Innovative Solutions Opening (ISO)

Rare Disease AI/ML for Precision Integrated Diagnostics (RAPID)

Proactive Health Office (PHO)

Advanced Research Projects Agency for Health

ARPA-H-SOL-25-119

January 10, 2025

TABLE OF CONTENTS

1.0 INNOVATIVE SOLUTIONS OPENING (ISO) SUMMARY INFORMATION

Federal Agency: Advanced Research Projects Agency for Health (ARPA-H), Proactive Health Office (PHO)

Program Title: Rare disease AI/ML and Precision Integrated Diagnostics (RAPID)

Announcement Type: Solicitation

ISO Solicitation Number: ARPA-H-SOL-25-119

Dates (all deadlines are 5pm EST):

- Proposers' Day: January 23, 2025
- Final date to submit ISO Questions: February 4, 2025
- Solution Summary Due Date: February 14, 2025
- Patients' Day: February 25, 2025
- Full Proposal Due Date: April 11, 2025

Concise Description of the Funding Opportunity: RAPID aims to accelerate rare disease diagnosis by catalyzing large-scale data curation to drive development of the world's most accurate and comprehensive diagnostic models, enabling the identification of undiagnosed patients at scale.

Anticipated Awards: Multiple Other Transaction Agreement awards.

Program Budget: ARPA-H will not publicly release the approved overall Program budget and has not established budget ceilings (or a range) for projects within the Program portfolio. Proposer funding will depend on the proposed statements of work as well as overall Program portfolio composition.

Cost Sharing Requirements: Cost sharing may be requested.

Agency Contact: All inquiries shall be sent to RAPID@arpa-h.gov.

1.1 ISO Purpose

ARPA-H seeks proposals from all eligible entities (see Section 3, *Eligibility Information*) to accomplish the RAPID 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

1.2.1 ARPA-H will post Questions and Answers (Q&As) to the RAPID 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.

1.2.3 Proposers' Day

1. ARPA-H will host a Proposers' Day in support of the RAPID Program as described in Special Notice ARPA-H-SN-25-124 (see SAM.gov). The purpose of the event is to provide potential Proposers with information on the RAPID program, promote discussion, and encourage team networking.

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

3. 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 RAPID PROGRAM INFORMATION

2.1 RAPID Background

An estimated 30 million Americans have one of 10,000 identified rare diseases, affecting 1 in 10 individuals in the US and more than 350 million people globally. It's estimated that 50% of individuals with a rare disease remain undiagnosed or misdiagnosed due to a combination of factors including disease heterogeneity, low disease prevalence, lack of awareness among healthcare professionals, and limited availability and use of confirmatory tests. The lengthy diagnostic "odyssey" endured by individuals with a rare disease lasts 6 years on average, but in many cases can extend for decades. The impact of delayed diagnosis on individuals and society is pronounced, often resulting in inappropriate care, irreversible disease progression, and significantly increased medical costs.

2.2 Program Description

2.2.1 RAPID is a 4.5-year (21-month base period and 33-month option period) program that aims to end or significantly reduce the prolonged diagnostic odysseys affecting millions of rare disease patients worldwide. RAPID seeks to develop novel diagnostic support tools for population-scale rare disease detection, systematically identifying and diagnosing rare disease patients more efficiently and accurately. This approach aims to overcome current barriers stemming from gaps in clinical assessment. By aggregating and harmonizing fragmented data and employing advanced analytic techniques, RAPID aims to drive the development and deployment of innovative rare disease detection models. These models will be designed to operate both within and outside traditional healthcare systems, enhancing the precision and scope of disease identification.

2.2.2 RAPID also emphasizes equitable access to rare disease diagnostics, focusing on reducing costs, improving accessibility, and enhancing user experiences. The program aims to democratize access to advanced diagnostic tools, ensuring that underserved and marginalized communities benefit from these innovations. By prospectively validating models in diverse clinical settings, RAPID seeks to transform the landscape of rare disease diagnosis, ensuring timely and effective care for millions of underserved patients worldwide and demonstrating the efficacy of advanced diagnostic systems.

2.2.3 Ultimately, RAPID aims to achieve measurable improvements in patient outcomes by reducing average diagnostic delays in target diseases by ≥50%, significantly decreasing the rate of misdiagnoses, and enhancing access to diagnostics for underserved populations. The program also seeks to increase clinical trial enrollment through earlier and more accurate patient identification and facilitate the discovery of actionable biomarkers to support therapeutic development. These outcome-driven targets are intended to alleviate the physical, emotional, and financial burdens of prolonged diagnostic uncertainty, improve quality of life for patients and families, and accelerate advancements across the rare disease ecosystem.

2.3 National Health Impact

Rare disease patients endure an average diagnostic odyssey of more than 6 years, including 17 medical interventions and 3 misdiagnoses. Delayed diagnosis can result in irreversible disease progression, worsening patient outcomes by increasing risk of preventable death and disability, as well as complicating treatment efforts. An accurate and timely diagnosis can result in better disease management, identification of potential therapeutics, and avoidance of unnecessary treatments and procedures. A rare disease diagnosis can also provide much-needed clarity and access to support networks and resources, improving the mental health and quality of life for patients, their families, and caregivers. More accurate prevalence estimates can also guide research and public health priorities, while faster patient identification supports clinical trial enrollment, accelerating treatment development – crucial for rare diseases lacking approved therapies.

2.4 RAPID Program Scope

2.4.1 The RAPID program takes an integrated approach to systematically identify undiagnosed rare disease patients at scale, leveraging novel training data, advanced AI/ML techniques, and real-world validation. The program will be conducted over two consecutive phases. At present, ARPA-H is soliciting innovative solutions for Phase I and Phase II that address the following Technical Areas (TAs): TA1, TA2, and TA3, introduced below. Proposers may apply to, and potentially be selected for, multiple TAs; however, each TA must be addressed by a separate solution summary and proposal. If submitting multiple proposals, clearly indicate this at the top of each submission. A subsequent solicitation for TA4 Effective Deployment and Real-World Validation will be issued separately at a later date. TA4 is anticipated to be an open solicitation, and subsequent

performers will only participate in Phase II. A Government Independent Verification and Validation (IV&V) partner will be selected separately and will provide continuous support and oversight throughout the duration of the program. The goals of each TA are outlined below:

1. Massive-Scale Rare Disease Dataset (TA1): Develop the largest curated dataset of longitudinal rare disease patient health data by integrating information from a fragmented data landscape. This extensive resource, spanning thousands of rare and ultra-rare diseases, is purpose-built to accelerate the development and validation of advanced detection algorithms and diagnostic tools. Sustainable systems will ensure the continuous aggregation and curation of patient data, driving transformative advancements in rare disease detection and diagnosis.

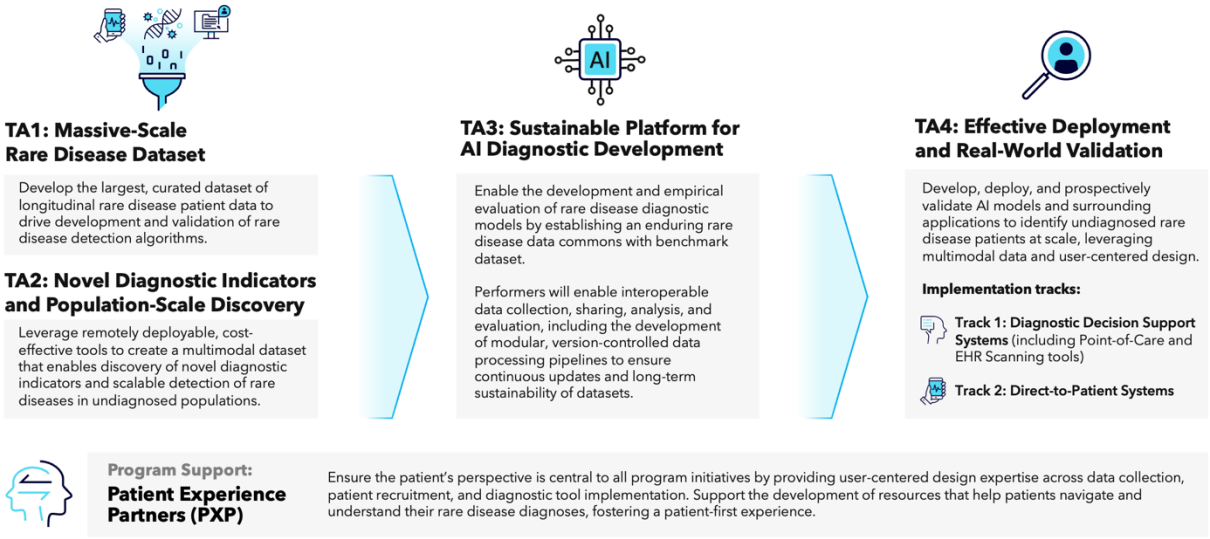
2. Novel Diagnostic Indicators and Population-Scale Discovery (TA2): Leverage cost-effective, widely accessible, and remotely deployable digital tools to collect data directly from patients, creating a comprehensive, multimodal dataset of rare disease patient health information. This dataset is designed to drive the discovery of novel diagnostic indicators and enable scalable detection of rare diseases in previously undiagnosed individuals, with an emphasis on reaching underrepresented and underserved populations.

3. Sustainable Platform for AI Diagnostic Development (TA3): Establish an enduring Rare Disease Data Commons (RDDC) with a benchmark dataset, enabling the accelerated development and empirical evaluation of rare disease diagnostic models. This dynamic, AI/ML-optimized platform will support interoperable data collection, sharing, analysis, and evaluation among key stakeholders, driving advancements in diagnostic decision support systems for rare diseases.

4. Model Benchmarking (IV&V): Following the initial phases of data collection and platform development, the RAPID Program will initiate a benchmarking effort to empirically evaluate rare disease detection models. The ARPA-H IV&V partner will facilitate the benchmarking process and collaborate with performers to integrate benchmarking tools, methodologies, and evaluation results into the TA3-developed platform. These results will provide critical insights to guide the selection of TA4 performers for Phase II.

2.4.2 In year two of the program, a Phase II solicitation will be released to solicit proposals for TA4: Effective Deployment and Real World Validation. TA4 performers will leverage data and infrastructure from TA1-3 to develop, deploy, and validate novel rare disease detection systems in both clinical and direct-to-patient settings, with real-world performance assessed through prospective validation. Data collection and processing for TA1-3 will begin in Phase I and continue through Phase II (refer to Figure 2 below for details).

Figure 1: RAPID Technical Areas (TAs) Overview. Data collected in TA1 and TA2 will be utilized by TA3 for further processing and normalization for use in the Rare Disease Data Commons and the Rare Disease Benchmark Dataset. This data will then be leveraged for model benchmarking and be available to TA4 performers for the training, testing, and validation of models in Phase II.



2.4.3 Proposers are encouraged to read the detailed description of the program's requirements for each TA below before responding to this solicitation.

2.5 Technical Approach and Structure

2.5.1 TA1: Massive Scale Rare Disease Dataset

1. TA1 will aggregate longitudinal health data of rare disease patients from diverse sources, including but not limited to Electronic Health Records (EHRs). TA1 data will enable the creation of the Rare Disease Benchmark Dataset a comprehensive data source optimized for developing and testing algorithms used in rare disease detection and diagnosis.

2. TA1 solutions must address the unique challenges of aggregating rare disease data, including fragmented data across institutions and organizations, misdiagnosis, underreporting, and limitations of medical coding systems like the International Classification of Diseases, Tenth Edition (ICD-10). Proposals should detail scalable strategies for integrating rare disease data across disparate sources, ensuring comprehensive coverage, and overcoming issues related to low prevalence and incomplete records.

3. Submissions must present a clear technological and strategic approach, with a focus on broad accessibility, patient engagement, and long-term sustainability. A detailed plan for overcoming data fragmentation, enabling scientific impact, and managing consent and Data Use Agreements (DUAs) is required.

4. TA1 proposals should address the following:

a. Disease Selection

1) A clear methodology for selecting rare diseases with a justification based on factors such as prevalence, etiology, availability of Human Phenotype Ontology (HPO) characterizations, and potential impact on under-diagnosed or under-characterized conditions.

2) An approach for collecting control data, including a justification for why the selected data is suitable as a control cohort and any additional data processing tasks required to achieve a suitable control dataset.

b. Data Format and Data Provider Selection

1) A comprehensive strategy for selecting and integrating diverse data sources and types, with the goal of maximizing the volume of usable data while navigating potential limitations imposed by data oversight requirements. This approach should detail methods for identifying, aggregating, and linking data from a wide spectrum of providers, including but not limited to healthcare organizations, insurers, diagnostic laboratories, patient advocacy groups, and research institutions.

2) Data should comprise diverse types, forming a comprehensive longitudinal medical record. Proposals should prioritize aggregating data in a format suitable for export from a health system, simulating a diagnostic support model using data from multiple providers. [Note: While structuring and normalization of data will be accomplished as part of TA3, aggregating both raw and standardized data is preferred when possible].

c. Data Accounting

Detailed methodologies for estimating and validating the content of unstructured data sources and assessing the completeness of individual patient records.

d. Data Curation and Annotation

1) A robust plan for expert curation of rare disease data, including approach to specialized disease coding (e.g., ORPHACODE, OMIM, ICD-11, ICD-10) and metadata annotation.

2) Strategy for accurately annotating patient data to identify pre- and post-diagnosis elements. Teams should develop approaches or tools capable of scaling the expert annotation process, ensuring high-quality data ready for further processing in TA3.

3) If developing novel tools for expert annotation, describe capabilities such as scalability, collaborative interfaces, machine learning assistance, and quality control methods to ensure consistent, high-quality curation across diverse diseases and data sources.

4) If developing or utilizing tools to enable expert annotation, describe strategies for integrating annotation tools into the broader data management workflow and ensuring their scalability as the program grows.

e. Data Usability and Access

1) Strategies to maximize the usability of aggregated data for use in the Rare Disease Benchmark Dataset, including approaches for de-identification, such as obtaining consent for TA3 to de-identify the data, or using synthetic data generation. Proposals should outline anticipated distributions of data access and acceptable use of aggregated data.

2) All data collected under TA1 must be available for processing and integration by TA3 performers as part of the development of the Rare Disease Data Commons. TA1 performers will be expected to collaborate with TA2 and TA3 performers to ensure data handoff for further processing in TA3.

f. Technical Infrastructure

1) A comprehensive technical infrastructure plan that supports scalable rare disease data aggregation. This plan should include strategies for managing data from varied sources, ensuring accessibility across data types.

2) Robust data processing workflows, including secure transfer methodologies to interface with TA2 and TA3 performers, and an outline of measures for ensuring data integrity, security, and privacy compliance - e.g. Health Insurance Portability and Accountability Act (HIPAA), General Data Protection Regulation (GDPR).

3) Explanation of how technical decisions support the program's strategic goals for data access, usability, and ownership rights throughout the program lifecycle.

4) Strategies for obtaining, tracking, and updating patient consent, including methods for implementing fine-grained access controls based on user roles and data sensitivity.

g. Teaming

Approaches to interfacing with external teams and subject matter experts, as well as ways to build collaboration among diverse stakeholders which may include health systems, patient advocacy groups, or patient registries.

h. Scalability and Sustainability

1) Describe how the proposed architecture will be highly scalable and adaptable for continuous growth and adaptation of rare disease data, including how the architecture accommodates external changes, such as evolving healthcare data systems, while addressing potential scalability limitations.

2) Describe approach for incorporating new data and newly diagnosed patients to enable sustainable scalability of operations beyond initial program metrics.

3) Detail plans for growing disease coverage based on early successes and emerging partnerships. Address scaling of operations and engagement strategies appropriate to the track (e.g. healthcare systems). Demonstrate how feedback from initial efforts will inform selection of new disease targets.

i. Ethics

Include an ethical framework that prioritizes patient trust and welfare. This framework should clearly delineate data ownership rights, ensure open access without imposing unfair financial barriers, and align with the program's core mission of improving patients' lives and advancing rare disease research and diagnosis.

2.5.2 TA2: Novel Diagnostic Indicators and Population-Scale Discovery

1. TA2 aims to develop a novel, large-scale, multi-modal dataset collected directly from rare disease patients through a user-friendly digital system. Solutions should be patient-centric including a highly usable interface for collecting novel and diverse data types, such as but not limited to, patient-reported outcomes, photos, video, audio, or other inputs that can be

utilized in the training and validation of rare disease diagnostic models. The dataset should enable the development of scalable models that support the diagnosis of patients who are underrepresented in EHRs or have limited access to the healthcare system, such as low-income households, racial/ethnic minorities, and rural residents. The data collection systems should also have the capability to obtain patient consent for collecting their EHR data. Submissions must include a comprehensive plan for collecting the appropriate consent and Data Use Agreements (DUAs) to enable broad access to aggregated data both during and after program completion.

2. TA2 proposals should address the following:

a. Targeted Population Selection

1) Describe and justify a methodology for selecting targeted rare diseases to reach the required metrics, emphasizing under-diagnosed conditions with identifiable multi-modal diagnostic signals or incomplete characterizations for advancing scientific understanding, demonstrating how the chosen diseases will advance diagnostics, improve patient outcomes, and potentially impact underserved populations.

2) Outline a methodology for selecting "control" populations and collecting relevant data, with justification for the intended selection methods to create a control group, such as age-matched populations.

b. Outreach Plans

Outline partnerships and strategies for patient identification and outreach, detailing plans to engage rare disease communities and ensure representation of historically underserved groups (e.g., low-income households, racial/ethnic minorities, rural residents) with the objective of improving rare disease diagnosis among underrepresented groups while maintaining the privacy of potentially vulnerable populations.

c. Data Definitions

Define a comprehensive data dictionary for the collection effort, including a core set of data elements required from all participants and any additional proposed elements. Justify each data point based on its relevance to diagnostic modalities, phenotyping potential, and early diagnosis capabilities. Outline the collection methodology and address mitigations for potential biases, especially for supplementary data requiring specialized tools.

d. Data Usability and Access

1) TA2 performers will be expected to collect data from both rare disease patients and patients without rare disease to serve as control data. Of the rare disease respondents, performers should obtain consent from >50% to collect EHR data for use in the Rare Disease Benchmark Dataset. Outline a consent management strategy on the collected data that includes both the immediate data collection and future research and development uses. This strategy should define which data can be used in a publicly released Rare Disease Benchmark Dataset and which data should be reserved for controlled research purposes. Explain how the consent strategy will have the flexibility to support potential future research.

2) All data collected under TA2 must be available for processing and integration by TA3 performers as part of the development of the Rare Disease Data Commons. TA2 performers will be expected to collaborate with TA1 and TA3 to ensure data handoff for further processing in TA3.

e. Data Collection Interface

1) Describe a patient-facing digital interface for data collection and patient interaction, with a primary focus on accessibility (i.e., cross-platform compatibility) and usability, including anticipated timelines for development. Detail the interface's design choices, explaining how they impact other aspects of the proposal, such as collected data quality, user engagement, and usability. This interface will serve as the central platform for executing data collection efforts.

2) Include details on interface adaptability to diverse user needs, including multi-language support, cultural adaptability, and intuitive design for both self-use and assisted data collection.

3) Discuss data collection capabilities, detailing potential technological limitations and their impact on data quality, and explain how these factors influence the overall data gathering strategy.

f. Data Validation

Propose a comprehensive data validation strategy encompassing both real-time and post-collection processes. Detail automated methods for immediate data validation during collection, ensuring

adherence to quality standards and content correctness. Include plans for analytical validation of collected data to maintain consistency across patients and uphold overall data fidelity.

g. Adaptability

1) Demonstrate an adaptable interface capable of evolving throughout the collection efforts, modifying data collection requirements as needed.

2) Define the ability to push updates, deploy multiple versions where necessary.

3) Outline how the system will incorporate new populations and findings, ensuring it remains agile and responsive to evolving research needs and discoveries throughout the project lifecycle.

4) Define a mechanism for re-contacting patients to gather new or updated information.

h. Security and Privacy

Describe robust security measures and privacy protocols for the collection, storage, and transfer of Protected Health Information (PHI), ensuring compliance with all relevant data protection regulations and industry standards (e.g., HIPAA, GDPR, NIST SP 800-53, ISO/IEC 27001, HITRUST).

i. Technical Infrastructure

Detail a comprehensive technical infrastructure capable of hosting and deploying the digital interface, managing patient data transfer and staging, handling user accounts and authentication, securely storing data, and facilitating transfers to authorized entities for analysis and processing.

j. Scalability and Sustainability

1) Proposals should prioritize extensible and sustainable systems over singular efforts, detailing long-term scalability and growth strategies including international expansion, leveraging the ubiquity of digital devices to facilitate global reach.

2) Detail plans for growing disease coverage based on early successes and emerging partnerships. Address scaling of operations and engagement strategies appropriate to the track (e.g. patient advocacy organizations). Demonstrate

how feedback from initial efforts will inform selection of new disease targets.

2.5.3 TA3: Sustainable Platform for AI Diagnostic Development

1. The TA3 performer will establish a Rare Disease Data Commons (RDDC), an AI/ML-optimized data platform designed to accelerate the development and evaluation of rare disease detection algorithms. A primary output of TA3 is the novel Rare Disease Benchmark Dataset to catalyze the research and development of diagnostic models by providing essential data and a common data source for comparing model performance.

2. The TA3 performer will work closely with the data collection initiatives (TA1 and TA2) to ingest, host, and process health and medical data, transforming it into the Rare Disease Benchmark Dataset, a research-grade resource optimized for machine learning. The performer will leverage advanced technologies for data structuring and normalization, while developing a user-friendly interface for accessing the Rare Disease Benchmark Dataset, supported by a sustainable and accessible protocol that manages all relevant DUAs. In collaboration with TA1 and TA2, TA3 will also oversee consent processes, ensure data de-identification, and coordinate data ingestion schedules.

3. TA3 proposals should address the following:

    a. Data Infrastructure

        1) Propose a technical infrastructure capable of securely handling patient data packets from diverse providers, accommodating multiple data formats and various data access methods, including federated access.

        2) Describe approach to pre-processing data and secure, efficient solutions to storing processed data.

        3) Address how the infrastructure will adapt to different interfacing systems (e.g., local vs. federated data sources).

    b. Data Processing

        1) Describe an advanced pipeline for structuring and normalizing heterogeneous medical data into standardized formats (e.g., HL7 FHIR, HPO, VCF/GA4GH), including immediate capabilities, performance metrics, and strategies for ongoing adaptation to evolving standards.

2) Include plans for ensuring data interoperability, such harmonizing through use of a Common Data Elements (CDE) dictionary.

3) Describe how you will enhance the Extract, Transform, Load (ETL) pipeline with external knowledge bases and graphical data elements to support downstream knowledge graph development.

4) Describe how you will establish a HIPAA-compliant de-identification plan, in collaboration with TA1 and TA2, leveraging existing services where applicable, and incorporating informed consent and privacy waivers as needed.

5) Propose processes to validate data accuracy and completeness, identifying and addressing gaps or inconsistencies.

c. Rare Disease Benchmark Dataset Access

1) Describe a Rare Disease Benchmark Dataset access interface and access protocol, including clear, ethical guidelines for data access, considering varied data use agreements and consent levels. A thoughtful protocol for managing data access should balance openness with necessary protections, ensuring that the Rare Disease Benchmark Dataset serves as a democratized resource in rare disease research.

2) Outline a comprehensive plan for managing researcher access to the platform that ensures robust data privacy and security while facilitating collaborative research. The RDDC should implement a granular access control system, granting researchers access only to the specific data and tools necessary for their approved projects, and should include provisions for creating multiple versions of the Rare Disease Benchmark Dataset, including a publicly accessible version.

3) Include a data governance framework that tracks data provenance/lineage, enables element-level access controls, and maintains secure linkages between identifiable and de-identified data while keeping them separated in storage and access.

Note: Once de-identified, Rare Disease Benchmark Dataset distribution may include a controlled public access protocol, such

as a contractual DUA and/or mandatory data privacy training, to uphold trust. Alternative methods of controlled public access could follow a broad IRB access protocol, such as the Clinical Data Science IRB (CDS-IRB). The Rare Disease Benchmark Dataset must be available for public use in perpetuity. Performers may not implement exclusionary or restrictive use requirements (e.g. processing data using proprietary methods).

d. Scalability and Sustainability

1) Outline how the infrastructure will address the data processing pipeline's sustainability in adapting to changing data standards and regulations, including ability to handle growing data volumes and expanding international data sources.

2) Scalability is crucial for the platform to accommodate the growing volume and variety of rare disease data. Describe the architectural design and infrastructure choices that will enable the platform to scale horizontally and vertically as data and user demands increase to ensure that the platform can handle increasing workloads without compromising performance or availability. Further, ARPA-H may negotiate use of the RDDC for broader health ecosystem data.

3) To ensure the long-term success and impact of the platform, proposals should include detailed plans for continued maintenance and updating of the system. This may involve the establishment of dedicated support and development teams, regular security audits and penetration testing, and the implementation of robust backup and disaster recovery procedures. Proposers should also outline their strategies for maintaining data privacy and security, including compliance with relevant regulations such as HIPAA and GDPR, and the implementation of industry-standard security controls such as encryption, access logging, and intrusion detection.

e. Financial Sustainability

1) Provide a sustainable financial model that ensures long-term viability without compromising data accessibility or the project's core mission of serving the rare disease community – including steps that would encumber data access because of intermediary data processing. This may include the exploration of non-rare disease applications, such as extending the platform's capabilities to support the

diagnosis and management of more common diseases. Proposals should also consider the potential for partnerships with academic institutions, healthcare organizations, and industry stakeholders to secure funding, expertise, and resources for the continued development and maintenance of the platform.

2) Outline a sustainable funding model that doesn't compromise data quality or create biased access with incentives that hamper the quality and accessibility of the Rare Disease Benchmark Dataset. Financial sustainability should be tied to technical and strategic plans, including Rare Disease Benchmark Dataset update cadences, access protocols, and hosting infrastructure.

f. Benchmarking Framework

1) Include a comprehensive framework for evaluating and benchmarking external models; this framework will be developed in partnership with the IV&V partner and should support a wide range of evaluation techniques, bias scores, noise-injection for robustness, performance benchmarking, and expert review, allowing for a thorough assessment of model quality and validity.

2) Privacy considerations should be considered in the external model evaluation architecture and the method for returning results. The model evaluation capabilities should also be able to support model comparisons, such as model leaderboards, for varying specific or general tasks.

g. Ethics

1) Explain methods for actively involving the rare disease community in shaping the Rare Disease Benchmark Dataset's evolution, from governance to feature development.

2) Describe safeguards and policies that promote responsible data use, protecting patient privacy while fostering open science.

3) Include a plan for establishing an Institutional Review Board (IRB) to oversee TA3 work and ensure compliance with informed consent procedures established by TA1 and TA2. Note: TA1and TA2 performers are responsible for obtaining data, and therefore for obtaining informed consent.

2.5.4 Additional Considerations (Applies to TAs 1-3)

1. Government Data Rights

   Data generated under this program, including de-identified and processed patient data, must be made available to the Government in accordance with the applicable Data Use Agreement (DUA). Unlimited Government Rights are preferred to maximize program impact, though not required. Data must be accessible to performer(s) of Technical Area 3 (TA3) and shared in compliance with all relevant legal, ethical, and contractual requirements, including patient consent agreements, and applicable regulations. Data sharing practices should be designed to align with the program's objectives, ensuring broad usability while upholding ethical and regulatory standards.

2. Optional Rights Negotiation

   Performers in TA1 and TA2 will have the opportunity to negotiate additional Government rights as part of the contracting process. These optional negotiations will specifically address the integration of data collected under the RAPID program into the ARPA-H data commons, fostering agency-wide impact and facilitating future data reuse.

3. Deidentified Data

   De-identified patient data collected or generated under this program must be accessible to other program performers and available as a public resource under controlled access, such as through restricted databases or access granted upon committee approval. Data must comply with applicable de-identification standards, such as HIPAA's Safe Harbor or Expert Determination methods, ensuring no information could reidentify patients. If additional consent requirements are specified in a DUA, these must also be met.

4. Identifiable Data

   Identifiable data, such as patient photographs, must only be shared with authorized entities under applicable DUAs and explicit patient consent agreements. Such sharing must adhere to all relevant legal, ethical, and contractual guidelines.

5. Management Plan

   Project teams must include a Principal Investigator (PI), or co-PIs, identified for the management team, as well as one designated primary point of contact (POC) who will serve as the Project Manager. Management plans should provide good faith estimates of metrics and target values that are appropriate and specific to proposed use-cases as well as detailed plans for meeting stated milestones on the prescribed program schedule (see Section 2.6 Program Timeline, Phases & Milestones). Technical risks along with mitigation strategies or alternative approaches should be included where appropriate.

6. Institutional Review Board
   Projects must include a draft Institutional Review Board (IRB) protocol or, at minimum, a plan for having an IRB protocol approved by month 6 of performing in the RAPID program for handling sensitive patient data. Program plans should address risk mitigation and compliance efforts related to handling such data.

2.5.5 Patient Experience and Engagement

1. Proposals for each TA should outline clear strategies for engaging patients and incorporating their perspectives through methods such as surveys, interviews, or focus groups, ensuring their input informs the development of key deliverables.

2. Continuous engagement and feedback loops should be described to ensure patient insights are consistently integrated throughout the project lifecycle, resulting in outcomes that align with patient needs and expectations.

3. Performers are expected to collaborate with Patient Experience Partners, described below, who will provide valuable guidance and resources to enhance engagement strategies. These partnerships will play a critical role in ensuring patient voices are effectively and consistently integrated throughout the program.

2.5.6 Program Support: Patient Experience (PX) Partner Network

1. Performers will be required to partner with PX Partners throughout the period of performance. The PX component of the RAPID program aims to ensure that patient perspectives, feedback, and lived experiences are integrated throughout the program. This component, solicited and funded through the IV&V RAPID Partner, will fund patient advocacy groups and organizations, which will serve as essential partners in fostering patient-centric design and participation, ensuring patient input is continuously incorporated into the development and deployment of RAPID tools and technologies. By leveraging their deep connections with patient communities, these organizations will help foster trust and drive patient participation, ultimately enhancing the success of the program.

2. **PX Partners are not eligible for ARPA-H awards under this solicitation and will be selected and funded independently. Entities must choose between serving as a PX Partner and performing under any TA, performance in one area will prevent performance in the other.** The RAPID IV&V partner will manage the PX Partner Network.

3. PX Partners will support and collaborate with RAPID program performers to facilitate patient-centered design and achieve the following:

a. Objectives:

1) *Amplify Patient Voices:* Ensure patient feedback, perspectives, and experiences are integrated into program decisions and technology development.

2) *Improve Data Relevance:* Align data collection, aggregation, and diagnostic models with the real-world conditions, symptoms, and challenges faced by rare disease patients.

3) *Promote Engagement:* Actively engage populations underrepresented in rare disease research and historically marginalized in healthcare, including racial and ethnic minorities and rural communities, to ensure their perspectives are reflected in data collection and analysis.

4) *Build Patient Trust:* Foster transparency and trust between the program and patients through active, ongoing engagement, championing responsible and ethical program practices.

b. Specifications and deliverables:

1) *Awareness and Outreach:* Partner with patient advocacy groups to raise awareness about the RAPID program within patient communities, increasing program visibility and engagement.

2) *Incentivize Data Participation:* Engage and motivate patients and patient advocacy groups to contribute data for TA1 and TA2, ensuring a diverse and representative dataset through patient outreach efforts.

3) *Usability Feedback:* Facilitate patient participation in user experience research (UXR), ensuring that patient perspectives are incorporated into the design and validation of user interfaces, and that tools are accessible and user-friendly.

4) *Trust Building:* Develop strategies that build patient trust in the program's new technologies and platforms, focusing on transparency, privacy, and the benefits of participation.

5) *Patient Resources:* Assist performers with the development of patient-facing resources such as tutorials, FAQs, and educational materials to help patients understand and

effectively use the tools and platforms developed in RAPID, maximizing their accessibility, utility, and benefit.

Organizations interested in becoming a PX Partner are invited to join an informational event to be held after Proposers' Day. For details about the event and instructions on applying to the PX Partner Network, please visit the RAPID program page: https://arpa-h.gov/research-and-funding/programs/rapid

2.6 Program Timeline, Phases & Milestones

RAPID is a 4.5 year (54-month), two-phase program with a 21-month Phase I period and an option for a 33-month Phase II period. Multiple awards are anticipated, and it is expected that fewer performers may be funded to participate in Phase II. For TA1, TA2, and TA3 the Phase II options may be exercised, at the Government's sole discretion, based on technical progress measured against the metrics (Table 1) and milestones defined in the Innovative Solutions Opening, and based on funding availability. Each Phase has key technical milestone goals. A description of the Phases, which are aligned with critical program milestones are described below:

2.6.1 Phase I (months 0-21): Foundation Building

At the start of Phase I, TA1 and TA2 performers will immediately commence data aggregation and collection efforts. TA2 performers will also design, test, and deploy scalable approaches for collecting multimodal data directly from patients. By the end of Phase I, TA1 and TA2 performers should have submitted data that has been validated by IV&V, satisfies all metrics, achieves all milestones, and is ready to support benchmarking and algorithm development for TA4 performers. Throughout the process, ARPA-H will be conducting periodic data assessments (to be defined after performer selection according to program needs), and performers should be ready to submit data Quality Assurance (QA) and progress reports. Initially, TA3 performers will prioritize the development of platform functionalities for processing data, as well as creating, maintaining, and hosting the Rare Disease Benchmark Dataset. The metrics define high-level goals, and the milestones outline a roadmap of features expected to be fully operational. Once baseline capabilities are established, TA3 performers will shift their efforts toward enabling the benchmarking of machine learning models.

2.6.2 Phase II (months 22-54): Development, Deployment, and Validation

1. During Phase II, TA1 and TA2 performers will build upon their initial efforts, with an expanded focus on scaling to address ultra-rare conditions and incorporating international data sources. Data QA and progress reports will continue to be conducted similarly to Phase I, along with similar IV&V analyses. TA3 performers will prioritize the continuous enhancement of core platform capabilities while advancing functionalities for real-time data exchange and collaboration with data providers, deploying models in clinical settings, and facilitating external model evaluation.

2. It is expected that TA4, solicited at a later date, will be incorporated during Phase II. TA4 model development will involve an iterative process with continuous cycles of model development and testing. At yearly intervals, model performance will be evaluated against baseline metrics, and improvements will be expected in subsequent intervals based on these assessments. Additionally, ARPA-H will conduct spot checks on model performance, and IV&V will analyze model architecture.

3. During the second half of Phase II, TA1 and TA2 performers will continue to scale their systems and finalize efforts to achieve the most challenging metrics and milestones. Their success will depend on the initial systems and groundwork established in the previous phase. TA3 performers will focus on continuous development of RDDC features to meet yearly metrics, while also deploying new functionalities for researcher access and clinical deployment. ARPA-H and IV&V analyses will proceed in a manner similar to the prior phases.

4. The ultimate objective of Phase II is to transition from controlled clinical validation to real-world deployment in its later stages. During the deployment period, performers will iteratively refine their methods to align with real-world conditions, leveraging techniques validated by the IV&V team to enhance their models. Performers will be evaluated based on their performance and outcomes in real-world applications.

2.6.3 Independent Verification and Validation (IV&V)

1. IV&V will be conducted by an ARPA-H identified entity with the necessary capabilities to evaluate performance during the program. Performers are expected to work closely with the IV&V team throughout the program's duration. In particular, evaluations will take place before scheduled Phase transitions to ensure validation and real-world performance of developed technologies in Phases I & II.

2. For TA1 and TA2, IV&V will focus on data quality and completeness, ensuring that the underlying data matches the high-level descriptive metrics. For TA3, IV&V will validate that the features function as described and that security standards are met. IV&V will also manage the Patient Experience Partners program support.

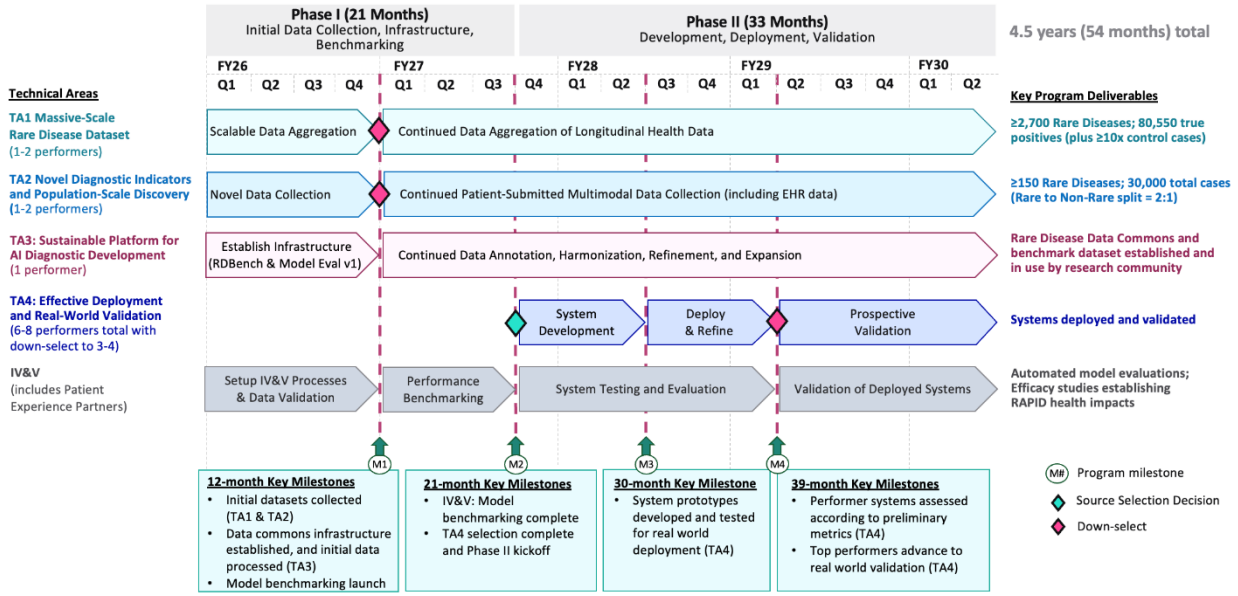
3. As noted above, the IV&V entity will also provide PX Partners for Performers.

2.6.4 Program Deliverables

RAPID anticipates several deliverables from the cumulative outputs of each TA. TA1 will produce the raw data to be used to develop an expertly curated, novel Rare Disease Benchmark Dataset, and ideally a sustainable system for identifying and aggregating rare disease data. TA2 will produce both a large-scale, diverse, multi-modal dataset representing several rare diseases and a control population

alongside a highly usable digital system for collecting the data. TA3 will produce a rare disease data commons that has the functionality to ingest various formats of health data and medical records to produce an AI-optimized dataset provided through a controlled access interface.

Figure 2: RAPID Program Timeline, Key Milestones and Deliverables across Phase I & II: TA1-TA4. Timeframes are relative to the start of the program. Note dotted red lines depict program phase transitions or key milestones, while gray-dotted lines depict end of fiscal-year.



2.6.5 Program Metrics

1. Specific metrics will be used to track progress as performers complete tasks for each individual TA. Performers will be required to report progress against these metrics as needed to the Program Manager, and to the designated IV&V team(s). These metrics will be used to evaluate success and will inform the Government team as they decide which performers will continue in the Program.

2. Table 1 defines the aggregation metrics by subcategory for the yearly target minimums. Proposers are also encouraged to include in their proposal any additional quantitative metrics and milestones, beyond those listed in Table 1, that they plan to use for tracking progress toward the final goals of each TA. If mutually agreed upon during negotiations, these additional metrics will be incorporated into the OT agreement alongside the established evaluation criteria. The ability to meet target metrics on time will be a major factor for advancing to later milestones of the RAPID Program. Clarifying details on specific metrics are provided in Table 2 and Table 3.

Table 1: RAPID Program Metrics across TA1. Timeframes are relative to the start of the program. Select metrics are explained in more detail in the following section.

TA1 AGGREGATION METRICS	SUB-CATEGORY	TARGET (Minimums)					
		Year 1	Year 2	Year 3	Year 4	Year 5	Grand Totals
Totals	**Total Disease Count**	**≥400**	**≥400**	**≥525**	**≥620**	**≥755**	**≥2,700 diseases**
	Total Sample Size	**≥22,000**	**≥21,500**	**≥20,100**	**≥11,200**	**≥5,750**	**≥80,550 samples**
Higher prevalence aggregation (likely in the range ~10-50/100k)	Disease Count	≥200	≥100	≥75	≥20	≥5	≥400 diseases
	Sample Size min.	≥100	≥200	≥250	≥500	≥1,000	≥73,750 samples
Lower prevalence aggregation (likely in the range ~0.1-9/100k)	Disease Count	≥200	≥300	≥450	≥600	≥750	≥2,300 diseases
	Sample Size min.	≥10	≥5	≥3	≥2	≥1	≥6,800 samples
Number of international sources	--	--	≥1	≥2	≥3	≥5	
Control Data	Control data must be collected annually at a minimum 1:10 ratio of rare to non-rare disease patients						≥805,500 samples

Table 2: RAPID Program Metrics across TA2. Timeframes are relative to the start of the program.

TA 2 METRICS	SUB-CATEGORY	TARGET				
		Year 1	Year 2	Year 3	Year 4	Year 5
Representation: Percent margin of error from US Census Bureau metrics	Demographic	≤30%	≤25%	≤20%	≤15%	≤10%
	Regional	≤30%	≤25%	≤20%	≤15%	≤10%
Total Sample Size: Cumulative number of distinct patients represented in the collected datasets. Ratio of rare disease to control data sample size should be 2:1		≥10,000	≥15,000	≥20,000	≥25,000	≥30,000
Disease Representation: Min. number of distinct rare diseases covered in the data		≥30	≥60	≥90	≥120	≥150

Table 3: RAPID Program Metrics across TA3. Timeframes are relative to the start of the program.

TA3 METRICS	SUB-CATEGORY	TARGET				
		Year 1	Year 2	Year 3	Year 4	Year 5
Harmonization: Percent of files that are normalized to required frameworks (metadata, OMOP, HPO, GA4GH) with ≥95% accuracy		≥75%	≥80%	≥85%	≥90%	≥95%
Enablement: Percent of patient records included in external model evaluation dataset		≥15%	≥35%	≥55%	≥75%	≥85%
Useability: Likert-scale assessment of usability, measured by user satisfaction		≥60%	≥70%	≥80%	≥90	≥95%

2.6.6 TA1 Data Aggregation

1. Metric: Higher Prevalence

   In the first year, a substantial sample size for a broad range of “prevalent” rare diseases is required to create a foundational dataset. As the program progresses, the focus will shift toward acquiring a significantly larger sample size for a smaller set of diseases, enabling the creation of a dataset with greater data depth. Only "complete" samples, defined by both comprehensive EHR elements and longitudinal availability, will contribute to the measured sample size. Performers are expected to propose target diseases ensuring their selections are grounded in strong, evidence-based justifications. This approach enables performers to leverage their expertise and resources, maximizing the impact and value of the data collected.

2. Metric: Lower Prevalence

   Initially, a small number of samples is expected to be collected for selected lower-prevalence diseases, establishing a foundation for future expansion and to achieve a dataset with high coverage across the spectrum of rare diseases. Over time, the metric will shift to include at least one sample for a substantial proportion of known rare conditions. Disease specific data counts will contribute to both higher and lower prevalence metrics, so that the 100 diseases aggregated for achieving high sample sizes also count towards this metric for wide disease coverage. This approach ensures the efforts to build the dataset do not overlook less common diseases, establishes infrastructure for collecting data on ultra-rare conditions, and positions the platform for future growth. By setting a target of including at least one sample for a large number of rare diseases, the program incentivizes broad participation from the rare disease community, fostering collaboration and knowledge-sharing.

3. Metric: International Sources

   International data sources are required to be a source for data aggregation, with a progressively increasing total number of sources during the program. There are no specific sample size requirements, but sources should include entities such as patient groups, academic centers, or research hospitals. International data integration is crucial for developing robust diagnostic tools, promoting global collaboration, and understanding the full spectrum of rare diseases across different populations. As the platform expands its global reach, it will attract more users worldwide, leading to internationally scalable growth and impact. Prioritizing the inclusion of international data sources is based the importance of diverse representation and global collaboration in addressing the complex nature of rare diseases.

2.6.7 TA2 Data Collection

1. Metric: Representation

   The collected data must align with the most recent US Census Bureau's demographic and regional distribution – with a shrinking margin of error over the course of the program- to ensure representativeness and serve historically underserved communities. However, overrepresentation of minority groups is encouraged and preferred to address disparities in data availability and provide robust, equitable training data for diagnostic models. Representation will be calculated based on a subset of data equal to the minimum annual sample size to maintain incentives for collecting data across all groups, promoting ongoing dataset expansion and refinement. Achieving diverse representation can also yield insights into effective outreach strategies for identifying underrepresented communities for subsequent proactive identification model development.

2. Metric: Total Records Collected

   To ensure this data collection effort reaches a substantial scale and supports robust model development, performers must meet a minimum target for the total number of individuals with complete data records. Data must pass QA checks for completeness, validity, and quality to count towards these requirements. Individuals with rare diseases should be asked to provide consent for the collection of their EHR data to enrich the rare disease benchmark dataset, helping to create a richer and more transformative dataset.

3. Metric: Disease Representation

   Performers will be required to encompass a diverse array of rare conditions in order to support developing robust diagnostic models that can accurately identify and differentiate between numerous rare disorders, creating a comprehensive tool to support proactive identification of rare diseases. The total number of distinct diseases increases year-to-year, to allow for scaling up of collection efforts. Performers can select specific rare diseases to target, leveraging their expertise to prioritize conditions based on factors such as disease characteristics, potential for novel insights, and anticipated impact of improved diagnostic tools. Instead of prescriptive sample size requirements per disease, performers must provide justification for their sample size determinations based on factors such as disease prevalence and data collection considerations. This approach balances representativeness with practical challenges in obtaining data for rare diseases with varying prevalence levels and support groups. This will also encourage performers to allocate resources strategically to maximize the dataset's impact and provide a solid foundation for future innovations in rare disease diagnostics, especially with alternative data.

2.6.8 TA3 Data Commons

1. Metric: Harmonization
   This metric assesses the effectiveness of the platform's data ingestion and normalization processes. To meet this metric, the ETL pipelines must coordinate with TA1 performers and apply de-identification and normalization techniques to extract and standardize data elements from incoming data sources. The extracted data should conform to established ontologies and standards, including HL7 FHIR (or the most current version) for healthcare data, HPO for phenotypic characterizations, and GA4GH Variant Representation Specification (VRS) for genomic data. By ensuring that the ingested data is properly de-identified and normalized to these standards, the RDDC can facilitate data interoperability, enable more effective data analysis, and support the development of accurate and robust diagnostic models for rare diseases. To allow for continuous development of these capabilities the metric starts lower and becomes more stringent over the course of the program. Evaluation will entail a combination of manual review and automated evaluation on labeled data from TA1 and public sources.

2. Metric: Enablement
   The Enablement metric evaluates the proportion of data within the platform that can be utilized for external model evaluation, promoting the development of innovative diagnostic support models for rare diseases. To achieve high Enablement scores, performers must secure increased consent for the direct use of patient data in machine learning and research applications or implement advanced data techniques that effectively de-identify patient data while preserving its utility for model evaluation. As the metric becomes more stringent over the course of the program, it incentivizes establishing a dynamic system that facilitates communication with data providers and patients, allowing for the continuous acquisition of new data and the expansion of data use permissions. To supplement this effort, performers can develop innovative methods and capabilities that maximize the usability of the data for model development (e.g. privacy-preserving techniques like homomorphic encryption or generating high-quality synthetic data). TA3 performers may collaborate with TA1 performers for obtaining additional patient consent and may also propose varied access protocols that provision different levels of access across different data types or individual patient data.

3. The preliminary list of priority data elements is identified in Appendix B.

2.7 General Requirements

It is expected that proposals will involve teams with the expertise needed to achieve the goals of TA1, TA2, and TA3 independently or in any combination. Specific content, communications, networking, and team formation are the sole responsibility of the

proposer. Proposers must submit a separate proposal for each TA they wish to apply for. Each proposal must be led by a Principal Investigator (PI) and must address all phases and metrics applicable to that specific TA. A single PI may lead multiple proposals, provided that each proposal is distinct and addresses the specific requirements of the corresponding TA.

To facilitate teaming, ARPA-H will hold a hybrid in-person and virtual Proposers' Day (see Section 1.2), encouraging the participation of a wide range of potential teams with cutting-edge approaches and enable sharing of information among interested proposers.

2.7.1 Data Standards

When obtaining or transferring relevant identifiable medical data, performers must either operate as Trusted Exchange Framework and Common Agreement (TEFCA) Qualified Health Information Networks (QHINs) or operate through existing QHINs. The target state data standards for this program include the most current versions of general healthcare data interoperability and ontologies and those specific to Rare Disease data elements. Currently, these standards are HL7 FHIR, GA4GH Variant Representation (VRS), and the Human Phenotype Ontology (HPO). For the purposes of this program, it is assumed that OMOP can be extracted from FHIR and that the required ontologies and models enable a Findable, Accessible, Interoperable, and Reusable (FAIR) implementation. Data processing and normalization pipelines are integral to this program and will ensure that all incoming data can be processed to be structured using the target data standards. This approach enables continuous improvements in data recognition and extraction tasks, as well as sustainable pipelines that can adapt to future changes. Incoming data should be available in its original form, where relevant, to allow processing using the same methods as all other data and to remain unaffected by changes in data standards. While having incoming data in both its original form and its relevant structured form is ideal, it is not a strict requirement given the processing capabilities. Proposers should demonstrate how their submissions directly enhance the ability to curate and structure data in the most usable form, aligning with the program's objective of harmonizing disparate data sources while adhering to the best practices outlined above.

2.7.2 Intellectual Property (IP) and Open Software Standards

1. The ARPA-H RAPID program will emphasize creating and leveraging open-source technology and architecture. Intellectual Property rights asserted by proposers are strongly encouraged to be aligned with open-source regimes. Thus, it is desired that all non-commercial software (including source code), software documentation, and technical data generated by the project are provided as deliverables to the Government with open-source or unlimited rights, as lesser rights may negatively impact the potential for this biomedical data ecosystem to become self-sustaining. Open-source code is highly encouraged using permissive, business-friendly open-source licenses such as CC-BY, BSD, MIT, Apache

2.0 or similar. Approaches that inhibit this objective are not desired and would adversely affect the project goals and objectives.

2. All 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 under the proposed effort. The information will be requested as part of a full proposal request.

3.0 ELIGIBILITY INFORMATION

3.1 Eligible Applicants

All responsible sources capable of satisfying the Government's needs may submit a proposal to the ISO. Specifically, universities, non-profit organizations, small businesses and other than small businesses are eligible and encouraged to propose to this ISO. While those that were discouraged during the Solution Summary phase are eligible to submit a proposal, it is ***strongly discouraged***. PX Partners are not eligible to perform under any TA as a Prime or subrecipient.

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

1. 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.

2. 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.

3. 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, contact this email address: RAPID@arpa-h.gov.

4. 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, the party should contact: RAPID@arpa-h.gov.

5. If a potential prime performer believes that an FFRDC has a unique capability without which their solution is unachievable, potential prime performers should be aware that they will have to provide documentation as part of their abstract submittal showing that they have exhausted all other options in order for ARPA-H to consider the inclusion of the FFRDC in the proposed solution.

3.1.2 Non-US Entities

ARPA-H will prioritize awards to entities (organization and/or individuals) that will conduct funded work in the United States. However, non-U.S. entities may participate to the extent that such participants comply with any necessary nondisclosure agreements, security regulations, export control laws, and other governing statutes applicable under the circumstances. In accordance with these laws and regulations, in no case will awards be made to entities organized under the laws of a covered foreign country [as defined in section 119C of the National Security Act of 1947 (50 U.S.C. Ch 44 § 3059)]; a foreign entity of concern meeting any of the criteria in section 10638(3) of the CHIPS and Science Act of 2022; [an individual that is party to a malign foreign talent recruitment program, as defined in Section 10638(4) of the CHIPS and Science Act of 2022; or entities suspended or debarred from business with the Government.

3.1.3 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 award negotiation.

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 and 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 SUBMISSION AND EVALUATION PROCESS

The RAPID selection process is based on the following steps designed to maximize efficiency, transparency, and integrity:

- Eligible entities submit Solution Summary packages
- Government verifies eligibility and then reviews eligible Solution Summaries to determine whether a full proposal is encouraged or discouraged.
- Proposers are notified whether they are encouraged to submit a full proposal or not.
- Eligible entities submit full proposals.
- The Government reviews full proposals to determine conformance to the ISO, including Program scope and minimum requirements.
- The Government reviews conforming full proposals against criteria 1-3 and determines the proposals that are most advantageous. The most advantageous

proposals will be selected for award negotiations based on available funding and Program needs.

- Proposers are notified whether a proposal (1) was determined non-conforming and was not considered further; (2) has been selected for award negotiations or (3) the proposal has not been selected for award negotiations. High-level feedback will be provided to proposers who submit conforming proposals, either verbally or in writing (subject to Government discretion).
- In addition to the notices mentioned above, the Government may request clarification from any proposer at any stage of the process. Requests for clarification do not allow for proposal revisions.

4.1 Solution Summary Submissions

Solution Summary submissions are required. See Appendix C for recommended formatting and Solution Summary guidance.

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 C (Solution Summary Format and Instructions) and Appendix D (Full Proposal Format and Instructions).

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 Solution Summary and proposal Submission Deadlines

4.3.1 The closing date of this solicitation, as established in Section 1, is the final date Solution Summaries will be accepted.

4.3.2 The due date for full proposals will be provided at the time of Solution Summary feedback.

4.4 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." Other incorrect markings (e.g., Confidential) will bear no weight.

5.0 REVIEW AND EVALUATION OF FULL PROPOSALS

5.1 Conforming Proposal Submissions

5.1.1 Conforming submissions contain all requirements detailed in this ISO. Full proposals that fail to include required information will be deemed non-

conforming and may be removed from further consideration. To be considered conforming, the proposal must meet the following elements:

- The proposed concept is applicable to the RAPID Program.
- The Proposer meets the eligibility requirements.
- The proposal meets the submission requirements.
- The proposal meets the content and formatting requirements in the attached Appendices.
- 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).
- The full proposal is submitted by a Proposer that submitted a timely and responsive Solution Summary.

5.1.2 Non-conforming 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.

5.2 Proposal Evaluation Criteria

The following criteria, listed in descending order of importance, will guide the Government's evaluation of proposals that have been determined to be conforming and thus eligible for further consideration.

5.2.1 Criterion 1: Overall Scientific and Technical Merit

The proposed technical approach is innovative, feasible, achievable, and complete. Task descriptions and associated technical elements provided are complete and in a logical sequence with all proposed deliverables clearly defined such that a final outcome that achieves the goal can be expected as a result of award. The proposal identifies major technical risks and planned mitigation efforts are clearly defined and feasible. In addition, the evaluation will take into consideration the extent to which the proposed intellectual property (IP) rights structure will contribute to the success of the Program.

5.2.2 Proposer's Capabilities and/or Related Experience

The proposed technical team has the expertise and experience to accomplish the proposed tasks. The proposer's prior experience in similar efforts clearly demonstrates an ability to deliver products that meet the proposed technical performance within the proposed budget and schedule. The proposed team has the expertise to manage the cost and schedule. Similar efforts completed/ongoing by the proposer in this area are fully described, including identification of other Government entities.

5.2.3 Budget Analysis

The proposed budget is reasonable and consistent with the proposed technical approach. When technical and value price analyses are insufficient, a cost realism 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 technical approach and reflect a sufficient understanding of the costs and level of effort needed to successfully accomplish the proposed technical approach.

5.3 Evaluation and Selection Process

5.3.1 It is the policy of ARPA-H to ensure impartial, equitable, comprehensive proposal evaluations based on the evaluation criteria listed above and to select the source (or sources) whose offer meets ARPA-H's mission objectives and programmatic goals.

5.3.2 ARPA-H will conduct a scientific and technical review of each conforming proposal. All proposal evaluations will be based solely on the evaluation criteria in Section 5.2.

5.3.3 Relative to the evaluation criteria, the Government will evaluate each conforming proposal in its entirety, documenting the strengths and weaknesses. Based on the identified strengths and weaknesses, ARPA-H will determine whether a proposal will be selected for award negotiation. Proposals will not be evaluated against each other during the scientific review process, but rather evaluated on their own individual merit to determine how well the proposal meets the criteria stated in RAPID ISO.

5.3.4 An award will be made to a proposer(s) whose proposal is determined to be the most advantageous to the Government, consistent with instructions and evaluation criteria specified herein and based on availability of funding.

5.3.5 The following definitions apply to the RAPID evaluation and selection process:

Selectable: A selectable proposal is a proposal that has been evaluated by the Government against the evaluation criteria listed in the ISO, and the positive aspects of the overall proposal outweigh its negative aspects. Additionally, there are no accumulated weaknesses that outweigh the positive aspects.

Non-Selectable: A proposal is considered non-selectable when the proposal has been evaluated by the Government against the evaluation criteria listed in the ISO, and the positive aspects of the overall proposal do not outweigh its negative aspects. Additionally, there may be accumulated weaknesses that would require extensive negotiations and/or a resubmitted proposal.

5.4 Handling of Selection-Sensitive Information

5.4.1 It is the policy of ARPA-H to protect all proposals as selection sensitive information and to disclose their contents only for the purpose of evaluation and only to screened personnel for authorized reasons, 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 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 General Guidelines

5.5.1 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.

5.5.2 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.

5.5.3 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 ADMINISTRATIVE AND NATIONAL POLICY REQUIREMENTS

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

1. 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.

2. 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

1. 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.

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

3. 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 intellectual property that will be utilized for the proposed effort. Proposers should appropriately identify any desired restrictions on the Government's use of any Intellectual Property contemplated under the award instrument in question. This includes both noncommercial items and commercial items. Respondents should utilize the prescribed format within the Administrative & National Policy Requirements Document Template (Volume 3 of Appendix D to this ISO) when asserting restrictions. If no restrictions are intended, then the proposal should state "NONE." It is expected that there will be deliverables tied to Intellectual Property management.

6.3 Human Subjects Research

6.3.1 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.

6.3.2 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 Electronic Invoicing and Payments

Performers will be required register in and to submit invoices for payment for invoicing in the Payment Management Services (PMS) system. PMS is a centralized payment and cash management system. ARPA-H other transaction payments are made by PMS, operated by PSC, in accordance with Department of the Treasury and OMB requirements. PMS guidance can be found here: https://pms.psc.gov/training/grant-recipient-training.html.

6.5 Government-Furnished Property/Equipment

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

6.6 Associate Performer Agreement

Associate Performer Agreements (APAs) will be required for proposers negotiating an award under the RAPID Program. An APA is an agreement between non-Federal entities working in furtherance of an ARPA-H agreement that requires the parties to share information, data, technical knowledge, expertise, or resources. See Appendix A for more information related to anticipated APAs in support of the RAPID Program.

APPENDIX A: ASSOCIATE PERFORMER AGREEMENT (APA)

1. An Associate Performer Agreement (APA) is an agreement between non-Federal entities or Federal performers (hereinafter Performer) working in furtherance of an ARPA-H agreement that requires the parties to share information, data, technical knowledge, expertise, or resources. An Associate Performer is defined as a party to an APA. ARPA-H is not a party to an APA.

2. Each resulting award will have the same or similar language:

3. Submission of a conforming proposal or receipt of an award under an ARPA-H solicitation is not conditioned on Associate Performers or their subcontractors selling, furnishing, or relinquishing proprietary information or confidential data (e.g., intellectual property).

    a. It is recognized that success of the research effort depends in part upon the open exchange of information between the various Associate Performers involved in the effort. This is intended to ensure that there will be appropriate coordination and integration of work by the Associate Performers to achieve complete compatibility and to prevent unnecessary duplication of effort. By executing this Agreement, the Performer assumes the responsibilities of an Associate Performer. For this APA, the term Performer includes subsidiaries, affiliates, and organizations under the control of the Performer (e.g., subcontractors).

    b. Work under this Agreement may involve access to proprietary information or confidential data from an Associate Performer. Associate Performer and their subcontractor(s) are not required to sell, furnish, or relinquish proprietary information or confidential data developed at private expense unless mutually agreed. To the extent that such data is received by the Performer from any Associate Performer for the performance of this agreement, the Performer hereby agrees that any proprietary information or confidential data received shall remain the property of the Associate Performer and shall be used solely for the purpose of the research effort. Only that information received from another contractor, in writing, and is clearly identified as proprietary or confidential shall be protected in accordance with this provision. A Performer's obligation to retain such information in confidence will be satisfied if the Contractor utilizes the same controls to avoid disclosure, publication, or dissemination of its own proprietary information. The receiving Performer agrees to hold such information in confidence as provided herein so long as such information is of a proprietary/confidential or limited rights nature.

    c. The Performer hereby agrees to closely cooperate as an Associate Performer with the other Associate Performers on this research effort. This involves as a minimum:

        - Maintenance of a close liaison and working relationship;
        - Maintenance of a free and open information network with all Government-identified associate Performers;
        - Delineation of detailed interface responsibilities;

- Entering into a written agreement with the other Associate Performer setting forth the substance and procedures relating to the foregoing, and promptly providing the Agreements Officer with a copy of same, and
- Receipt of proprietary information from the Associate Performer and transmittal of Performer proprietary information to the Associate Performers subject to any applicable proprietary information exchange agreements between associate contractors when, in either case, those actions are necessary for the performance of either

d. In the event that the Performer and the Associate Performers are unable to agree upon any such interface matter of substance, or if the technical data identified is not provided as scheduled, the Performer shall promptly notify the ARPA-H Program Manager. The Government will determine the appropriate corrective action and will issue written guidance to the affected Performer.

e. The Performer agrees to insert in all subcontracts hereunder which require access to proprietary information belonging to the Associate Performer, a clause which shall conform substantially to this language, including this paragraph (e).

f. Associate Performers for this research effort include:

Contractor (POC Details)	Technical Area

APPENDIX B: DATA OF INTEREST

This is a non-exhaustive list that represents data of interest and is subject to refinement and expansion as the project progresses:

1. Clinical Information

Clinical Notes
Intake Forms
Anamnesis/Patient History
Family History
Exposure History
Entries on Allergies
Symptoms
Assessments
Visit Notes
Nurses' Notes
Specialist Findings
Scanned in Notes from Other Providers
Patient Reported Outcomes
Therapeutic Response
Referral Notes
Discharge Letter
Reports (Surgical, Pathology, Radiology, Metabolomics, Proteomics)

2. Laboratory Data

Wound Reports
Lab Reports (values and/or full reports)
Clinical Biochemistry
Hematology
Microbiology
Immunology/Serology
Cytopathy/Histopathology
Genetic Testing/Molecular Pathology
Toxicology
Endocrinology
Urinalysis
Blood Banking/Transfusion Medicine

3. Genomics and Molecular Data

Genetic Data (including Transcriptomics adhering to GA4GH Ontologies)
Raw Data
Variant Reports
Findings Reports

4. Phenotypic Data
   Phenotypic Data (adhering to GA4GH Ontologies)

5. Administrative Data

   Entries on departments visited and case ID
   ICD-codes/ SNOMED
   Procedure codes
   Vitals and other measurements
   List of medications
   Administrative patient profile
   Entries on social habits/risk factors

APPENDIX C: SOLUTION SUMMARY FORMAT & INSTRUCTIONS

1. General Information

a. 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 three pages, exclusive of a cover page, Rough Order of Magnitude, and References. No table of content shall be provided. The Government may not review pages beyond three (3) total; and any Solution Summary submitted that exceeds 3 pages will only be reviewed at ARPA-H's discretion.

b. Solution Summaries should be submitted in a PDF format to the ARPA-H Solution Submission Portal. Attachments and embedded links shall not be included. The Solution Summary should address why the proposed idea is relevant to the ARPA-H mission and the proposed RAPID program.

c. Solution summaries must address only one specific TA.

2. Cover Page

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

1	Solicitation #	ARPA-H-SOL-25-119
2	Solution Summary Title	
3	Technical Approach (TA) Selection	
4	Submitter Organization	
5	Type of Organization and website URL if applicable	Choose all that apply: Large Business, Small Disadvantaged Business, Other Small Business, HBCU, MI, Other Educational, or Other Nonprofit
6	Technical Point of Contact (POC)	Name: Mailing Address: Telephone: Email:
7	Administrative POC	Name: Mailing Address: Telephone: Email:
8	Total Estimated Budget	Total: $
9	Place(s) of Performance	
10	Other Team Members (sub-performers, including consultants) if any	Technical POC Name: Organization: Organization Type:

3. Proposed Work

a. 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.

b. Describe the final deliverable(s) for the project, one or two key interim milestones, and the overall technical approach used to achieve project objectives. Applicants submitting proposals for TA1 or TA2 are required to provide a description for how they plan to prioritize rare disease that will be captured as part of their proposal efforts. Identify adoption challenges to be overcome for the proposed solutions to be successful. Describe key risks.

4. 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.

5. Rough Order of Magnitude (ROM)

a. Please include a basis of estimate (BOE) to support the proposed project budget/ROM as well as the total project cost including cost sharing, if applicable. The BOE should also include a breakdown of the work by fully burdened labor (inclusive of fringe), subcontracts, materials, equipment, other direct costs (e.g., travel), indirect costs, profit, cost sharing, and any other relevant costs. Also, estimate the total number of labor hours anticipated per phase in the labor hours row. All subcontracts should total together in the subcontracts line. The below table may be used for this breakdown:

Categories	TA 1 Amount	TA 2 Amount	TA 3 Amount	Total
Direct Labor (including fringe)				
Subcontracts				
Materials				
Equipment				
Travel				
Other Direct Costs				
Indirect Costs				
Profit/Fee				
Total				
Cost Sharing (if applicable/appropriate)				
Labor hours (in hours)				

b. 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 D: FULL PROPOSAL FORMAT AND INSTRUCTIONS

1. General Instructions

a. All Proposals 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.

b. 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: "TA #, Volume I_XYZ Institution", "Volume II_XYZ Institution", "Volume II Supporting Documents", etc. Proposals must address one specific Technical Area.

c. Conforming full proposals should consist of three volumes as follows plus three attachments as described:

- Appendix D: Volume I, Technical and Management Proposal,
- Appendix D: Volume II, Cost Proposal, and
- Appendix D: Volume III, Administrative and Policy Requirements Submission
- Attachment: Cost Spreadsheet
- Attachment: Statement of Work (SOW)
- Attachment: Rare Disease Prioritization Spreadsheet (applies to TA1 & TA2)

2. Summary of Full Proposal Requirements, including page limits:

Volume I, Technical and Management Proposal	
Volume Element	Page Limit
Cover Page	1
A. Executive Summary	15
B. Solution Fit with RAPID	
C. Technical Plan	
D. Management Plan	
E. Capabilities	
F. Commercialization Plan	
G. Rare Disease Prioritization Spreadsheet (TA1 and TA2)	N/A, use provided template/format
H. Statement of Work (SOW)	N/A, use provided template/format
I. Schedule and Milestones	N/A use provided template/format
J. Data Management and Sharing Plan (DMSP)	N/A (estimated 2 pages)
K. References	N/A

Volume II, Cost Proposal	
Volume Element	Page Limit
Cover Page	1
A. Cost Proposal Spreadsheet(s), including for subcontractors 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
B. OCI Affirmations and Disclosure	
C. Research Security Disclosure	
D. Novelty of Proposed Work	
E. Intellectual Property (IP)	
F. Technical Data and Computer Software	
G. Patents	
H. Ability to Meet Programmatic Goals with IP/Patent Implications	
I. Human Subjects Research	
J. Representations Regarding Unpaid Delinquent Tax Liability or a Felony Conviction Under any Federal Law	
K. Software Component Standards	
L. Cybersecurity	

3. Volume I: Technical and Management Proposal

a. **The maximum page count for Volume I is fifteen (15) pages**, with exclusions as noted in the table above. ARPA-H encourages conciseness to the maximum extent practicable. No other supporting materials may be submitted for review. 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.

b. Volume I should include the following components:

1) Cover Page

1	Solicitation #	ARPA-H-SOL-25-119
2	Full Proposal Title	
3	Technical Approach (TA) Selection	
4	Prime Awardee/entity submitting the proposal	
5	Unique Entity Identifier of primer proposer/awardee (UEI)	
6	Type of Organization and website URL if applicable	**Choose all that apply:** Large Business, 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 or not 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 Submission	
8	Technical Point of Contact (POC)	Include salutation Last Name: First Name Mailing Address: Telephone: Email:

9	Administrative POC	Include salutation Last Name: First Name Mailing Address: Telephone: Email:
10	Other Team Members (sub-performers, including consultants) if applicable.	Technical POC Name: Organization: Organization Type:
11	Total funds requested from ARPA-H, and the amount of cost share (if any)	Total: $
12	Place(s) of Performance	

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

- What is the proposed work attempting to accomplish or solve?
- How is it done today? What are the limitations of present approaches?
- What are the key technical challenges in your approach, and how do you plan to overcome these?
- What is new about your approach? Why do you think you can be successful at this time?
- Who cares? If you succeed, what difference will it make?
- 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.
- How much will your project cost?
- What are your milestones to check for success consistent with RAPID metrics
- To ensure equitable access for all people, how will cost, accessibility, and user experience be addressed in your project?
- How might this program be misperceived or misused (and how can we prevent that from happening)?

3) Solution Fit with RAPID

Clearly describe what the team is trying to achieve and the difference it will make (qualitatively and quantitatively) if successful relative to RAPID'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.

4) 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.

5) Management Plan

a) 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 for the following responsibilities:

- 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/Agreements Officer),
- coordinate the effort across the team,
- organize regular Performer meetings or discussions,
- facilitate data sharing, and
- ensure timely completion of milestones and deliverables.

b) 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.

c) Provide a detailed plan for coordination, including explicit guidelines for interaction among collaborators/sub-performers of the proposed effort. Include risk management approaches.

Describe any formal teaming agreements required to execute this program.

6) Capabilities

Describe organizational experience in relevant subject area(s), existing intellectual property, specialized facilities, and any Government-furnished materials or information. Discuss any work in closely related research areas and previous accomplishments.

7) Commercialization Plan

Briefly outline your current understanding of your technologies target market and the size of that market. Identify 2-3 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 RAPID Program (Government Purpose, Unlimited, Limited.)	Name of Person or Entity Asserting Restrictions (who owns the IP?)	Funding Source (Federal Government, other, or Mix**)

8) Statement of Work

a) 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.

b) 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.

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

9) Schedule and Milestones
Using the provided format, provide a detailed schedule showing tasks (task name, duration, work breakdown structure element as applicable, and 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.

10) Rare Disease Prioritization

a) To ensure alignment with the objectives of the program, applicants submitting proposals for TA1 or TA2 are required to provide documentation for the initial prioritization and justification of rare diseases that will be captured as part of their proposed efforts.

- TA1 Proposals must include documentation for a **minimum of 100 diseases.**
- TA2 Proposals must include documentation for a **minimum of 100 diseases.**

b) RAPID seeks to build a diverse and representative portfolio of rare diseases that balances immediate clinical impact with opportunities for novel discovery. By prioritizing diseases with the highest potential to enhance public health, accelerate translational research, and drive innovation in rare disease diagnosis, applicants will demonstrate their alignment with RAPID's mission and their capacity to deliver transformative and impactful solutions. For each disease included, applicants must provide a clear, concise, and well-supported justification. Justification may be based on several factors, including but not limited to:

- Diseases with clear diagnostic criteria and validated biomarkers with a high potential for early intervention using accurate AI models
- Diseases with significant diagnostic delays or conditions where earlier diagnosis enables critical interventions

- Under-diagnosed diseases with phenotypic heterogeneity or suspected subtypes
- TA1: Volume and availability of known data sources
- TA2: Diseases suitable for digital phenotyping approaches.

c) Proposals may identify groups of diseases that have similar justifications for prioritization.

11) Data Management and Sharing Plan (DMSP)

a) This is recommended to be no more than 2 pages.

b) 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 inform feedback for proposals who are selected for award negotiations.

12) References
Add a list with the cited literature.

4. 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.

a. Cover Page

1	Solicitation #	ARPA-H-SOL-25-119
2	Full Proposal Title	
3	Technical Approach (TA) Selection (TA1 or TA2 – must select only one)	
4	Prime Awardee/entity submitting the proposal	
5	Unique Entity Identifier of primer proposer/awardee (UEI)	
6	Type of Organization and website URL if applicable	**Choose all that apply:** Large Business, 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 or not 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	Technical Point of Contact (POC)	Include salutation Last Name: First Name: Mailing Address: Telephone: Email:
8	Administrative POC	Include salutation Last Name: First Name: Mailing Address: Telephone: Email:
9	Other Team Members (sub-performers, including consultants) if applicable and type of organization for each	Technical POC Name: Organization: Organization Type:
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	Commercial and Government Entity (CAGE) Code	
14	Proposal validity period (Minimum of 120 days)	

b. Cost Proposal Spreadsheet

1) ARPA-H Standard Excel Cost Proposal Spreadsheet (See Attachments). 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 cost proposal. The cost proposal spreadsheet must be used by the prime organization and all subcontractors at any tier.

2) While the prime proposer is ultimately responsible for submission of all required documents, subcontractor cost proposal spreadsheets may be submitted directly to the Government by the proposed subcontractor via email to RAPID@ARPA-H.gov. Subcontractor proposals should include Interdivisional Work Transfer Agreements or similar arrangements between the awardee and divisions within the same organization as the awardee. Please ensure the associated Prime performer is annotated on any subcontractor documents for traceability.

c. 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).

5. Volume III: Administrative & National Policy Requirements Document Template

- The Administrative and National Policy Requirements document must be completed in full. Do not delete any portion of this document.
- All pages shall be formatted for printing on 8-1/2 by 11-inch paper with 1-inch margins and font size not smaller than 11-point. Font sizes of 8- or 10-point may be used for figures, tables, and charts. There is no page limit for this document.
- The Administrative and National Policy Requirements document must be in .pdf, .odx, .doc, or .docx formats. Submissions must be written in English.

a. Cover Page

1	Solicitation #	ARPA-H-SOL-25-119
2	Proposal Title	
3	Proposer Organization	
4	Technical Point of Contact (POC)	Name: Address: Telephone: Email:
5	Administrative POC	Name: Address: Telephone: Email:
6	Date of Proposal Submission	
7	Proposal Validity Period (minimum 120 days)	

b. Team Member Identification

[Provide a list of all team members including the prime, subawardee(s) (including consultant(s)), as applicable. Identify specifically whether any are a non-US organization or individual. Use the following format for this list. Note: Consultants (e.g., 1099s) are considered subperformers and must be listed.]

PRIME				
Individual Name:	Organization:	Non-U.S. Organization: Non-U.S. Individual:	☐ Yes ☐ Yes	☐No ☐No
SUBAWARDEES/CONSULTANTS				
Individual Name:	Organization:	Non-U.S. Organization: Non-U.S. Individual:	☐ Yes ☐ Yes	☐No ☐No
Individual Name:	Organization:	Non-U.S. Organization: Non-U.S. Individual:	☐ Yes ☐ Yes	☐No ☐No

c. Organizational Conflict of Interest Affirmations and Disclosure

[In accordance with the ISO, provide the following information.]

1) Are any of the proposed individual team members or their respective organizations (whether prime or subawardee or consultant) currently providing Systems Engineering Technical Assistance (SETA), Partnership Intermediary Agreement (PIA) or similar support to ARPA-H?

☐ No ☐ Yes

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

☐ No ☐ Yes

[If you answered "Yes" to c.1) OR c.2), 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 (subawardee, consultant) 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 subawardee or consultant)?

☐ No ☐ Yes

[If yes, provide the following information for each applicable team member: Identification of applicable team member; and an OCI mitigation plan.]

d. Research Security Disclosure

[In accordance with National Security Presidential Memorandum (NSPM)-33 and the associated White House Office of Science and Technology Policy Implementation Guidance[1], which requires certain individuals to disclose potential conflicts of interest (COI) and commitment (COC), PIs and other senior/key personnel[2] that will serve as prime and subawardees are required to complete the Current and Pending (other) Support Common Form as well as the Biographical Sketch Common Form. These forms can be found at: https://www.nsf.gov/bfa/dias/policy/nstc_disclosure.jsp].

1) In populating these forms, the following is required for each PI and other Senior/Key Personnel (whether they are supporting the prime or a subawardee (at any tier)).

- Other organizational affiliations and employment
- Other positions and appointments[3]
- Participation in any foreign Government-sponsored talent recruitment program(s)[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:
  - 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;
  - 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
  - Private equity, venture, or other capital financing.

2) For consultants, please additionally list the following (Note: current, pending, and other support not required):
- Other organizational affiliations and employment
- Other positions and appointments
- Participation in any foreign Government-sponsored talent recruitment program(s)

3) Foreign Participation

a) Do any members of the proposed team have any contracts associated with participation in programs sponsored by foreign Governments, instrumentalities, or entities, including foreign Government-sponsored talent recruitment programs? If yes, please provide a list of contracts and the nature of the sponsorship.

☐No ☐ Yes

b) Do any members of the proposed team receive direct or indirect support (including, but not limited to, financial) that is funded by a foreign Government-sponsored talent recruitment program, even where the support is provided through an intermediary and does not require membership in the foreign Government-sponsored talent recruitment program. If yes, please provide a list of individuals and the nature of the support received.

☐ No ☐ Yes

c) Do any members of the proposed team have/participate in any other foreign Government sponsored or affiliated activities. In accordance with 42 USC § 19232, individuals are prohibited from being a party in a malign foreign talent recruitment program.

☐ No ☐ Yes

d) Do any of the proposed individual team members or their respective organizations (whether prime or subawardee or consultant) participate in any foreign Government-sponsored talent recruitment program(s)?

☐ No ☐ Yes

By submitting this document to ARPA-H, you are certifying that the information provided in this section is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. §6605.

By submitting this document to ARPA-H, you are also certifying that, at the time of submission, no members of the proposed team are a party in a malign foreign talent recruitment program.

By submitting this document to ARPA-H, you acknowledge that misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

e. Novelty of Proposed Work

[Performers shall not receive alternative funding for the same purposes as an agreed upon ARPA-H award. At the discretion of the program team and the Agreement Officer, additional reporting may be required.]

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

f. Intellectual Property (IP)

[Note: The Government will assume unlimited rights to all IP not explicitly identified as restricted in the proposal.]

g. 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, 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.]

NONCOMMERCIAL				
Technical Data and/or Computer Software To be Delivered with Restrictions	Summary of Intended Use in the Conduct of the Research	Basis for Assertion	Asserted Rights Category	Name of Person Asserting Restrictions

COMMERCIAL				
Technical Data and/or Computer Software To be Delivered with Restrictions	Summary of Intended Use in the Conduct of the Research	Basis for Assertion	Asserted Rights Category	Name of Person Asserting Restrictions

h. 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, 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).]

i. Ability to Meet Programmatic Goals with IP/Patent Implications
[Describe how IP assertions and/or patent implications impact the ARPA-H RAPID programmatic goals.]

j. Human Subjects Research
Does the proposed work involve Human Subject Research?

☐ No ☐ Yes

[If yes, provide evidence of or a plan for review by an institutional review board (IRB). Please include evidence of a Federalwide Assurance for the Protection of human subjects. Please also complete the below table for each organization, including team members and subawardees, performing HSR. Add row as needed.]

Organization Performing HSR	Federalwide Assurance Number	Approved IRB Protocol (Y/N)

k. Representations Regarding Unpaid Delinquent Tax Liability or a Felony Conviction Under Any Federal Law
[Complete the following statements.]

The Proposer represents that –

(i) 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,

(ii) It is ☐ is not ☐ a corporation that was convicted of a felony criminal violation under a Federal law within the preceding 24 months.

l. Software Component Standards
Does your solution include software components that are proprietary or do not include commercial-friendly-open-source licenses?

☐ No ☐ Yes

[If you answered yes, please provide a technical plan in accordance with Section 6.1 of the ISO.]

m. Cybersecurity
Does your organization implement a cybersecurity program leveraging industry and/or Government standards to secure and defend your systems, networks, and/or data?

☐ No ☐ Yes

[If yes, provide a brief description of the program in your DMSP, including the specific standard(s) that guide the program, the abilities of the organization to respond to a cybersecurity incident, and how the organization assesses the security posture of their systems and/or networks. If no, provide an explanation.]

Appendix E: Acronyms

APA	Associate Performer Agreement
ARPA-H	Advanced Research Projects Agency for Health
ASR	Animal Subjects Research
BOE	Basis of Estimate
CAGE	Commercial and Government Entity Code
CDE	Common Data Elements
CDS	Clinical Data Science
CFR	Code of Federal Regulations
CHIPS	Creating Helpful Incentives to Produce Semiconductors
COC	Conflict of Commitment
COI	Conflict of Interest
COTS	Commercial off-the-shelf
DMSP	Data Management and Sharing Plan
DUA	Data Use Agreement
EHR	Electronic Health Records
ETL	Extract, Transform, Load
FAIR	Findable, Accessible, Interoperable, and Reusable
FDA	Food and Drug Administration
FFRDC	Federally Funded Research and Development Centers
FHIR	Fast Healthcare Interoperability Resources
GA4GH	Global Alliance for Genomics and Health
GDPR	General Data Protection Regulation
GFE	Government Furnished Equipment

GFP	Government Furnished Property
HBCU	Historically Black Colleges and Universities
HHS	Health and Human Services
HIPPA	Health Insurance Portability and Accountability Act
HITRUST	Health Information Trust Alliance
HPO	Human Phenotype Ontology
HSR	Human Subjects Research
ICD	International Classification of Diseases
IEC	International Electrotechnical Commission
IOS	International Organization for Standardization
IP	Intellectual Property
IRB	Institutional Review Board
ISO	Innovative Solutions Opening
IV&V	Independent Verification & Validation
MI	Minority Institution
NIST	National Institute of Standards and Technology
NIH	National Institutes of Health
NSPM	National Security Presidential Memorandum
OMIM	Online Mendelian Inheritance in Man
OMOP	Observational Medical Outcomes Partnership
OT	Other Transaction
PHI	Protected Health Information
PHO	Proactive Health Office
PI	Principal Investigator

PIA	Partnership Intermediary Agreement
PII	Personally Identifiable Information
POC	Point of Contact
PMS	Payment Management Services
PSC	Program Support Center
PX	Patient Experience
QA	Quality Assurance
QHIN	Qualified Health Information Network
RAPID	Rare Disease AI/ML and Precision Integrated Diagnostics
RDDC	Rare Disease Data Commons
ROM	Rough Order of Magnitude
SAM	System for Award Management
SBA	Small Business Administration
SETA	Systems Engineering Technical Assistance
SOW	Statement of Work
SNOWMED	Systematized Nomenclature of Medicine
TA	Technical Area
TEFCA	Trusted Exchange Framework and Common Agreement
UEI	Unique Entity Identifier
UXR	User Experience Research
VCF	Variant Call Format
VRS	Variation Representation Specification