreach and Engagement Summary* Reports 9. Generate the "*Race and Ethnicity Diversity Plan for Clinical Studies*" for submission to the FDA
[Q13-Q17]	Phase 2: Nonclinical Testing
Meets or exceeds all criteria from Phase 1	
ADME-Tox	1. Produce an *IND-enabling Study Summary* Report including ADME/PK (Absorption, Distribution, Metabolism, Excretion and Pharmacokinetics) evaluation, determination of acute, chronic, local, and systemic toxicities and sensor immunogenicity 2. Demonstrate that the sensor administration modality does not alter ADME/PK and safety profiles of sensor/reporter libraries under conditions that mimic at home testing 3. Identify a safe dose range for clinical testing.
Manufacturing	1. cGMP grade manufacturing of material for ≥130 patients. 2. Document plans to scale up to ≥10,000 patients for Phase 2b clinical studies.
Software Integration	Integrate individual software modules and perform system level testing and validation per *FDA standards for Software as Medical Device*, IEC 62304, and other relevant regulatory guidelines.
Analytical Validation	Demonstrate that the integrated digital app accurately processes input data to generate accurate, reliable, and precise output data per FDA guidelines for technical and analytical validation of medical software.
Test Evolution & Data Sharing	Produce AI/ML-based analytics to improve post-market test performance using real-world data sets and an integrated data sharing strategy with dedicated partners.
Commercialization and Regulatory Engagement	1. IND/IDE application to the FDA by Q4 of FY4 at the latest. 2. *IPDM* and *Care Summary* Reports with updated phase 3 plans. 3. IRB approved protocols and consent forms for the Phase 1b/2a clinical study. 4. Submit a revised TPP, a draft GTM strategy and an optimized MVP design
Equity and Accessibility	1. Demonstrate adherence to Phase 1 equity and accessibility metrics. 2. Provide evidence that clinical trial demographic requirements defined in the *Race and Ethnicity Diversity Plan* are met. 3. Generate the Cancer Outreach Program Phase 2 progress report.
[Q18-Q20]	Phase 3: Clinical testing
Phase 1b Clinical Trial	1. Double blind, randomized, placebo controlled multiple ascending dose study on up to 30 healthy, asymptomatic individuals. 2. Identify *Dose Limiting Toxicities* (DLT), *Maximum Tolerable Dose* (MTD) and recommended Phase 2 doses (P2Ds)
Phase 2a Clinical Trial	1. Open label, multi-dose study on ≥100 patients with confirmed stage 1 diagnoses. 2. Demonstrate that test meets/exceeds predefined test performance metrics: stage I detection with ≥90% sensitivity, ≥99.9% specificity and ≥95% Tissue of Origin (TOO) prediction accuracy. 3. Identify recommended dose for Phase 2b clinical study

Commercialization and Regulatory Engagement	1. Produce a Comprehensive Commercial Viability Assessment Report 2. Submit the Final TPP and a finalized GTM strategy
Equity and Accessibility	Demonstrate continued adherence to equity and accessibility metrics and clinical trial demographic requirements.

3.0 Eligibility Information

3.1 Eligible Proposers

All responsible sources capable of satisfying the government's needs may submit a Solution Summary in response to this ISO.

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

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

(a) FFRDCs and government entities, including federal government employees, are not permitted to respond to this solicitation as a prime or sub- Performer on a proposed Performer team.

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

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

3.1.2 Non-U.S. Entities

Non-U.S. entities may participate to the extent that such participants comply with any necessary non-disclosure agreements, security regulations, export control laws, and other governing statutes applicable under the circumstances. However, non-U.S. entities are encouraged to collaborate with domestic U.S. entities. In no case will awards be made to entities organized under the laws of a covered foreign country (as defined in section 119C of the National Security Act of 1947 (50 U.S.C. § 3059)) or entities suspended or debarred from business with the government.

3.1.3 Proposer Teaming Structures

The proposer team will ideally be led by a single corporation or other commercial entity. The ideal proposer characteristics may include the proven capability and established infrastructure to produce, manufacture, translate, commercialize, and deliver upon all technical components of the program. Alternatively, a strong team led by a small and/or non-commercial entity (e.g., a university or small business) may submit a proposal but may be required to negotiate a multi-party teaming agreement to receive an award (i.e., all proposed key team members will be required to be bound by this agreement).

3.1.4 Award Limitations

While there is statutory language that may suggest ARPA-H is limited in the number of awards it may make to one entity, there are circumstances in which ARPA-H may make more than three awards to a particular person or organization. ARPA-H encourages organizations to submit their research ideas notwithstanding this perceived limitation. Any proposal received will be fairly considered for award and, if it is of interest to ARPA-H, will be selected for an award.

3.2 System for Award Management (SAM)

A Proposer must have an active registration in SAM (www.sam.gov) for its proposal to be found conforming. Proposers must maintain an active registration in SAM.gov with current information at all times during which a proposal is under consideration or a current award from ARPA-H is held. Information on SAM.gov registration is available at SAM.gov.

NOTE: New registrations and renewals may take more than 14 business days to process in SAM. The SAM is independent of ARPA-H and thus ARPA-H representatives have no influence over processing timeframes.

4.0 POSEIDON Submission and Evaluation Process Overview

The POSEIDON evaluation and selection process is based on the following steps:

1. Eligible entities submit Solution Summary Packages*
2. Government verifies eligibility and then reviews eligible/conforming Solution Summaries to determine those that are advantageous given Criteria 1-3.
3. Proposers are notified whether they are encouraged to submit a full proposal (which includes a Solution Pitch) or not.
4. The government reviews full proposals, including Solution Pitches, against criteria 1-3 and determines the Solution Proposals that are most advantageous. The most advantageous proposals will be selected for award negotiations based on available funding and Program needs.

*This process is based on receipt of Solution Summaries by the Priority Submission Date. Should it be in the government's interest to consider submissions received after this date (but prior to the ISO Closing Date), it will follow the same evaluation and selection process.

4.1 Solution Summary Submissions

Solution Summary submissions are required. See Appendix A (required for submissions) and Appendix B (recommended format for Solution Summary).

4.2 Solution Summary- and Proposal Submission Information

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

4.2.1 **General.** All Solution Summaries and proposals submitted in response to this solicitation must be submitted in English and must be consistent with the content and formatting requirements of Appendix B (Solution Summary Format and Instructions) and Appendix C (Full Proposal Format and Instructions). All Solution Summaries and full proposals must include the Appendix A Eligibility and Conformance Certification Sheet.

4.2.2 **Submission Portal.** All Solution Summaries and full proposals shall be submitted via the ARPA-H Solution Submission Portal (https://solutions.arpa-h.gov/). Proposers must register in advance of submissions.

4.3 Full Proposal Solution Pitch Planning

Virtual Solution Pitches are a required element of full proposals. Proposers submitting full proposals should also plan to give virtual Solution Pitches during the month of February 2025 (subject to change). The specific date and time for a Proposer's Pitch is expected to be given at the time Solution Summary feedback is provided. See Appendix C for information related to Pitch content and logistics.

4.4 Solution Summary and proposal Submission Deadlines

4.4.1 **General.** The closing date of this solicitation, as established in Section 1, is the final date Solution Summaries will be accepted. To reflect the government's commitment to realizing solutions for American patients through the POSEIDON program as quickly as possible, the government will begin the review and selection process with Solution Summaries received by the Priority Submission date (see Section 1). All submissions received by this date will be considered and will receive a feedback response.

4.4.2 **Late Submissions.** Should it be in the government's interest to consider

submissions received after the Priority Submission date (but prior to the ISO Closing Date), it will consider all submissions received by the closing date. Proposers in this group will thus only receive a feedback response if the government considers submissions beyond the Priority Submission deadline.

4.4.3 Proposal Submission Deadline. The full proposal submission deadline will be provided to Proposers at the time of Solution Summary feedback. The government anticipates the due date for full proposals will be no later than approximately 8 January 2025.

4.5 Proprietary Information

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

5.0 Solution Summary Review and Evaluation of Full Proposals

5.1 Conforming Solution Summaries and Proposal Submissions

Conforming submissions contain all requirements detailed in this ISO. Solution Summaries or full proposals that fail to include required information will be deemed non-conforming and may be removed from further consideration. A Solution Summary or proposal will be deemed non-conforming under this ISO unless it meets the following solicitation requirements:

1. The proposed concept is applicable to the POSEIDON Program.
2. The Proposer meets the eligibility requirements.
3. The Solution Summary/proposal meets the submission requirements.
4. The Solution Summary/proposal meets the content and formatting requirements in the attached Appendices (including for Solution Pitches).
5. The Proposer's concept has not already received funding or been selected for award negotiations for another funding opportunity (whether from ARPA-H or another government agency).
6. The full proposal is submitted by a Proposer that submitted a timely and responsive Solution Summary.
7. The Proposer's Eligibility and Conformance Certification sheet (Appendix A) indicates a responsive solution.

Non-conforming Solution Summary and proposal submissions may be removed from consideration. Proposers will be notified of non-conforming determinations via email correspondence if the determination results in the submission not moving forward for further consideration because it is not responsive to this ISO.

5.2 Review, and Evaluation Criteria

The following criteria, listed in descending order of importance, will guide the government's review and evaluation of Solution Summaries and Proposals that have been determined responsive to the solicitation, and thus eligible for further consideration.

5.2.1 Criterion 1: Overall Scientific and Technical Merit

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

The proposal includes a clear commercialization strategy and addresses the proposer's intended intellectual property (IP) rights structure. *Note: Program metrics include scientific/technical, accessibility, regulatory, and commercial.

5.2.2 Criterion 2: Proposer's Capabilities and/or Related Experience

Factors considered may include: The proposed technical team has the expertise and experience to accomplish the proposed tasks; the Proposer's prior experience in similar efforts clearly demonstrates an ability to deliver products that meet the proposed technical performance within the proposed budget and schedule; and the proposed team has the expertise to manage the cost and schedule with similar efforts completed/ongoing by the Proposer in this area fully described.

If the Proposer is not a commercial entity with the capability to facilitate at least early commercialization efforts, the proposal shall describe the proposed teaming arrangement to ensure all applicable terms and conditions of a resulting OT will be met and will be binding, as applicable, on all team members (e.g., intended multi-party teaming agreement between academic team(s) and commercial entities).

In terms of capability, the government shall assess the Volume III biosketches provided for the Project Manager, Engagements Officer, Outreach Coordinator, Regulatory expert, Commercialization experts, and other key personnel on the project team.

5.2.3 Criterion 3: Price/Cost Analysis

Proposals will be evaluated to determine the reasonableness of the estimated budget and the anticipated value received by the government. Cost realism and/or technical

analysis may be performed to ensure proposed costs are realistic for the technical and management approach, accurately reflect the technical goals and objectives of the solicitation, the proposed costs are consistent with the Proposer's Scope of Work and reflect a sufficient understanding of the costs and level of effort needed to successfully accomplish the proposed technical approach. The costs for the prime Proposer and proposed subperformers should be substantiated by the details provided in the proposal (e.g., the type and number of labor hours proposed per task, the types and quantities of materials, equipment and fabrication costs, travel and any other applicable costs including the basis for the estimates).

It is expected the effort will leverage all available relevant prior research to obtain the maximum benefit from the available funding. Based on the Program structure as well as the ultimate benefits anticipated for the Performer(s), the government may negotiate resource sharing arrangements with successful Proposers. Accordingly, proposals that include resource sharing will be considered favorably.

5.3 Review, Evaluation, and Selection Process

It is the policy of ARPA-H to ensure an impartial, equitable, and comprehensive scientific review process based on the criteria listed above, and to select the proposals whose solutions are most advantageous to the government. ARPA-H will review and respond to all Proposers submitting Solution Summaries by the Priority Submission date. Solution Summaries will be reviewed on a high-level (given page limitations) against all three criteria, except as described in Section 5.3.2. At no point in the merit assessment and review process will Solution Summaries be compared with one another. All timely responsive proposals will be evaluated against the criteria above except as described in Section 5.3.2. Proposals will not be evaluated against each other, but rather evaluated on their own individual merit to determine how well the submission meets the criteria stated in this ISO.

5.3.1 Selectable or Non-Selectable Determination

A selection for award negotiations will be made to Proposers whose proposal is determined to be most advantageous by the government. For the purposes of this solicitation, selectable and non-selectable are defined as follows:

SELECTABLE: A selectable proposal is a proposal that has been evaluated by the government against the evaluation criteria listed in this ISO, and the positive aspects of the overall proposal outweigh its negative aspects.

NON-SELECTABLE: A proposal is considered non-selectable when the proposal has been evaluated by the government against the evaluation criteria listed in this ISO, and the positive aspects of the overall proposal do not outweigh its negative aspects. Any Solution Summary or Proposal

that lacks merit in relation to Criterion 1 will be deemed non-selectable overall.

5.3.2 Non-Selectable Criterion 1 Solutions

If a submission that is reviewed or evaluated as lacking scientific or technical merit to a degree sufficient to determine the submission overall will be non-selectable, the government may not evaluate Criteria 2 and 3 (as applicable for the submission type). Thus, any feedback provided will be limited to that of the government's review/evaluation (e.g., no more than Criterion 1).

5.3.3 Review and Evaluation Timelines

ARPA-H's intent is to review Solution Summaries and proposals as soon as possible after the applicable submission date.

5.4 Handling of Competitive Sensitive Information

5.4.1 It is the policy of ARPA-H to protect all Solution Summaries and proposals as competitive sensitive information and to disclose their contents only for the purpose of evaluation and/or only to screened personnel for authorized reasons, to the extent permitted under applicable laws. Restrictive notices notwithstanding, during the evaluation process, submissions may be handled by ARPA-H support contractors for administrative purposes and/or to assist with technical evaluation.

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

5.5 Evaluation and Award Disclaimers

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

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

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

6.0 Policy Requirements and Miscellaneous Other Information

6.1 Organizational Conflicts of Interest (OCI)

Proposers are required to identify and disclose all facts relevant to potential or actual OCIs involving the Proposer's organization and any proposed team member (proposed sub-awardee). Although the FAR does not apply to OTs or this ISO overall, ARPA-H requires OCIs be addressed in the same manner prescribed in FAR subpart 9.5. Regardless of whether the Proposer has identified potential or actual OCIs under this section, the Proposer is responsible for providing a disclosure with its proposal. If a potential or actual OCI has been identified, the disclosure must include the Proposers', and as applicable, proposed team members' OCI mitigation plans. The OCI mitigation plan(s) must include a description of the actions the Proposer has taken, or intends to take, to prevent the existence of conflicting roles that might bias the Proposer's judgment and to prevent the Proposer from having unfair competitive advantage. The OCI mitigation plan will specifically discuss the disclosed OCI in the context of each of the OCI limitations outlined in FAR 9.505-1 through FAR 9.505-4. The disclosure and mitigation plan(s) do not count toward the page limit.

6.1.1 Agency Supplemental OCI Policy

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

Proposers shall follow the instructions in, and complete, Volume III (see Appendix C) to address the requirements of this ISO Section.

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

6.1.2 Government OCI Procedures

The government will evaluate OCI mitigation plans to avoid, neutralize, or mitigate potential OCI issues before award and to determine whether it is in the government's interest to grant a waiver. The government will only evaluate OCI mitigation plans for proposals selected for potential award based on the evaluation criteria and funding availability.

The government may require Proposers to provide additional information to assist the government in evaluating the OCI mitigation plan.

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

6.2 Intellectual Property

Proposers must provide a good faith representation that the Proposer either owns or possesses the appropriate licensing rights to all IP that will be utilized for the proposed effort. ARPA-H strongly encourages IP rights to be aligned with open-source regimes. Further, it is desired that all non-commercial software (including source code), software documentation, and technical data generated and/or developed under the proposed

project is provided as a deliverable to the government. IP delivered to the government should align with project or Program goals.

NOTE: IP rights assertions will be reviewed under Criterion 1.

6.3 Human Subjects Research

All entities submitting a proposal for funding that will involve engagement in human subjects research (as defined in 45 CFR § 46) must provide documentation of one or more current Assurance of Compliance with federal regulations for human subjects protection, including at least a Department of Health and Human Services (HHS), Office of Human Research Protection Federal Wide Assurance. All human subjects research must be reviewed and approved by an Institutional Review Board (IRB), as applicable under 45 CFR § 46 and/or 21 CFR § 56. The entities human subjects research protocol must include a detailed description of the research plan, study population, risks and benefits of study participation, recruitment and consent process, data collection, and data analysis. Recipients of ARPA-H funding must comply with all applicable laws, regulations, and policies for the ARPA-H funded work. This includes, but is not limited to, laws, regulations, and policies regarding the conduct of human subjects research, such as the U.S. federal regulations protecting human subjects in research (e.g., 45 CFR § 46, 21 CFR § 50, § 56, § 312, § 812) and any other equivalent requirements of the applicable jurisdiction.

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

6.4 Animal Subjects Research

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

Proposers must provide documentation of a current Animal Welfare Assurance (AWA) on file with the Office of Laboratory Animal Welfare (OLAW).

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

All Animal Use Research must undergo review and approval by the local Institutional Animal Care Use Committee (IACUC) prior to incurring any costs related to the animal use research. For all proposed research anticipating animal use, proposals should briefly describe plans for IACUC review and approval.

6.5 Electronic Invoicing and Payments

Performers will be required to submit invoices in a designated electronic payment system as described in the award document.

6.6 Government-Furnished Property/Equipment/Information

Government-furnished property/equipment/information may be provided to selected Performers. Any instances of GFP/GFE will be specifically negotiated.

Appendix A: Eligibility and Conformance Certification Sheet

Prime Entity Name:	
Prime Entity's Unique Entity Identification (UEI):	
Names of ALL subperformer institutions, entities, and/or companies:	
If Prime is not a commercial entity, have all team members agreed to sign a legally binding multi-party teaming agreement accepting the terms and condition of the resulting ARPA-H award?	Choose an item.
Does your experimental plan include ALL 25 cancer types as required by the solicitation?	Choose an item.
Does your experimental plan include the additional 5 cancer types (selected by you) as required by the solicitation?	List ALL 5 here: 1) 2) 3) 4) 5)
Which bodily fluids does your approach test? (check all that apply)	☐Breath ☐Urine ☐Blood ☐Other (Specify:)
How will your sensors be administered systemically for the urine test?	☐Intramuscular ☐Transdermal (microneedle) ☐Transdermal (other) ☐Oral ☐Intranasal ☐Intravenous ☐Other (Specify:)
How will your sensors be administered systemically for the breath test?	☐Intramuscular ☐Transdermal (microneedle) ☐Transdermal (other) ☐Oral ☐Intranasal ☐Intravenous ☐Other (Specify:)
Which TAs are you proposing to address? (Select all that apply)	☐TA1 ☐TA2
Which Technical Approach are you proposing to address? (Select all that apply)	☐A ☐B ☐C
Do you have a planned IND-enabling study?	Choose an item.
What is your experimental system for the IND-enabling study?	

Appendix B: Solution Summary Format and Instructions

A. General Instructions

All Solution Summaries must be submitted in English and use a non-serif font type with a readability like that of Calibri, Avenir Next LT Pro Light, Arial, or New Century 11-point font. Smaller non-serif fonts may be used for figures, tables, and charts. Margins may be no less than one inch in width. Solution Summaries are limited to one page written and one page for the infographic/preliminary data, exclusive of a cover page and Rough Order of Magnitude. No tables of content shall be provided. The government may not review pages beyond two (2) total; and any Solution Summary submitted that exceeds 2 pages will only be reviewed at ARPA-H's discretion. All solution summaries must also include the Eligibility and Conformance Certification sheet (Appendix A).

B. Cover Page

The cover page should follow the format below. The cover page does not count towards the page limit.

Solicitation #	ARPA-H-SOL-24-109
Solution Summary Title	
Submitter Organization	
Type of Organization	Choose all that apply: Large Business, Small Disadvantaged Business, Other Small Business, HBCU, MI, Other Educational, or Other Nonprofit
Technical Point of Contact (POC)	Name: Mailing Address: Telephone: Email:
Administrative POC	Name: Mailing Address: Telephone: Email:
Total Estimated Budget	Total: $
Place(s) of Performance	
Other Team Members (subperformers, including consultants) if any	Technical POC Name: Organization: Organization Type:

C. Proposed Work

1. Describe the Solution Summary concept with minimal jargon and explain how it addresses the technical areas of the POSEIDON program. Clearly identify the problem(s) to be solved and the outcome(s) sought with the proposed technology concept. Explain the concept's potential to be disruptive compared to existing or emerging technologies, including anything with pre-existing funding, and how the proposed approach will go far beyond current commercial capabilities.

2. Describe the final deliverable(s) for the project, one or two key interim milestones, and the overall technical approach used to achieve project objectives. Describe the background, theory, simulation, modeling, experimental data, or other sound engineering and scientific practices or principles that support the proposed approach. Identify adoption challenges to be overcome for the proposed technology to be successful. Describe key technical risks.

3. At a minimum, the Solution Summary should address:
   - Technical plan to produce breath and/or urine test that identifies 30+ cancers
   - Plan to translate developed tests; and
   - Supporting information to justify selection of Technical Approach A, B, or C.

D. Team Organization and Capabilities

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

E. Rough Order of Magnitude (ROM)

Please include a basis of estimate (BOE) to support the proposed project budget, as well as the total project cost including cost sharing, if applicable. The BOE should also include a breakdown of the work by direct labor, labor hours, subcontracts, materials, equipment, other direct costs (e.g., travel), profit, cost sharing, and any other relevant costs. The below table may be used for this breakdown:

Categories	Phase I Amount	Phase II* Amount	Phase III* Amount	Total
Direct Labor (Fully burden)				
Labor hours				

Subperformers				
Materials				
Equipment				
Travel				
Other Direct Costs				
Profit				
Total				
Cost Sharing (if applicable/appropriate)				

Proposers must ensure the BOE encompasses all applicable costs and should modify the above to best reflect the Proposer's expected costs. The BOE does not count toward the page limit.

NOTE: Delete all formatting and content instructions prior to submission.

Appendix C: Full Proposal Format and Instructions

I. Summary

A. Full proposals must follow the guidance in this Appendix. Conforming proposals shall consist of the Eligibility and Conformance Certification sheet (Appendix A), as well as the following:

a. Volume I, Technical and Management Proposal,
b. Volume II, Cost Proposal,
c. Volume III, Administrative and Policy Requirements Submission, and
d. Solution Pitch Deck

B. All required proposal templates/formats (e.g., standard ARPA-H cost spreadsheet) will be provided at the time of Solution Summary feedback.

Summary of Full Proposal requirements, including page limits.

Volume I, Technical and Management Proposal	
Volume Element	Page Limit
Cover Page	1
ii. Executive Summary	15
iii. Solution Fit with POSEIDON	
iv. Technical Plan	
v. Management Plan	
vi. Capabilities	
vii. Commercialization Plan	
viii. Statement of Work (SOW)	N/A, use provided template/format
ix. Schedule and Milestones	N/A use provided template/format
x. Data Management and Sharing Plan (DMSP)	N/A (estimated 2 pages)
xi. References	N/A
Volume II, Cost Proposal	
Volume Element	Page Limit
Cover Page	1
A. Cost Proposal Spreadsheet(s), including for subperformers at any tier	N/A, use provided template/format
B. Cost and Pricing Data Support	N/A

Volume III, Administrative and Policy Requirements Submission	
Volume Element	Page Limit
Cover Page	1
A. Team Member Identification	N/A, use provided template/format
A. OCI Affirmations and Disclosure	
B. National Security Disclosure and associated biosketches	
C. Novelty of Proposed Work	
F. Intellectual Property (IP)	
G. Human Subjects Research	
H. Animal Subjects Research	
I. Representations Regarding Unpaid Delinquent Tax Liability or a Felony Conviction Under any Federal Law	

C. The page limitation includes all figures, tables, and charts. All pages shall be formatted for printing on 8-1/2 by 11- inch paper. Margins must be 1-inch on all sides, using a sans serif font with readability similar to that of 11 pt Arial, Avenir Next LT Pro Light, or Calibri, with a page number at the bottom of each page.

D. Documents must be clearly labeled with the ISO number, Proposer organization, and proposal title/proposal short title (in the header of each page). Use the following Title Format: "Volume I_XYZ Institution", "Volume II_XYZ Institution", "Volume II, Supporting Documents", etc.

II. Volume I, Technical and Management Proposal

The maximum page count for Volume I is fifteen (15) pages, with exclusions as noted in the table within this Appendix. The cover page and sections 8-11 (Statement of Work through References) are not included in the page count. However, for all sections, conciseness to the maximum extent practicable is encouraged. No other supporting materials may be submitted for review. Note that while the government's evaluation of Volume I against criteria 1-3 is limited to the sections included in the page count limitations, it will be reviewing all sections. The other documents may be used to cross-check the proposal and will also inform feedback for Proposers whose full proposals are determined most advantageous and selected for award negotiations. Volume I should include the following components:

Cover Page

1. ISO number ARPA-H-SOL-24-109.
2. Proposed Technical Approach (A, B, or C);
3. Proposal title.
4. Prime Awardee/entity submitting proposal.

5. Unique Entity Identifier of prime proposer/awardee (UEI);
6. Type of organization of the prime, selected among the following categories:

    - Large
    - Small, Disadvantaged Business
    - Other Small Business
    - Historically Black Colleges and Universities (HBCUs)
    - Minority Institution (MI)
    - Other Educational, or Other Non-Profit (including non-educational government entities)

    NOTE: The Small Business Administration's (SBA) size standards determine whether a business qualifies as small. Size standards may be found here: https://www.ecfr.gov/current/title-13/chapter-I/part-121#121.201

7. Date of proposal submission.
8. Other team members (if applicable) and type of organization for each.
9. Technical point of contact (POC) to include salutation, last name, first name, street address, city, state, zip code, telephone, e-mail.
10. Administrative POC to include salutation, last name, first name, street address, city, state, zip code, telephone, e-mail; and
11. Total funds requested from ARPA-H, and the amount of resource share (if any).

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

1. What is the proposed work attempting to accomplish or solve?
2. How is it done today? What are the limitations of present approaches?
3. What are the key technical challenges in your approach and how do you plan to overcome these?
4. What is new about your approach? Why do you think you can be successful at this time?
5. Who cares? If you succeed, what difference will it make?
6. What are the risks? Identify any risks that may prevent you from reaching your objectives, as well as any risks the program itself may present. Please also describe plans to mitigate these risks at a high level.
7. How much will your project cost?
8. What are your milestones to check for success consistent with POSEIDON metrics?

9. To ensure equitable access for all people, how will cost, accessibility, and user experience be addressed in your project?
10. How might this program be misperceived or misused (and how can we prevent that from happening)?

B. Solution Fit with POSEIDON: Clearly describe what the team is trying to achieve and the difference it will make (qualitatively and quantitatively) if successful relative to POSEIDON's vision and metrics. Provide an overview of the current and previous research and development (R&D) efforts related to the proposed research and identify any challenges associated with such efforts, including any scientific or technical barriers encountered during such efforts or challenges in securing sources of funding, as applicable. Describe the innovative aspects of the project in the context of existing capabilities and approaches, clearly delineating the uniqueness and benefits of this project in the context of the state of the art, alternative approaches, and other projects from the past and present. Describe how the proposed project is revolutionary and how it significantly rises above the current state-of-the-art. Describe the deliverables associated with the proposed project as well as how the project will integrate into existing clinical workflows and successfully improve patient care.

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

D. Management Plan:

1. Provide a summary of the expertise of the team, including any subperformers, and key personnel who will be doing the work. A Principal Investigator (PI) for the project must be identified, along with a description of the team's organization, including the breakdown by TA. All teams are required to identify a Project Manager/Integrator to

    - serve as the primary point of contact (POC) to communicate with the ARPA-H PM team and OT/Contracts equivalent for each award instrument (e.g., Contracting Officer),
    - coordinate the effort across the team,
    - organize regular Performer meetings or discussions,

- facilitate data sharing, and
- ensure timely completion of milestones and deliverables.

2. Provide a clear description of the team's organization including an organization chart that includes, as applicable:
   - the programmatic relationship of team members
   - the unique capabilities of team members
   - the task responsibilities of team members
   - the teaming strategy among the team members and
   - key personnel with the amount of effort to be expended by each person during each year.

3. Provide a detailed plan for coordination, including explicit guidelines for interaction among collaborators/subperformers of the proposed effort. Include risk management approaches. Describe any formal teaming agreements required to execute this program.

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

F. Commercialization Plan: Briefly outline your current understanding of your technologies target market and the size of that market. Identify two- to three key competitive technologies operating in the market and their limitations. Outline ownership plans for existing and future IP across the team. Identify ideal partners (e.g. private industry, investors, etc.), that may be pursued to secure funding, manufacturing, and marketing following the award period. Plans shall include completion of the following table:

IP Category (Trade Secret, Patent, or Data)	USPTO# and Docket # and Application #	IP Title	Summary of Intended Use in Project	Asserted rights for government related to POSEIDON Program(Government Purpose, Unlimited, Limited.)	Name of Person or Entity Asserting Restrictions (who owns the IP?)	Funding Source (federal government, other, or Mix**)

G. Statement of Work (SOW):

1. The SOW should provide a detailed task breakdown, citing specific tasks for each TA, and their connection to the milestones and program metrics. Each Phase of the program should be separately defined. The SOW must not include proprietary information. Please note the technical proposal must stand on its own as the SOW cannot be used to supplement the 15 pages of the technical proposal.

2. For each task/subtask, provide:
   - A detailed description of the approach to be taken to accomplish each defined task/subtask.
   - Identification of the primary organization responsible for task execution (prime awardee, sub-awardee(s), by name).
   - A measurable milestone, i.e., a deliverable, demonstration, or other event/activity that marks task completion. Include completion dates for all milestones. Include quantitative metrics.
   - A definition of all deliverables (e.g., data, reports, software) to be provided to the government in support of the proposed tasks/subtasks.

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

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

I. Data Management and Sharing Plan (DMSP) (recommend NTE 2 pages) The DMSP shall include all information included in the 6-Element plan format recommended by the National Institutes of Health (to view the 6-Element suggested format visit https://grants.nih.gov/grants/forms/data-management-and-sharing-plan-format-page). Note: this plan will not be specifically evaluated against Criteria 1-3 but will likely be used to give feedback for proposals that are selected for award negotiations.

J. References: Add a list with the cited literature.

III. Volume II, Cost Proposal

There is no maximum page count for Volume II. The Cost Proposal shall be comprised of the editable Excel Cost Proposal spreadsheet and associated supporting materials, ideally provided in a single attachment (e.g., Adobe pdf) led by a cover page as follows.

Cover Page

1. ISO number ARPA-H-SOL-24-109.
2. Technical area.
3. Prime Awardee/entity submitting proposal.
4. UEI of prime awardee/Proposer.
5. Type of organization of the prime, selected among the following categories:

    - Large
    - Small, Disadvantaged Business
    - Other Small Business
    - Historically Black Colleges and Universities (HBCUs)
    - Minority Institution (MI)
    - Other Educational, or Other Non-Profit (including non-educational government entities)

6. Other team members (if applicable) and type of organization for each.
7. Proposal title.
8. Technical POC to include salutation, last name, first name, street address, city, state, zip code, telephone, e-mail.
9. Administrative POC to include salutation, last name, first name, street address, city, state, zip code, telephone, and e-mail.
10. Total proposed cost separated by base and option(s) (if any).
11. Name, address, and telephone number of the Proposer's cognizant auditor (as applicable).
12. Date proposal was submitted.
13. Proposal validity period (Minimum of 120 days).

A. Cost Proposal Spreadsheet:

1. *ARPA-H Standard Excel Cost Proposal Spreadsheet* shall be submitted with all full proposals. All tabs and tables in the cost proposal spreadsheet should be developed in an editable format with calculation formulas intact to allow traceability of the elements of the cost proposal. The cost proposal spreadsheet must be used by the prime organization and all subperformers at any tier.

2. While the prime Proposer is ultimately responsible for submission of all required documents, subperformer cost proposal spreadsheets may be submitted directly to the government by the proposed subperformer via email to POSEIDON@ARPA-H.gov. Subperformer proposals should include Interdivisional Work Transfer Agreements or similar arrangements between the awardee and divisions within the same organization as the awardee.

B. Cost and Pricing Data Support:

1. In addition to using the cost proposal spreadsheet, the cost proposal must include documentation to support the proposed price/budget. Supporting documentation must be in sufficient detail to substantiate the summary cost estimates and should include a description of the method used to estimate costs (e.g., vendor quotes). For indirect costs provide the most current indirect cost agreement (e.g., Colleges and Universities Rate Agreement, Forward Pricing Agreement, Provisional Billing Rates, etc.).

2. Cost and pricing support may also facilitate a value analysis by the government through information other than detailed cost and pricing data. Proposers are encouraged to include information related to value-added resources or conditions that are not immediately obvious in the Cost Proposal Spreadsheet or the traditional forms of cost and pricing support information like vendor quotes (e.g., intended intellectual property terms and conditions with perceived future value).

IV. Volume III, Administrative and Policy Requirements Submission

Cover Page

1. ISO number ARPA-H-SOL-24-109.
2. Technical area.
3. Prime Awardee/entity submitting proposal.
4. UEI of prime awardee/Proposer:
5. Type of organization of the prime, selected among the following categories:

- Large
- Small, Disadvantaged Business
- Other Small Business
- Historically Black Colleges and Universities (HBCUs)
- Minority Institution (MI)

- Other Educational, or Other Non-Profit (including non-educational government entities)

6. Other team members (if applicable) and type of organization for each.
7. Proposal title.
8. Technical POC to include salutation, last name, first name, street address, city, state, zip code, telephone, e-mail.
9. Administrative POC to include salutation, last name, first name, street address, city, state, zip code, telephone, and e-mail.
10 Total proposed cost separated by base and option(s) (if any).
11. Name, address, and telephone number of the Proposer's cognizant auditor (as applicable).
12. Date proposal was submitted.
13. Proposal validity period (minimum of 120 days).

A. TEAM MEMBER IDENTIFICATION

[Using the following table as a template, provide a list of all entities as well as specific Key Personnel (PI, Project Manager, other investigators, etc.). Note: Consultants (e.g., 1099s) are considered subperformers and must be listed.

PRIME		
Individual Name:	Organization:	Non-U.S. Organization: ☐ Yes ☐ No Non-U.S. Individual: ☐ Yes ☐ No
SUBPERFORMERS, INCLUDING CONSULTANTS		
Individual Name:	Organization:	Non-U.S. Organization: ☐ Yes ☐ No Non-U.S. Individual: ☐ Yes ☐ No
Individual Name:	Organization:	Non-U.S. Organization: ☐ Yes ☐ No Non-U.S. Individual: ☐ Yes ☐ No

B. ORGANIZATIONAL CONFLICT OF INTEREST AFFIRMATIONS AND DISCLOSURE

1. Are any of the proposed individual team members or their respective organizations (whether prime or subperformer) currently providing support services to ARPA-H?

☐ No ☐ Yes

2. Did any of the proposed individual team members or their respective organizations (whether prime or subperformer) provide support services to ARPA-H within one calendar year of this proposal submission?

☐ No ☐ Yes

[If you answered "Yes" to B1. OR B2., provide the following information for each applicable team member:

- The name of the ARPA-H office receiving the support.
- The prime contract number.
- Identification of proposed team member (subperformer) providing the support; and
- An OCI mitigation plan.]

3. Are there any other potential Organizational Conflicts of Interest involving any of the proposed individual team members *or* their respective organizations (whether prime or subperformer)?

☐ No ☐ Yes

[If yes, provide the following information for each applicable team member:

- Identification of applicable team member; and
- An OCI mitigation plan.]

C. NATIONAL SECURITY DISCLOSURE

[In accordance with National Security Presidential Memorandum (NSPM)-33 and the associated White House Office of Science and Technology Policy Implementation Guidance, which requires certain individuals to disclose potential conflicts of interest (COI) and commitment (COC), individuals designated as PIs and other senior/key personnel (e.g., Project Manager) under prime and subperformers are required to complete the Common Form for Current and Pending (other) Support as well as the Common Form for Biographical Sketch[1]:]

1. For PIs and other senior/key personnel (in both prime and subperformers, including consultants), please list:

    1. Other organizational affiliations and employment
    2. Other positions and appointments[2]

[1] Other Support: https://www.nsf.gov/bfa/dias/policy/researchprotection/commonform_cps.pdf; Biographical Sketch: https://www.nsf.gov/bfa/dias/policy/researchprotection/commonform_biographicalsketch.pdf

[2] Both foreign and domestic, including affiliations with foreign entities and governments. This includes titled academic, professional, or institutional appointments whether or not remuneration is received, and whether full-time, part-time, or voluntary (including adjunct, visiting, or honorary).

3. Participation in any foreign government-sponsored talent recruitment program(s)[3]
4. Current and pending support/Other support. For researchers, "Other Support" includes all resources made available to a researcher in support of and/or related to all of their professional R&D efforts, including resources provided directly to the individual rather than through the research organization, and regardless of whether or not they have monetary value (e.g., even if the support received is only in-kind, such as office/laboratory space, equipment, supplies, or employees).] This support includes:

    i. all resources made available, or expected to be made available, to an individual in support of the individual's research and development efforts, regardless of (i) whether the source is foreign or domestic; (ii) whether the resource is made available through the entity applying for a research and development award or directly to the individual; or (iii) whether the resource has monetary value;
    ii. in-kind contributions requiring a commitment of time and directly supporting the individual's research and development efforts, such as the provision of office or laboratory space, equipment, supplies, employees, or students. This includes resource and/or financial support from all foreign and domestic entities, including but not limited to, (i) gifts provided with terms or conditions, (ii) financial support for laboratory personnel, and (iii) participation of student and visiting researchers supported by other sources of funding; and
    iii. Private equity, venture, or other capital financing.

2. For consultants, please additionally list the following (Note: current, pending, and other support not required):

    1. Other organizational affiliations and employment
    2. Other positions and appointments Error! Bookmark not defined.

[3] The term "foreign government-sponsored talent recruitment program" or "foreign government-sponsored talent recruitment programs" means an effort directly or indirectly organized, managed, or funded by a foreign government or institution to recruit S&T professionals or students (regardless of citizenship or national origin, and whether having a full-time or part-time position). Compensation could take many forms including cash, research funding, complimentary foreign travel, honorific titles, career advancement opportunities, promised future compensation, or other types of remuneration or consideration, including in-kind compensation.

3. Participation in any foreign government-sponsored talent recruitment program(s)

D. NOVELTY OF PROPOSED WORK

Has the proposed work been submitted to any other government solicitation?

☐ No ☐ Yes

If yes, provide the following information:

- Solicitation number _____
- Agency/Office _____
- Proposed work has already received funding or a positive funding decision.

☐ No ☐ Yes ☐ Decision pending

E. INTELLECTUAL PROPERTY (IP)

[Provide the following information, as applicable. The IP table in this section should match the table provided with the Commercialization Plan in Volume II and should include any background IP as well as intended IP related to deliverables under the intended OT. The table should be completed appropriately for each type (e.g., background/foreground. Additionally, the government will assume delivery of Data related to each patent based on the license rights asserted. Thus, data in the table below is intended to relate to items not associated with a patent]

IP Category (Trade Secret, Patent, or Data)	USPTO# and Docket # and Application #	IP Title	Summary of Intended Use in Project	Asserted rights for government related to POSEIDON Program(Government Purpose, Unlimited, Limited.)	Name of Person or Entity Asserting Restrictions (who owns the IP?)	Funding Source (federal government, other, or Mix**)

1. TECHNICAL DATA AND COMPUTER SOFTWARE

Are you asserting any IP restrictions on any technical data or computer software that will be delivered to the government?

☐ No ☐ Yes

[If yes, in the table above list all anticipated proprietary claims to results,

prototypes, deliverables, or systems supporting and/or necessary for the use of the proposed research, results, prototypes and/or deliverables. Provide a short summary for each item asserted with less than unlimited rights that describes the nature of the restriction and the intended use of the intellectual property in the conduct of the proposed research. Use the following format for these lists.]

2. PATENTS

Does the proposed effort involve using patented inventions that are owned by or assigned to the proposing organization or individual?

☐ No ☐ Yes

[If yes, in addition to completing the above table, provide documentation proving ownership or possession of appropriate licensing rights to all patented inventions to be used for the proposed project. If a patent application has been filed for an invention, but it includes proprietary information and is not publicly available, provide documentation that includes: the patent number, inventor name(s), assignee names (if any), filing date, filing date of any related provisional application, and summary of the patent title, with either: (1) a representation of invention ownership; or (2) proof of possession of appropriate licensing rights in the invention (i.e., an agreement from the owner of the patent granting license to the Proposer).]

3. ABILITY TO MEET PROGRAMMATIC GOALS WITH IP/PATENT IMPLICATIONS

[Describe how IP assertions and/or patent implications impact the applicable ARPA-H programmatic goals.]

F. HUMAN SUBJECTS RESEARCH

Does the proposed work involve Human Subject Research?

☐ No ☐ Yes

[If yes, provide the Federal-wide Assurance (FWA) number and the plan for Institutional Review Board (IRB) review and approval.]

G. ANIMAL SUBJECTS RESEARCH

Does the proposed work involve Animal Subject Research?

☐ No ☐ Yes

[If yes, provide the Animal Welfare Assurance (AWA) number, the Vertebrate Animals Section (VAS), and the plan for Institutional Animal Care and Use Committee (IACUC) review and approval.]

H. REPRESENTATIONS REGARDING UNPAID DELINQUENT TAX LIABILITY OR A FELONY CONVICTION UNDER ANY FEDERAL LAW

[Complete the following statements.]

The Proposer represents that –

1. It is ☐ / is not ☐ a corporation that has any unpaid federal tax liability that has been assessed, for which all judicial and administrative remedies have been exhausted or have lapsed, and that is not being paid in a timely manner pursuant to an agreement with the authority responsible for collecting the tax liability,

2. It is ☐ / is not ☐ a corporation that was convicted of a felony criminal violation under a federal law within the preceding 24 months.

VI. Solution Pitches

Information related to Solution Pitch logistics and pitch deck composition will be provided to Proposers at the time of Solution Summary feedback.

Appendix D: Acronyms

ADME/PK	Absorption, Distribution, Metabolism, Excretion/ Pharmacokinetic
AI/ML	Artificial Intelligence/ Machine Learning
AO	Agreements Officer
ARPA-H	Advanced Research Projects Agency for Health
CAB	Commercialization Advisory Board (CAB)
CBER	Center for Biologics Evaluation and Research
CDRH	Center for Devices and Radiologic Health
cGMP	current Good Manufacturing Practice
CMMI	Center for Medicare and Medicaid Innovation
CMS	Centers for Medicare & Medicaid Services
COP	Cancer Outreach Program
CP	Commercialization Plan
CSRN	Cancer Screening Research Network
CX/UX	Customer Experience/ User Experience
DLT	Dose Limiting Toxicities
EHR	Electronic Health Record
EO	Engagements Officer
FDA	Food and Drug Administration
FIH	First in Human
GLP	Good Laboratory Practice
GTM	Go-to-Market
HCP	Health Care Provider
HIPAA	Health Insurance Portability and Accountability
HSF	Health Science Futures
IEC	International Electrotechnical Commission
IHS	Indian Health Service
IND	Investigational New Drug
IND/IDE	Investigational Drug and Devices
INTERACT	INitial Targeted Engagement for Regulatory Advice on CBER ProducTs
IP	Intellectual Property
IPDM	IP Development and Management (IPDM),
IPSF	Intellectual Property Success Framework (IPSF),
IRB	Institutional Review Board
IV	Intravenous
KPI	Key Performance Indicators
MCED	Multi-Cancer Early Detection
MOU	Memorandum of Understanding
MTD	*Maximum Tolerable Dose*
MVP	Minimum Viable Product
NCI	National Cancer Institute
NDA	Non-Disclosure Agreement
OC	Outreach Coordinator
PM	Program Manager
POSEIDON	Platform Optimizing SynBio for Early Intervention and Detection in Oncology
R&D	Research and Development

RFD	Request for Designation
SEER	Surveillance, Epidemiology and End Results
TA	Technical Area
TCET	Transitional Coverage for Emerging Technologies
TOO	Tissue of Origin
TPP	Target Product Profile
U.S.	United States