Innovative Solutions Opening (ISO)

# Systems for Phenotypic Evaluation, Clinical Trajectories, Response, and Agency (SPECTRA)

Proactive Health Office (PHO)

Advanced Research Projects Agency for Health

ARPA-H-SOL-26-163

September 17, 2026

# Contents

# INNOVATIVE SOLUTIONS OPENING (ISO)

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

**Program Title:** Systems for Phenotypic Evaluation, Clinical Trajectories, Response, and Agency (SPECTRA)

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**Solution Summary Submission Deadline:**

TA 4: October 18, 2026 at 5pm ET (submission portal opens Oct 4, 2026)

TA 1 and TA 2: December 2, 2026 at 5pm ET (submission portal opens Nov 18, 2026)

- Anticipated ISO Amendment late Oct

TA 3: January 18, 2027 at 5pm ET (submission portal opens Jan 4, 2027)

- Anticipated ISO Amendment early Dec

*Proposal deadline information will be forthcoming.*

**Where to Submit:**

**Solution Summaries:** **https://solutions.arpa-h.gov**

**Questions:** **https://solutions.arpa-h.gov/Ask-A-Question/**

*Registration is required to submit documents via the ARPA-H Solutions site. Late submissions may not be considered.*

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**Award Instrument:** Other Transaction (OT)

**Resource Sharing:** Resource sharing is encouraged but not required.

# PART I: OVERVIEW AND PROGRAM DESCRIPTION

## 1.1 Program Summary

Autistic people are valued members of their families and communities across the United States, contributing strengths, skills, and perspectives to family life, work, science, the arts, and civic life. Yet, there is much we do not understand about autism. One in 31 American children has been diagnosed with autism spectrum disorder (ASD), and autism affects individuals, families, and caregivers across the full lifespan. Co-occurring health conditions are common: for example, roughly 30 percent of autistic people have co-occurring intellectual disability, sleep problems affect approximately 60 percent of children and adolescents, gastrointestinal symptoms affect at least one third, epilepsy affects approximately 1 in 10, and anxiety disorders affect approximately 1 in 5, with higher estimates reported in children and adolescents. Converging evidence indicates that autism arises from the interplay of many factors, including genetic, biological, behavioral, environmental, and iatrogenic (medical) influences, rather than from any single cause. How these factors combine to produce autism and its co-occurring conditions, and why they converge most profoundly in some individuals, is not yet understood. Existing research has produced compelling findings, but it has largely examined these factors in isolation and has not addressed the complexity of their nonlinear interactions or how those interactions unfold as trajectories across the lifespan. As a result, current care often leaves families without timely answers about cause, trajectory, communication, co-occurring conditions, and likely response to intervention.

The Advanced Research Projects Agency for Health (ARPA-H) seeks submissions for the Systems for Phenotypic Evaluation, Clinical Trajectories, Response, and Agency (SPECTRA) program. SPECTRA will identify and act on autism trajectories, the evolving developmental paths individuals follow across the lifespan from the prenatal period through aging, spanning autism characteristics, co-occurring conditions, and functional outcomes together with the genetic, biological, behavioral, iatrogenic (medical influences), environmental factors and their nonlinear interactions. Rather than examining these factors in isolation, SPECTRA will examine how they combine and interact, including their nonlinear interactions, to produce autism and its co-occurring conditions over time. Because different trajectories arise from different combinations of biomarkers and factors, SPECTRA encourages examining them in combination, whether assembled within one team or through partnership. By resolving these trajectories, SPECTRA aims to move autism care from one-size-fits-all management to biologically and behaviorally informed intervention: to explain not only what a person experiences but why, to enable earlier identification of autism and co-occurring conditions, and to guide personalized support and treatment that reduce the impact of co-occurring conditions and improve quality of life across every life stage. Understanding how these factors converge also opens opportunities to intervene before the most disabling features take hold. Where a modifiable combination of influences drives a trajectory toward regression, medical crisis, or profound impairment, resolving it early could reduce the severity of these outcomes and, in some cases, prevent them.

SPECTRA will also develop technologies that serve two purposes at once: extending reliable assessment beyond the clinic while improving everyday communication, function, and quality of

life. The same tools people use to live more fully will also generate the data that drive measurement and personalized care.

**SPECTRA supports and respects autistic people and their families.** The program works to understand developmental trajectories and to improve health, communication, function, and quality of life across the full range of the spectrum. Consultation with the community and co-design where applicable will be key components of the program. SPECTRA gives particular attention to those with the highest support needs, including people with profound autism, who are most often excluded from research and least well served by current tools.

**A note on scope.** In this solicitation, medical exposures refers to therapeutic, prophylactic, and procedural exposures encountered in the course of clinical care across the lifespan, assessed with dose and timing resolution, both beneficial and iatrogenic. Immune refers to infection, fever, inflammatory and autoimmune processes, and immune activation from any source, in the parent or the individual. SPECTRA prejudges no factor and excludes none from examination.

***A note on language.*** *In alignment with major autism advocacy organizations, ARPA-H acknowledges that preferences regarding autism terminology vary within the autism community. Some individuals prefer person-first language (for example, "person with autism"), while others prefer identity-first language (for example, "autistic person"). ARPA-H does not endorse one convention over the other and may use both forms interchangeably across its publications, while respecting individuals' stated language preferences. Where this document uses the term "profound autism," it does so descriptively, to refer to autistic people with high support needs, including those with co-occurring intellectual disability and minimal or no reliable speech. The term is not a formal diagnostic category, and ARPA-H uses it to make explicit that SPECTRA includes this population, not to define a subtype.*

**The Gap**

Current research rarely examines the complex, nonlinear interactions among the genetic, biological, behavioral, environmental, and iatrogenic (medical) influences that shape autism, and it seldom connects them to the everyday outcomes families care about across the lifespan. Assessment also happens largely in the clinic rather than in the real-world settings where people live, learn, and work, which limits what can be measured and when. ARPA-H believes this gap is now bridgeable. Converging advances in artificial intelligence and machine learning (AI/ML), genetic and biological markers, biosensing wearables, and voice and speech technology make it possible to resolve these interactions, match risk to phenotype, identify autism sooner, and deliver precision therapies beyond the clinic.

SPECTRA will pursue four Technical Areas (TAs) of research and development. TA1, Multi-Factor Analysis and Trajectory Identification, uses deep phenotyping to identify, measure, and model how the many contributing factors combine, and to define the trajectories and the harmful combinations that drive negative outcomes. TA2, Population-Scale Modeling and Data Integration, builds durable, secure national infrastructure that integrates and characterizes data across populations, so trajectories can be assessed for representativeness and people can be followed as they age. TA3, Precision Intervention and Trajectory Testing, tests in rigorous trials whether acting

on these trajectories changes outcomes, including the co-occurring conditions that drive the most harm. TA4, Technologies for Communication, Quality of Life, and Embedded Assessment, develops tools such as wearables, communication and speech interfaces, eye tracking, low-channel EEG, and camera-based movement analysis that improve everyday communication and function while generating the real-world measurements that assessment now lacks.

TA1 and TA4 are designed to answer each other's central question. Today neither is sufficient on its own: the measurements needed to observe trajectories in daily life do not yet exist, and the models needed to interpret those measurements are nonlinear and incomplete. SPECTRA breaks this dependency through deliberate co-development. TA1 defines and models the trajectories worth measuring, which tells TA4 what to build; TA4 develops novel real-world measurements, which TA1 incorporates and tests against its models. In effect, each supplies the other's answer key. Each iteration sharpens both, until the program converges on a functional definition of the causal trajectories and outcomes that matter and the measurements needed to assess them. These same measures will be used in TA3 to assess effectiveness of therapeutic approaches.

A separate, non-solicited program element will support data coordination, independent verification and validation, community co-design, responsible-use controls, and transition support (see Section 2.2 for more on the non-solicited program elements).

## 1.2 Problem Statement

Current approaches to improving diagnostic capabilities and precision care for individuals affected by autism fall short in five significant ways:

**First, diagnosis comes too late.** Autism can often be reliably identified only well after the earliest signs emerge, and in many cases diagnosis is delayed by years, particularly for girls, those with subtler presentations, and those with limited access to specialty diagnostic care. Because the earliest years of life represent a period of exceptional neurodevelopmental plasticity, late identification narrows the window in which intervention can meaningfully improve developmental trajectories. Delay also allows secondary and comorbid conditions, such as anxiety, gastrointestinal disorders, epilepsy, and self-injurious behavior, to take hold and compound, worsening long-term outcomes that earlier action might have prevented or mitigated.

**Second, environmental and developmental exposures are not integrated with host biology.** Autism does not follow a single cause or pathway; it likely reflects a dynamic interplay among an individual's biology, genetics, the developing brain and body, and environmental and developmental exposures accumulated over time, combining differently from one person to the next. Yet current approaches largely evaluate these dimensions in isolation, if at all. Current methodologies rarely capture how exposures interact with an individual's biology across development, and as a result cannot represent the full, longitudinal context that shapes each person's phenotype. This leaves clinicians and researchers without a mechanistic picture of why a given trajectory unfolds as it does.

**Third, the data that would reveal trajectories are siloed.** The multi-modal data needed to see how autism unfolds are fragmented across health systems, research cohorts, and administrative records, held in incompatible formats and under separate governance. Because these sources

cannot be analyzed together, no single view captures a representative population at sufficient scale, and patterns that would emerge only across combined data remain invisible. This leaves the field without the population-level foundation that trajectory identification and precision care require.

**Fourth, data do not reliably translate into action.** Even where rich developmental data exist, existing prediction models do not adequately capture the nonlinear, branching, and highly individual nature of developmental processes. They tend to describe risk or category membership rather than forecast an individual's trajectory, and they offer little guidance on which intervention is likely to help which individual at which point in time. Consequently, data can characterize a person without informing what should actually be done to improve their outcomes.

**Fifth, current assessments fail many of the people who most need them.** Most instruments were designed around a narrow profile using a structured assessment in the clinic, and they capture only a thin slice of function and behavior, usually verbal and behavioral performance in a single setting, rather than the full range of function, self-regulation, sensory and behavioral needs, health and safety, learning, social participation, and communication. These assessments also conflate distinct domains: they conflate motor speech, cognition, and communicative competence, so that a difference in one domain is read as a deficit in another. This falls hardest on those with the highest support needs. An estimated 25 to 30 percent of autistic people are minimally verbal or nonspeaking, and standard tools were not designed for them; the same tools also underserve people with intellectual disability, co-occurring conditions, and atypical presentations. This mismatch limits both the ecological validity of assessment and the durability and relevance of intervention.

Together, these limitations leave autism care without a robust path from early, ecologically valid, multidimensional measurement to individualized prediction and precision intervention delivered when and where they can do the most good. SPECTRA is motivated by the hypothesis that autism can be understood as a dynamic developmental trajectory, one whose phenotypic features, biological and environmental drivers, and responses to intervention can be measured early and continuously in real-world settings, integrated across host biology and exposure, and used to forecast and adaptively shape outcomes toward greater health and agency.

## 1.3 Program Vision and Impact

If successful, SPECTRA will deliver personalized, evidence-based care and support for people with autism across the lifespan. It will improve understanding of the causal and modifiable influences that shape developmental, health, and functional trajectories, and translate that understanding into biologically and behaviorally grounded tools for earlier identification and precision intervention. The program moves autism care beyond a single diagnostic label toward trajectory-guided treatment that improves communication, health, independence, autonomy, and quality of life while preventing avoidable morbidity.

**SPECTRA will deliver the following outcomes:**

- Evidence on the factors and phenotypes that shape individual trajectories and which of them are potentially modifiable. This will enable care to target what drives outcomes rather than the diagnostic label alone (TA1).
- Trajectory-guided precision intervention that tests what works for whom, including when to safely start, adjust, or stop treatment. This will replace the trial-and-error approach that is the current standard of care (TA3).
- Assessment and diagnostics that work in everyday settings, including home, school, clinic, and community, measuring communication, function, and treatment response during daily life. This will allow the ability to intervene with issues such as distress, pain, sensory overload, sleep disruption, and seizures before they become crises (TA4).
- Communication and functional supports that preserve the person's intent, autonomy, and agency across the full range of support needs (TA4).
- Durable, privacy-preserving learning systems that improve tools and care models as longitudinal data accumulate, without forcing personal data into central custody (TA2).

- Family and caregiver quality of life treated as an explicit outcome, not an assumed consequence of care (cross-cutting).

Together, these outcomes will identify treatable conditions earlier, including but not limited to sleep disorders, seizures, gastrointestinal symptoms, anxiety, and pain, and support earlier action to prevent avoidable morbidity, regression, crisis, and loss of function across the lifespan.

**Evidence Tiers:**

All performers are bound to common, clear, agreed-upon language denoting the strength of evidence for causality for all publications, materials, or public communication. All work supported by the program will adhere to a three-tier evidence standard, which the program will publish. For clarity, language about *cause* is reserved for the tier three evidence this program will generate. Nothing at tier one or two may be described as driving, causing, or leading to an outcome.

| Tier | Definition | Permitted language |
|---|---|---|
| I: Associated | Observed in data, not replicated, confounding not excluded | associated with, observed in |
| II: Replicated | Reproduced in independent samples and at more than one site, using data not used to derive the original finding | consistently associated, replicated |
| III: Tested experimentally | Modifying the target produced the pre-specified change in the predicted group | drives, causal, modifiable target |

# PART II: TECHNICAL AREAS AND REQUIREMENTS

## 2.1 Solicited Components: SPECTRA Technical Areas

SPECTRA comprises four technical areas (TAs) that together address the five limitations of current practice, described as problem statements in Section 1.2. Proposers may submit to one or more technical areas; submissions addressing a single technical area are welcome and expected. Proposing institutions wishing to respond to more than one TA may do so as separate submissions. Such submissions may discuss any synergies if they exist, but each must stand on its own should only one be funded.

Across all four technical areas, SPECTRA encourages interdisciplinary approaches that combine the scientific, clinical, engineering, and lived-experience expertise each problem requires. The strongest contributions will often sit at the boundaries between disciplines. Proposers should expect to coordinate and collaborate with performers in other technical areas once the program starts.

| TA | Title | Limitation(s) answered | Function |
|---|---|---|---|
| TA1 | Multi-Factor Analysis and Trajectory Identification | Limitations 1 and 2: measurement comes too late, and factors are studied in isolation | Analyze |
| TA2 | Population-Scale Modeling and Data Integration | Limitation 3: the data that would reveal trajectories is siloed | Integrate |
| TA3 | Precision Intervention and Trajectory Testing | Limitation 4: data does not turn into action | Act |
| TA4 | Technologies for Communication, Quality of Life, and Embedded Assessment | Limitation 5: function is measured where it least occurs | Enable |

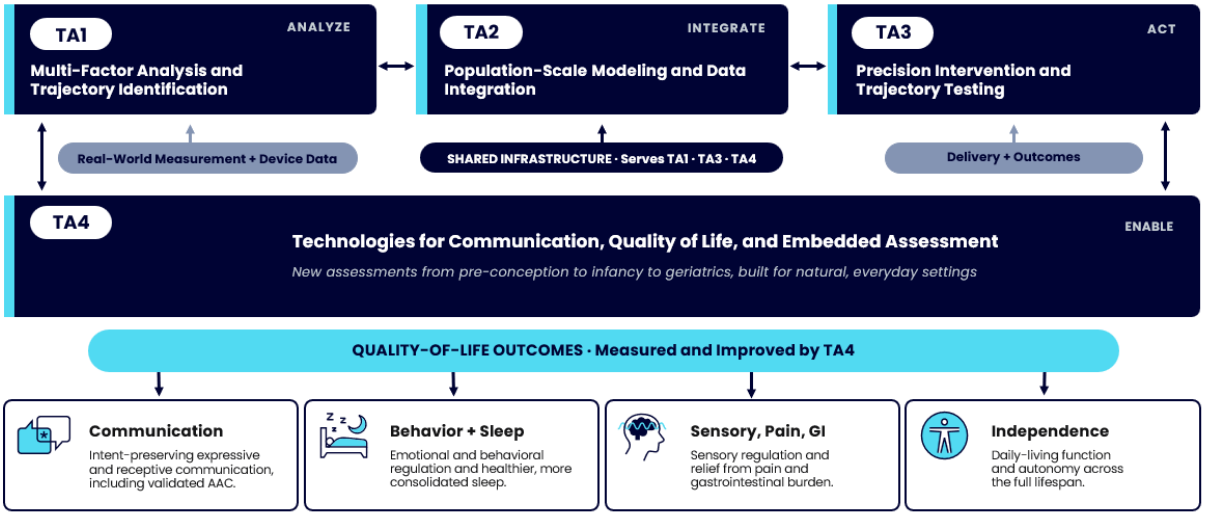


*Figure 1: SPECTRA Program Structure and Technical Areas*

### 2.1.1 Technical Area 1 (TA1): Multi-Factor Analysis and Trajectory Identification

**Objective.** SPECTRA addresses the first two limitations by identifying distinct autism-related trajectories and by integrating and analyzing comprehensive, multimodal datasets that resolve complex interactions among environmental, infectious, iatrogenic, genetic, epigenetic, microbiome, immune, metabolic, prenatal, and perinatal factors. These domains span biological propensity and responses to exposure and are typically measured and studied apart. Trajectory definitions may include sex, race, income, support-need level, and communication ability, with coverage reported. Thus, TA1 supplies the trajectory structure that TA3 requires in order to stratify treatment. Analyses should take a broad view that allows for identification of non-intuitive, nonlinear effects and that includes, but is not limited to, brain development as an endpoint. For example, assessments that identify stress signatures and predisposition to dysregulated immune inflammation, and connect them to developmental and behavioral trajectories, are encouraged. A core goal is individual-level trajectory assessment and causal impact of the above factors, with the understanding that initial conclusions are likely to be drawn at the subgroup level.

TA1 is an analysis technical area. TA1 will produce trajectory definitions and the interaction patterns that give rise to them; TA1 is not intended to produce clinical assessments or instruments. TA1 is inherently interdisciplinary, requiring analytic and computational methodologists to work alongside domain scientists across genetics, exposure science, immunology, metabolism, and developmental measurement. The program may pair complementary analytic and domain strengths across awardees. Because few groups can measure the full range of relevant biomarkers on their own, proposers are encouraged to span multiple biomarker and exposure domains within a single proposal, or to team so that different combinations of markers and factors can be measured and analyzed together.

**What TA1 Does and Does Not Do**
Three technical areas contribute to trajectory identification. The boundaries are stated here to prevent duplication.

| Area | Contribution to trajectories | Boundary |
|---|---|---|
| TA1 | Identifies candidate trajectories from complex interactions among biological, environmental, and developmental factors | Analyzes and applies measures. Does not develop measurement technology or assessments of any type. |
| TA2 | Integrates and harmonizes data across institutions at population scale, and characterizes the population the data represent | Provides the data substrate, the federation, and the scale, and characterizes representativeness. Does not build individual causal or mechanistic trajectory models; that is TA1. |
| TA4 | Develops the real-world measurement technologies that supply richer, denser, and more ecologically valid data over time | Builds and validates instruments. Does not define trajectories. |

*TA1 is focused on biological measurement and assessment of exposures. Performers may apply novel biological and exposure assays where existing ones are inadequate, and must justify the validity and reproducibility of any proprietary or non-standard assay methods.* ***Development of real-world measurement technology, including home-based and device-derived capture, is the responsibility of TA4 and is not funded under TA1.***

**Approach: Start Immediately, Integrate Progressively**
TA1 begins producing results in Year 1 and does not wait for TA4 technology to mature, nor for TA2 to provide datasets. Proposers should have already identified data sets specific to their chosen approach and established partnerships or teaming arrangements with sources of retrospective data, patient cohorts for prospective studies, and biobanked samples for further analysis using methods under development in TA4.

Year 1: Analysis with existing and novel measures.

- Examine complex interactions among environmental, infectious, iatrogenic, genetic, epigenetic, microbiome, immune, metabolic, prenatal, and perinatal factors using existing data resources and established measures.
- Apply novel biological and exposure assays where existing measurement is inadequate to resolve a hypothesized interaction.
- Produce first-generation candidate trajectory definitions with explicit uncertainty, delivered to TA2 for replication at scale and to TA3 as provisional strata.
- Specify, jointly with TA4, which measurement gaps most constrain trajectory resolution, stated as a requirement on TA4 rather than a wish list.

Year 2 and beyond: Integration of TA4 measurement.

- Integrate TA4 real-world measures into the analysis as they are validated, progressively increasing the density, ecological validity, and lifespan reach of the data underlying trajectory definitions.
- Re-estimate trajectories with the enriched measurement and report how definitions change, including where earlier definitions do not survive.

- Maintain continuity of measurement so that trajectories defined in Year 1 remain comparable to those defined in Year 4.

This sequencing gives TA1 immediate traction, connects it directly to TA4, and creates the concurrent measurement period needed to establish that both new and established measures point to the same underlying causal structure.

**Factors in Scope**

- Genetic and epigenetic contributions, including inherited, de novo, and polygenic factors, assessed across both parents where relevant.
- Environmental, infectious, and iatrogenic exposure across development, captured prospectively where possible and integrated with host biology rather than analyzed separately.
- Microbiome, immune and inflammatory, and metabolic measurement at defined developmental windows.
- Prenatal and perinatal factors, scoped to modifiable maternal and infant health rather than to prediction of autism.
- Behavioral, developmental, communication, and functional measurement, initially from established instruments and progressively incorporating TA4-derived data.
- Social and service context, including care access, intervention exposure, and educational placement, which shape outcomes and confound naive comparison.

**Analytic Requirements**

- TA1 aims at defining interactions in a way that allows for inference of causality and mechanism, not merely association. Submissions that reduce to single-factor analysis across many factors are unlikely to be responsive.
- Interactions among domains conventionally analyzed in isolation should be modeled using novel tools aimed at identifying higher-order, nonlinear, and time-dependent interactions where the data support it, even if that data is not yet available, but might be produced by TA4 teams.
- TA1 submissions should aim to distinguish trajectories that arise from a single dominant driver from those arising from multiple interacting contributions.
- Characterize trajectories at the individual level with calibrated uncertainty, including within-person variability over time, in addition to clustering trajectory-based subgroups.
- Pre-register analysis plans and report candidate structures that fail, since selective reporting of surviving patterns would corrupt replication and independent validation.
- Move beyond association toward causal inference by design, using approaches such as within-family and sibling comparison, natural experiments, temporal ordering, negative controls, multisite replication, and independent validation.

**Technical Area Recap**

The technical areas are sequentially dependent but not sequentially executed. TA1 identifies candidate trajectories from the nonlinear interaction of many factors, including genetic, biological, behavioral, environmental, and iatrogenic (medical) influences, applying new modeling techniques to existing data rather than examining factors in isolation, and it begins in Year 1 without waiting for new measurement. TA2 builds durable, secure infrastructure that integrates and harmonizes data across institutions, characterizes the population that data

represents, follows people as they age, and serves the other areas as shared infrastructure. TA3 runs rigorous trials that act on trajectories, concentrating on the co-occurring conditions that drive the most harm, and uses each intervention as a test of the mechanism it targets. TA4 develops the real-world measurement and support technologies that improve communication and daily function while generating the measurements TA1 and TA2 need, progressively enriching them from Year 2 onward, and it provides the delivery and endpoint-measurement technology TA3 requires.

Several feedback loops are structural (see Figure 1): TA4 returns real-world data to TA1 and TA2; TA4 returns delivery and outcome data to TA3; and, internal to TA4, assessment data improves the technologies themselves through personalization.

**Deliverables**

- Integration of at least three data modalities from among the factors named above.
- First-generation candidate trajectory definitions delivered in Year 1, with uncertainty bounds and pre-registered analysis plans.
- Successive trajectory revisions as TA4 measurement is integrated, with documented crosswalks establishing comparability across program years.
- A specification of the interaction patterns underlying each trajectory, in a form TA2 can test at population scale and TA3 can use to stratify.
- An annual measurement-requirements document for TA4, identifying which gaps most limit trajectory resolution.
- Analysis code and analytic protocols released for independent reproduction.

**Metrics**

| Metric | Target |
|---|---|
| Retrospective data access | By 3 months: demonstrated access to datasets sufficient to fulfil all relevant TA1 metrics, meeting requirements for balanced sex, race, income, support-need level, and communication-ability distribution. |
| Trajectory classification | By 6 months: at least three classification schemes, each defining at least three mutually diverging trajectories relative to a baseline of factor-matched non-autistic individuals, delivered to TA2 and TA3. By 18 months: at least one expanded (more than three trajectories) and refined scheme incorporating Year 1 marker-validation results, with at least one additional trajectory or scheme every 6 months thereafter. By 2 years: IV&V reproduces a classification scheme from provided code and held-out data. |
| Interaction hypotheses | By 6 months: verifiable biomarkers or environmental factors that could predict, or serve as targets for, mechanism-based intervention for at least five non-trivial trajectories, delivered to TA2 and TA4. By 2 years: at least five refined trajectory marker sets, with at least one additional set each year thereafter. |
| Trajectory marker validation | By 1 year: validated association of at least three trajectory markers using held-out retrospective data, biobanked samples, prospective sampling, |

| Metric | Target |
|---|---|
| | or a combination. By 3 years: at least two validated sets of marker interactions that, measured in combination, nonlinearly improve trajectory prediction, with one additional set in Year 4. |
| Measurement-gap identification | Annually: an assessment, delivered to TA4, of the measurement gaps most limiting trajectory resolution. |

**Out of Scope**

- Analyses based on single-modality datasets, or datasets uniquely focused on a single factor.
- Single-factor association studies, or panels of single-factor analyses presented as interaction analysis.
- Development of measurement devices, home-based capture systems, or assistive technology, which fall under TA4. Teams may apply to multiple TAs.
- Construction or operation of the federated data infrastructure, which falls under TA2. Teams may apply to multiple TAs.
- Prenatal or perinatal analysis framed as autism risk prediction rather than modifiable health risk.
- Trajectory definitions derived from cohorts that systematically exclude people with high support needs or without reliable speech.

**Interfaces**

- To TA2: candidate trajectory definitions and interaction specifications for population-scale characterization and integration.
- To TA3: provisional strata in Year 1, refined definitions thereafter.
- To TA4: an annual statement of the measurement gaps most limiting trajectory resolution.
- From TA4: validated real-world measures for integration from Year 2 onward.
- From TA2: population-scale characterization and representativeness assessments, including how derivation cohorts differ from the broader population, against which cohort findings are judged.

### 2.1.2 Technical Area 2 (TA2): Population-Scale Modeling and Data Integration

**Objective:** Much of the data that would reveal how autism unfolds across the population are fragmented across institutions and cannot be analyzed jointly in a harmonized, privacy-preserving way. TA2 removes that barrier by serving as the data integration and federation backbone of SPECTRA. TA2 federates existing and newly generated data across institutions without moving records, applies common data standards and stringent quality control, and carries out population- and cohort-level analyses that describe prevalence, incidence and epidemiologically relevant trends across the full range of autism-affected people and support levels. Because autism unfolds over years, TA2 is built to house longitudinal, multi-domain data safely and securely over time, so that the same individuals and populations can be followed as they age. Notably, the federated data network is intended to become self-sustaining and to persist as durable national infrastructure

beyond the life of the program. TA2 addresses Limitation 3, that the multi-modal data that would reveal trajectories is fragmented across institutions and cannot be analyzed together.

The federated analysis is built on an established clinical-data standard such as FHIR and OMOP and SPECTRA TA2 performers will work with the community to develop new data standards as required for new data types where established data standards do not exist. SPECTRA extends federation beyond records and claims into environmental exposure, multi-omics, behavioral, longitudinal, and sensor data and other modalities collected from TA4.

**TA2 provides Shared Infrastructure:**

TA2 has internal customers. Its purpose is not only to produce findings but to enable the other technical areas. A substantial share of TA2 milestones is therefore defined by whether TA1, TA3, and TA4 can execute against it.

| Serves | TA2 must provide | Failure mode if not delivered |
|---|---|---|
| TA1 | Harmonization of cohort measures, an analytic environment, and population-scale comparison against which cohort patterns are tested | TA1 patterns remain single-cohort findings and cannot be generalized |
| TA3 | Trial-ready stratification, participant identification against eligibility criteria, and endpoint data drawn from routine care | Trials cannot open stratified arms and revert to unstratified enrollment |
| TA4 | Federated learning substrate, telemetry ingestion in the common schema, and a versioned model registry | Device personalization cannot be validated, and TA4 data cannot return data to TAs 1 and 3. |
| External researchers | Documented access under governance, after the program's own use | The commons does not outlive the program |

***Submissions must state explicitly how and when these services become available.***

**Federation and Harmonization:**

- Mapping federated data sources to a common data model. Submissions should describe their approach to mapping every federated data source into a common data model that supports federated learning across both retrospective and prospective data. The engineering effort to bring a data source into the common model is a program cost; closing the representational gap between source's native format and the common model is part of the proposed work, not a precondition of participation.

- Extend the data model beyond its observational health care data origins. SPECTRA will collect complex, continuous, and high dimensional data types such as sensor streams, eye tracking, acoustic data, genomics, education, and environmental exposure that do not fit conventional clinical tables. TA2 will require innovative approaches to link stores with defined relationships these modalities require.
- Submissions should detail how they plan to build the privacy architecture and publish the technical architecture specifications. Specifications should include, but not be limited to, privacy-preserving linkage techniques, federated learning enablement at scale, differential privacy and secure execution. The privacy architecture must be published when operational, not merely described.
- Part of program performance will require development of a plan for financially sustainable maintenance of the infrastructure that keeps the privacy posture intact. This is expected to be developed during the program, rather than enumerated in the proposal. Proposals should detail plans for co-design of governance, consent, standards, and common data elements with the autism and data-contributing communities, so that the network reflects the priorities and privacy expectations of those whose data it holds.

**Population-Scale Analysis and Methods:**

SPECTRA seeks advances in method, not only application of existing methods to a new disease area. Submissions that solely apply standard supervised learning to assembled data will not be responsive.

- Population- and cohort-level statistical models that characterize prevalence, incidence and epidemiologically relevant trends across subgroups and support levels.
- Methods for measurement error, missing data and differences in ascertainment across sources, so that heterogeneous datasets can be analyzed together validly.
- Federated modeling across nodes with heterogeneous data availability, where no single site holds all modalities.
- Characterization of who is and is not represented in the federated data, and assessment of how the cohorts in which TA1 trajectories were derived differ from the broader population.
- Explicit reporting of uncertainty, bias, subgroup performance and failure, including where models do not work.

**Deliverables:**

- An operating federated network with a minimum of ten live nodes that has demonstrated cross-query functionality, published privacy architecture, and documented onboarding sufficient for new nodes to join without program assistance.
- Agreed common data elements, data models, and crosswalks, versioned and published under an open license for use beyond the program.

- Population characterization of the autistic population and its subgroups, including prevalence, incidence and the representativeness of the federated data, reported across the full range of support needs.
- A written report on how TA1 derivation cohorts differ from the broader population, delivered to TA1 and TA3 to bound generalizability of TA1 trajectories.
- A versioned model registry to validate TA4 personalization and to independently reproduce registered models, demonstrated by at least one independent reproduction from the registry alone.
- An analytic environment used by the other technical areas throughout the program and made available to external researchers. This environment will eventually need to be supported by a robust sustainability and transition plan that ensures documented, governed access remains available and demonstrates the long-term viability and success of the analytical environment beyond the program.

**Metrics:**

| Metric | Target |
|---|---|
| Nodes live | Minimum ten live nodes with data flowing and cross-node query enabled by the end of program with interim targets. |
| Harmonization | >95% of committed sources mapped to the common model and passing quality checks by end of program. |
| Service delivery | On-time delivery of stratification, cohorts, and endpoint extracts delivered to TA3 and TA4 against dates agreed upon by the program; target of 95% on-time, zero missed dependencies that block a TA3 trial opening. |
| Query performance | ≤5 sec multisite query across 10+ sites. |
| Representativeness | On-time delivery of the target autism population represented in the federated data, with gaps characterized by subgroup. |
| Privacy | No successful re-identification under adversarial red-team testing by an independent team, repeated yearly at minimum and after each major architecture change. |
| Reuse | 5 external research groups executing analyses against the SPECTRA platform by the end of the program. |

**Out of Scope:**

- Centralized repositories requiring custodians to relinquish custody of their data.
- Re-aggregation of datasets already assembled by other federal programs. TA2 will consume and interoperate with those resources rather than duplicate them.
- Causal or mechanistic trajectory modeling on deeply phenotyped individuals, which is the scope of TA1. TA2 provides the sub-population and broader population context, not the individual causal model.
- Analytic environments accessible only to the performer that built them.

### 2.1.3 Technical Area 3 (TA3): Precision Intervention and Trajectory Testing

**Objective:** Test interventions within trajectories rather than against the autism label, establish which options work for whom, and use each intervention as a test of the mechanism it targets. TA3 answers Limitation 4, that we do not turn data into action and treatment is chosen by trial and error.

**Intervention as Causal Test**

Every TA3 trial serves twice. It is a treatment trial, and it is an experimental test of a candidate driver nominated by TA1. This dual purpose is a program requirement and distinguishes TA3 from conventional intervention research.

For each arm, proposers must register in advance the target being modified, the predicted direction and magnitude of effect, the subgroup in which the effect is predicted, and the subgroup in which it is predicted not to occur. A trial that improves outcomes without testing its stated mechanism is a partial result. A trial whose prediction fails is a reportable finding and is not a program failure.

**Trial Architecture**

- Adaptive platform trials operating under a master protocol with a shared control, so that arms can be added and dropped without standing up new trials.
- Sequential multiple-assignment randomized designs for building treatment sequences, since real care is sequential and the operative question is what to try next when the first option does not work.
- Real-world conditions: delivery in ordinary clinics, schools and homes, broad eligibility, usual-care comparators, and outcomes measured in daily life.
- Confirmatory stages designed to support regulatory and coverage decisions.

**Open Broad, Then Sharpen**

Trials open with broader eligibility and add trajectory stratification as trajectories are confirmed by TA1 and their population representativeness is established by TA2. This sequencing is deliberate. It allows TA3 to begin without waiting for final trajectory definitions, and it means a delay in TA1 or the supporting data infrastructure slows the refinement of TA3 rather than halting it.

**Targets and Intervention Classes**

TA3 gives priority to the co-occurring conditions that cause the most harm and are most often missed, including those overlooked when their symptoms are misattributed to autism rather than investigated as distinct, treatable conditions. These include, and are not limited to, sleep disruption and disorders, seizures and epilepsy, gastrointestinal disease, chronic pain, anxiety and mood conditions, self-harm and behavioral crisis, immune and metabolic conditions, and regression or loss of function. Proposers may address other conditions where they can show comparable harm and a testable mechanism. TA3 does not prescribe which interventions to test; proposers select them and justify each against the mechanism it targets. Because many autistic people, especially those with intellectual disability, carry a heavy and sometimes thinly evidenced medication burden, testing when to safely reduce or stop medication, not only when to start it, is within scope and is held to the same evidentiary standard.

**Endpoints**

Endpoints must align across the program. Each trial draws its outcome measures from the trajectory outcomes defined in TA1, expresses them wherever possible through the TA4 measures that capture behavior in daily life, and reports them so they can be read against the population characterized by TA2. Where a shared program measure exists, trials use it rather than inventing a standalone endpoint.

- Health and morbidity: e.g., seizure frequency, sleep architecture, gastrointestinal symptom burden, pain, crisis, and hospitalization.
- Function and participation: daily living, school and workplace participation, independence, and prompt dependence over time.
- Communication and language: functional communication in daily life across all modalities, including speech, augmentative and alternative communication (AAC), and gestural or behavioral signals. Measures capture initiation and not only prompted response, apply to people with and without reliable speech, and use TA4-derived real-world measures validated against structured assessment.
- Quality of life, reported by the person wherever possible and by proxy only where necessary, with the method stated.
- Family quality of life and caregiver health, measured with validated instruments rather than assumed.
- Durability at twelve months in ordinary settings. In-clinic performance at the end of an intervention period is not a sufficient endpoint.
- Medication burden and adverse drug effects, so that benefit is weighed against the harms of treatment and of polypharmacy.
- Each endpoint is defined in advance in full: the population it applies to, the outcome measured, how the analysis treats events such as rescue treatment, added medication, or dropping out,

and how results are summarized across participants, so that treatment changes and attrition in real-world settings do not obscure the effect being measured.

Endpoint selection, eligibility criteria, and the definition of meaningful benefit are to be co-designed with autistic people and families, so that trials measure outcomes the community values rather than outcomes that are merely convenient to measure.

**Deliverables**

- An operating platform trial with at least two trajectory-stratified arms and endpoints aligned with regulatory expectations.
- At least one trajectory-matched intervention with a confirmatory result.
- Registered causal tests with results reported in full, including predictions that failed.
- A coverage evidence dossier suitable for payer review, supporting expansion of covered services.
- Trial infrastructure and protocols released for continued use after the program period.
- Targets are stated as outcomes a performer demonstrates against pre-specified thresholds fixed at award and reported by program gate. Values marked as conditions of milestone acceptance gate continuation.

**Metrics**

| Metric | Target |
|---|---|
| Stratification benefit (primary) | Pre-registered effect-size advantage for trajectory-matched treatment over unstratified care, meeting a pre-specified margin in a confirmatory arm. |
| Mechanism confirmation | Proportion of pre-registered mechanism predictions confirmed in the predicted direction and magnitude, against a stated threshold, with disconfirmed predictions reported in full. |
| Stratification-rule validity | The stratification rule shown to be predictive rather than prognostic and locked before the confirmatory stage, with responder-rule sensitivity and specificity reported and analytical and clinical validation demonstrated. |
| Sequential treatment benefit | Improvement from sequential, multiple-assignment strategies over fixed first-line care among participants who did not respond to the initial option. |
| Endpoint validity | Trial endpoints validated against structured assessment at a pre-specified threshold using TA4-derived real-world measures, and person-reported wherever possible. |
| Arm throughput | Time from a TA1 candidate-driver nomination to arm activation under the master protocol, against a stated threshold and reported by gate. |
| Enrollment representativeness | People with high support needs, intellectual disability, and without reliable speech enrolled at pre-specified minimum proportions, reported by stratum. |

| Metric | Target |
|---|---|
| Safety and harm surveillance | Adverse-event and harm monitoring across all arms under an independent data safety monitoring board, with pre-specified stopping rules, and no intervention that narrows expressive range or reduces autonomy. |
| Durability | Proportion of demonstrated benefits sustained at twelve months in ordinary settings. |
| Clinical significance | Absolute benefit reported alongside relative effect, including number needed to treat and, where relevant, number needed to harm. |
| Medication burden | Where medication is safely reduced or stopped, function and quality of life maintained or improved with lower medication burden and fewer adverse drug effects, against a pre-specified threshold. |
| Family and caregiver outcomes | Change in family quality of life and caregiver health measured with validated instruments, reported alongside participant outcomes. |
| Regulatory and coverage readiness | Confirmatory results structured to regulatory expectations, with coverage dossiers filed and coverage determinations obtained. |
| Full-result reporting | All registered causal tests and predictions reported, confirmed and disconfirmed alike, with trial infrastructure and protocols released for continued use. |

**Out of Scope**

- Trials enrolling on the autism label alone with no stratification and no plan to add it.
- Interventions whose stated endpoint is reduction of autistic traits rather than health, function, communication, participation or quality of life.
- Trials measuring only in-clinic performance without a real-world durability endpoint.
- Trials excluding people with high support needs, intellectual disability, or without reliable speech, absent a stated scientific justification.

**Interfaces**

From TA1: ranked candidate drivers with pre-specified tests, predicted responder subgroups, participant phenotype supporting eligibility, and trial-ready stratification.

From TA2: federated data support and characterization of the trial population's representativeness.

From TA4: intervention delivery and continuous real-world endpoint measurement.

To TA1: trial outcomes returned as evidence that moves candidate drivers to tier three, or removes them, refining trajectory models.

### 2.1.4 Technical Area 4 (TA4): Technologies for Communication, Quality of Life, and Embedded Assessment

**Objective**

Develop technologies that people want in their daily lives, across the full lifespan, and that generate assessment data as a byproduct of ordinary use. These are everyday technologies: wearables that track sleep, movement, and autonomic state; augmentative and alternative communication (AAC) and speech interfaces; eye tracking on tablets and phones; low-channel EEG usable outside a research center; camera-based analysis of movement, gait, and behavior; and immersive and virtual-environment tools for practice and participation. Used daily, each yields continuous, ecologically valid measurement of domains that are assessed today only in the clinic, the setting that predicts a person's actual life least well, and each improves with that use through AI-driven personalization. Together they span the assessment and support that daily life requires, including everyday function and independence, self-regulation, sensory and behavioral needs, health and safety, learning and social participation, and communication.

TA4 treats measurement, personalization, and sustained use as one system: measurement enables personalization, personalization drives retention, and retention makes longitudinal measurement possible. Because acceptance and sustained use are the test, TA4 technologies are co-designed with the people who will use them and, where relevant, their caregivers and communication partners, from the earliest design stage rather than evaluated on them at the end. Proposers should describe their plans for engagement across the product lifecycle, with particular attention to design.

The strongest approaches will often combine modalities, for example pairing wearable physiological sensing with speech recognition and behavioral analysis to capture more of daily function than any one modality alone. Such integration may require interdisciplinary teams that the program assembles across awardees after submission.

#### Measurement Outside the Clinic

Every TA4 capability must produce measurement as a byproduct of ordinary use, without imposing a separate assessment task. This is a scoping rule: a capability that requires someone to perform a task in order to be measured belongs in TA1. And because a capability that nobody sustains produces no data, abandonment is both a measurement failure and a quality-of-life failure.

Assessment data generated by TA4 serves three purposes at once. Submissions must address all three.

1. Identification and characterization. Continuous, ecologically valid measurement feeds TA1 analysis and TA2 population characterization, extending both into settings and populations that clinic-based instruments cannot reach.
2. Therapeutic effectiveness. Real-world outcome data supplies TA3 with endpoints measured in daily life, including durability, and makes trajectory-matched treatment testable at the individual level.

3. Device improvement and personalization. Data returns to the technology itself, supporting AI-driven adaptation to the individual user and improvement of the underlying models for all users.

Proposers must solve the following technical problems: cold start, so the technology is useful from first use and improves quickly from sparse examples; few-shot personalization from very small individual datasets; non-stationarity across the lifespan, since the same person changes with development, aging, illness, and medication; adaptive drift, where a system that adapts to a shutdown or low-engagement state can narrow what it offers and entrench that state; and on-device constraints on compute, memory, and power consistent with all-day wearable and mobile use.

### Early Identification

SPECTRA seeks identification beginning as soon after birth as is technically feasible and validated in selected populations by 24 months. Today nothing is validated below 16 months, the strongest early signals come from modalities that do not scale, such as MRI, and the sub-16-month evidence derives from high-familial-likelihood infant-sibling cohorts rather than unselected populations. TA4 must push validated performance roughly ten months earlier, in selected populations, using modalities that work outside a research center, such as low-channel EEG and tablet or phone-based eye tracking.

**Acceptance and Sustained Use**

The test is acceptance and sustained use, not stated preference. The parties who must accept a technology will change across the lifespan (from parents to the person themselves).

| Life stage | Who must sustain it | What it must deliver to them |
|---|---|---|
| Infancy and early toddlerhood | The family, in the home | Indirect benefit such as sleep and feeding insight, reassurance, faster access to support, reduced clinic burden. The caregiver and infant benefit. |
| Early and middle childhood | The child and the family together | Direct benefit to the child in communication, participation, or regulation, with manageable burden for the family and school. |
| Adolescence through adulthood | The person themselves | Direct benefit the person values enough to keep using, with control over what is collected and shared. |

In the birth-to-24-month window, some capabilities are primarily instrumentation: an infant does not choose an EEG cap or a wearable, and no amount of design will turn one into an assistive device. SPECTRA accepts primarily measurement-oriented capabilities in this window when the submission meets the following criteria:

- the burden is minimal
- the technology is easy to use

- affordable and runs on widely available hardware
- that the family receives something of value during a period when no diagnosis exists and none should be assigned
    - E.g., sleep, feeding, and developmental insight, reduced clinic time, faster access to support if concerns emerge
- that sustained real-world use is demonstrated, with retention reported over months rather than adherence over a single visit.

*Reducing diagnostic delay is a sufficient justification on its own. Submissions in this window should not claim quality-of-life benefit to the infant that the technology does not deliver.*

**The measurement-validity problem.** Personalization and stable measurement are in tension, and resolving that tension is a required deliverable. If the device adapts while it measures, the instrument is not fixed: a drop in selection latency may reflect the user improving, the model improving, or both. Performers must deliver methods that separate observed change into device-attributable and user-attributable components. Submissions that report improvement without separating these sources will not satisfy the assessment return.

- Specify the personalization mechanism explicitly: what is learned from an individual, over what timescale, what changes as a result, and how improvement is verified rather than assumed.
- Report device-attributable and user-attributable change separately in all outcomes.
- Version, log, and make auditable the model state behind any measurement used by TA1, TA2, or TA3.
- Demonstrate personalization gain as a measured quantity, not a design claim.
- Include safeguards against adaptive drift that narrows expression or entrenches an impaired state.

**Speech and Language Models**

Automatic speech recognition (ASR) and related language models underpin many TA4 capabilities, including voice interfaces, dictation, captioning, voice-controlled assistive technology, speech-derived measurement of communication, and communication systems that incorporate a visual band for nonverbal elements of communication. Current systems are trained predominantly on fluent adult speech from neurotypical speakers. Performance degrades on children's speech and further on speech marked by disfluency, atypical prosody, articulation and phonological differences, dysarthria or childhood apraxia of speech, reduced intelligibility, and minimal or emerging speech. This excludes a substantial share of the population the program serves, and it does not resolve by scaling adult data. Autistic communication may also include echolalia and scripted or gestalt language, which mainstream models handle poorly.

SPECTRA will accept submissions that address this need, focused on open models, data, and benchmarks and on easy integration with devices rather than a fielded standalone device. Closed commercial models cannot be inspected for failure modes, fine-tuned on device, or used in federated personalization, so they cannot meet SPECTRA's personalization and on-device requirements. Performers will coordinate with TA2 on data standards and privacy-preserving infrastructure. A component may be proposed on its own or as part of a broader TA4 effort. It should deliver:

- Open-source, openly licensed acoustic, language, and multimodal models, small enough for on-device deployment and fine-tunable so that per-speaker adaptation occurs on device without raw data leaving the home.
- Stated coverage across age, from infancy through older adulthood, and across speech and language profiles, which may include pre-linguistic vocalization, disfluency, atypical prosody, articulation and phonological differences, dysarthria and apraxia, reduced intelligibility, minimally speaking and nonspeaking communication, and speech that alternates with AAC. A submission need not cover the full range but should state its target populations and profiles.
- A consented, shareable speech corpus and a public benchmark reporting word error rate and phoneme error rate stratified by age band and speech profile. Submissions should state a target error-rate reduction on child and atypical speech relative to mainstream systems, measured on this benchmark. The corpus and benchmark are program deliverables expected to outlast the program.

*Corpus construction must follow the program's consent and governance requirements. Speech is biometric and identifiable, and in this population is often collected from people who may not be able to consent conventionally. Submissions must address consent, assent, revocation, and re-identification risk directly.*

**Deliverables**

**Per-award deliverables.** Each award delivers:

- One or more technologies that people adopt and sustain in daily life, demonstrating durable functional benefit at 12 months of use with no loss of user agency.
- A validated profile of the communication and function domains the technology targets, stating where on the continuum it applies, from fluent speech with impairment through intermittent speech loss to no reliable expressive method, and reporting expressive ability and, where the approach allows, receptive ability.
- A demonstrated individual personalization loop: measured improvement in the individual's device performance attributable to adaptation, reported separately from user change, with versioned model state.
- An operating closed-loop data return into TA1 and TA2 through the common data model.

**Program-level outcomes.** Across the portfolio and shared infrastructure, the program delivers:

- At least three technologies demonstrating durable functional benefit at 12 months of use, spanning the communication and function continuum and the lifespan from fluent speech with impairment through intermittent speech loss to no reliable expressive method.
- Demonstrated population transfer: improvement in base-model performance for new users arising from federated learning across the cohort.
- Open speech models, a consented and shareable speech corpus, and a public benchmark, released under open license and expected to outlast the program.

**Metrics**

*Targets are stated as outcomes a performer demonstrates against pre-specified thresholds. For each metric below, the direction of effect and the required evidence are fixed by the program; the numeric threshold is proposed by the performer and set with the program team and Program Manager at award. Each proposal must state the improvement its technology is predicted to deliver over current practice, including how much earlier it is expected to enable identification, and must*

*define how each gain is measured. Metrics are assessed at the program gates shown (G1 at Month 12, G2 at Month 24, Final at Month 48).*

**Graded performance metrics.**

| Metric | Success criterion | Verified |
|---|---|---|
| **Earlier validated identification** | Reduction in the age at which the condition can be validly identified, below the current 16-month floor, with robust performance by 24 months in unselected, real-world populations. | G2, Final |
| **Subgroup representation** | Detection and device performance hold within the performer's pre-specified margin across sex, genetic ancestry, income, and communication and cognitive profile. | G2, Final |
| **Adoption, retention, and burden** | A performer-set reduction in abandonment at 6 months relative to current assistive-technology practice, with setup time, wear time, and user and caregiver effort reported as measured quantities in representative users. | G1, G2, Final |
| **Real-world measurement validity** | Embedded measures correlate with structured assessment at the performer's pre-specified threshold, with an established minimum detectable change, in at least two settings and at least two independent deployment sites (for example a clinic, a school, or a home or community program). | G2, Final |
| **Measurement integrity** | Observed change is decomposed into device-attributable and user-attributable components to a stated accuracy, supported by versioned, logged, and auditable model state. | G2, Final |
| **Learning performance** | Usable at first use before any individual data exists; a stated per-user adaptation rate to reach a defined benefit from sparse data; and measured gain for new users from federated learning without centralizing raw data. | G1, G2, Final |
| **Integration with TA1 and TA2** | Embedded measures map to defined TA1 trajectory constructs as versioned, validated data fields; TA4 data conform to TA2 standards and enter population-scale models by federated learning. Contribution reported as cohort coverage and as improvement in models for new users, to performer-set targets. | G2, Final |
| **Functional performance** | Capability-specific gains over current practice to performer-set targets, for example reduced word error rate on child and atypical speech on the program benchmark, communication throughput in words per minute, or time from speech loss to an available alternative modality. | G2, Final |
| **Safety** | Adverse events at or below a stated rate, and, for alerting capabilities, lead time for events such as overload or seizure at a stated sensitivity and false-alarm rate. Reviewed by an independent safety monitor. | G1, G2, Final |

**Out of Scope**

- Deployment of unvalidated measures or methods as established practice. SPECTRA funds approaches supported by current evidence of validity, and will fund rigorous testing to establish validity where it is in question, but will not fund the deployment of methods that lack that evidence.
- Systems that log or transmit without user-controlled consent, or that restrict what a user is able to express.
- Devices evaluated only on in-clinic performance without a real-world durability endpoint.
- Closed ecosystems that cannot export interaction data in the program schema.
- Capabilities that impose an assessment task on the user rather than measuring as a byproduct of use.

**Interfaces**

- To TA1: validated real-world measures for integration into trajectory analysis from Year 2 onward.
- To TA2: consented telemetry in the common data model, and model state for the versioned registry.
- To TA3: intervention delivery and continuous real-world endpoint measurement, including durability.
- From TA1: an annual statement of the measurement gaps most limiting trajectory resolution.
- From TA2: federated learning substrate and model registry services.

## 2.2 Shared Non-Solicited Program Resources

To ensure that SPECTRA functions as a coherent ecosystem rather than a collection of independent efforts, ARPA-H anticipates providing a set of shared, non-solicited program resources that operate across all four TAs. These resources are not solicited under this ISO and are described here for reference only, so that proposers understand the broader SPECTRA ecosystem and expected interfaces. The shared resources are: (1) Program-Wide Data Coordination; (2) Community Co-Design; (3) Responsible-Use Controls; (4) Independent Evaluation; and (5) Transition Support.

Proposers should not assume that all shared resources will be fully available at the start of performance. Performers will receive rolling access, as appropriate, to shared standards, benchmark targets, common testbed capabilities, and early harmonized data and analytic outputs as those resources are established, with more mature, shared datasets, models, and evaluation resources expected to become available progressively thereafter. Accordingly, submissions should describe how the proposed effort will (a) leverage these shared resources as they become available and (b) remain technically credible and executable as such resources are phased in over time. ARPA-H expects to provide additional details on the sequencing, content, and intended use of shared resources through subsequent amendments to this ISO and/or after performers are selected and as the execution phase of the program gets underway.

### 2.2.1 Program-wide Data Coordination

A dedicated data-coordination function will support alignment of performer-generated data to the SPECTRA common data model and data standards established by TA2 and assess shared test-bed needs for benchmarking and evaluation. It complements—but does not duplicate—the federation and harmonization work solicited under TA2; its role is program-level coordination and translation of outputs into forms usable across teams, ensuring that trajectory definitions (TA1), trial-ready data (TA3), and real-world telemetry (TA4) remain mutually intelligible over the life of the program.

### 2.2.2 Community Engagement and Co-Design

SPECTRA treats acceptance and sustained use, not stated preference, as the test of success. A program-wide engagement and co-design resource will connect the program to the full stakeholder community: autistic people across all support needs, including those with profound autism and those who are minimally speaking or nonspeaking; their families and caregivers; autistic-led self-advocacy organizations and autism advocacy and service organizations; and clinicians, educators, and other providers. Autistic people, families, and caregivers act as co-design partners who shape governance, consent, common data elements, assessment design, and technology development from the outset; other stakeholders are engaged for structured input and review. The resource reinforces the co-design expectations in individual technical areas, notably TA2 governance and TA4 technology development, and provides shared methods so community priorities and privacy expectations are reflected consistently across the program. Decisions about the autistic community are made with that community, not for it.

### 2.2.3 Responsible-Use Controls

Because SPECTRA collects sensitive, identifiable, and longitudinal data—including biometric speech, physiological, genomic, and behavioral data—often from individuals who may not be able to provide conventional consent, a shared responsible-use function will maintain program-wide safeguards governing how SPECTRA data, models, and tools are used. This includes consent, assent, and revocation practices; re-identification risk management; a granular, revocable consent-and-agency layer; and enforcement of intended-use and use-limitation policies. Consistent with the interpretation limits stated for TA4, SPECTRA outputs will not be validated or advanced for determining legal capacity, guardianship, educational placement, or service eligibility, and absence of demonstrated ability will not be treated as evidence of absence of ability. This resource works alongside TA2's privacy architecture to ensure that responsible-use requirements are applied uniformly across all performers.

### 2.2.4 Independent Evaluation (IV&V)

A separate Independent Verification and Validation (IV&V) capability will provide objective, arms-length assessment of technical progress across the program. Its functions include independent assessment of technical progress against pre-specified thresholds; evaluation of integration readiness across technical areas; independent reproduction of registered models and trajectory derivations from provided code and held-out data; and data quality assurance and quality control.

The IV&V capability supports the Program Phase Reviews and down-select decisions described in Part III and reinforces SPECTRA's emphasis on replication, full-result reporting, and reproducibility.

### 2.2.5 Transition Support

A program-wide transition function will help de-risk and accelerate the movement of SPECTRA outputs toward real-world adoption and sustainability. This includes regulatory planning support (e.g., FDA engagement strategy for diagnostic and therapeutic capabilities), coverage and reimbursement evidence planning for payer review, coordination with potential industry and health-system partners, and support for the long-term governance and sustainability of shared assets—such as the TA2 federated network, model registry, analytic environment, and the open speech corpus and benchmarks—so that these commons outlive the program. This resource complements the commercialization and transition planning required of individual performers rather than replacing it.

# PART III: PROGRAM STRUCTURE AND SCHEDULE

ARPA-H anticipates a phased program structure with Program Phase Review decision points at the end of each phase and may conduct down-selects at phase transitions based on items such as technical progress, integration readiness, and alignment with program objectives.

Periodic Reporting and Progress Review: Detailed cadence and content requirements will be set by the Program Manager in consultation with the IV&V teams. These may include (but are not limited to) written reports, slide presentations, quad charts, data, software or schema deposition, demonstrations (virtual, or at site visits) and/or oral presentations. IV&V teams and Subject Matter Experts will review monthly reports and provide feedback to the Program Manager and the TA performer teams.

Periodic Program-Wide Events and Phase Reviews: SPECTRA program events may include (but are not limited to) kick-off events, evaluation events in each phase, and site visits.

## 3.1 Program Metrics

Program metrics are referenced in Section 2.1, which defines the performance expectations for the TAs across the SPECTRA program. Additional metrics may be applied program-wide and to technical areas as needed. These metrics are intended to guide evaluation of technical progress and assess whether proposed solutions are advancing toward clinically meaningful, usable, and translatable capabilities aligned with SPECTRA program objectives.

# PART IV: PROPOSAL REQUIREMENTS

## 4.1 Eligibility

ARPA-H is primarily interested in proposals from commercial performers, academic institutions, and non-profit organizations. Federally Funded Research and Development Centers (FFRDCs) and government entities, including federal employees, are **not permitted** to respond to this ISO as a prime or sub-performer.

ARPA-H must prioritize awards to entities that will conduct funded work in the United States. Non-domestic performers are encouraged to collaborate with a domestic entity. ARPA-H will not make awards to entities organized under the laws of a covered foreign country per 42 U.S.C. 290c(n)(1)(D).

**System for Award Management (SAM)**: An active SAM.gov registration and Unique Entity Identifier (UEI) is required to receive an award. NOTE: SAM actions may take more than 14 business days to process; at times it may take up to 90 days. SAM is independent of ARPA-H and thus ARPA-H representatives have no influence over processing timeframes.

## 4.2 Award Instruments

ARPA-H may award Other Transaction (OTs) agreements resulting from proposals submitted in response to this ISO.

## 4.3 Solution Summaries (Pre-Proposal Submissions)

**ARPA-H requires submission of a Solution Summary prior to submission of a Proposal for all Technical Areas.** Solution Summaries allow ARPA-H to assess the viability of proposed concepts prior to Proposals.

Submission of a Solution Summary is mandatory. ARPA-H will review submitted Solution Summaries and either encourage submission of a Proposal or discourage submission of a Proposal. Note that a Solution Summary may be evaluated to be of merit but discouraged from submitting a Proposal. Although a Proposal may be submitted regardless of ARPA-H's determination, potential proposers are advised to give the government's determination significant weight when deciding whether to invest time and resources in the development of a Proposal. Additional feedback on Solution Summaries may not be provided.

**Solution Summary Format (Attachment A):**

**Use of Attachment A – Solution Summary Format is required.** All solution summaries submitted in response to this ISO must comply with the content, page, and formatting requirements outlined in Attachment A. Potential proposers are required to use the template provided. Information not explicitly requested in this ISO may not be reviewed.

**ARPA-H will amend this ISO at a future date to add Attachment A for TAs 1-3. A separate Attachment A will be issued for each TA. Proposers must review and use the Attachment A that corresponds to the TA they are addressing. The amendments will be posted on SAM.gov, and proposers should monitor SAM.gov for its release.**

- Submit to: https://solutions.arpa-h.gov
    - Solution Summary Due Dates:
        - TA 4: October 18, 2026 at 5pm ET (submission portal opens Oct 4, 2026)
        - TA 1 and TA 2: December 2, 2026 at 5pm ET (submission portal opens Nov 18, 2026)
        - TA 3: January 18, 2027 at 5pm ET (submission portal opens Jan 4, 2027)

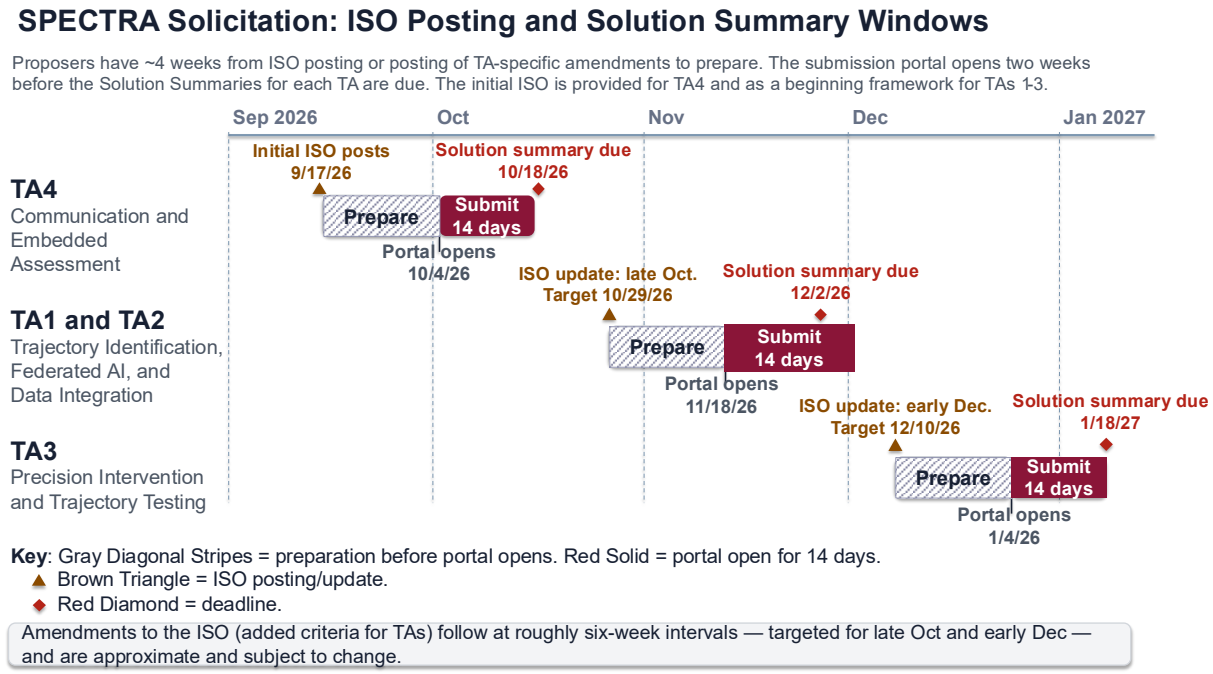


*Figure 2: SPECTRA Solicitation: ISO Posting and Solution Summary Windows*

## 4.4 Proposal Requirements

As noted above, following Solution Summary evaluation, proposers will be either encouraged to, or discouraged from, submitting a Proposal. Although a Proposal may be submitted regardless of ARPA-H's determination, potential proposers are advised to give the government's determination significant weight when deciding whether to invest time and resources in the development of a Proposal.

ARPA-H will amend this ISO at a future date, following the evaluation of Solution Summaries, to add Attachment B – Proposal Requirements. A separate Attachment B will be issued for each TA. Proposers must review and use the Attachment B that corresponds to the TA they are addressing. The amendments will be posted on SAM.gov, and proposers should monitor SAM.gov for its release.

## 4.5 Full Proposal Submission Requirements

More information and guidance will be provided with the posting of Attachment B – Proposal Requirements. The amendment will be posted on SAM.gov, and proposers should monitor SAM.gov for its release.

# PART V: EVALUATION CRITERIA AND SELECTION

## 5.1 Solution Summary Evaluation

ARPA-H will review and respond to each conforming Solution Summary submission. Solution Summaries will be reviewed for the purpose of providing feedback regarding whether ARPA-H is interested in the Solution Summary concept. At a minimum, the government's response will indicate whether submission of a Proposal is encouraged or discouraged. Although a Proposal may be submitted regardless of the feedback provided, potential proposers are advised to give the government's decision significant weight when determining whether to invest time and resources in the development of a Proposal.

Non-conforming Solution Summaries submissions may be removed from consideration. If a submission is determined to be non-conforming and will not advance for further consideration, the proposer will be notified via email. No additional feedback will be provided.

## 5.2 Proposal Evaluation

All conforming Proposals will be evaluated by qualified Government Evaluators through ARPA-H's Scientific Review Process. **ARPA-H will evaluate Proposals based on consideration of overall scientific and technical merit, proposer's capabilities and relevant experience, price/value analysis, and relevance to the ARPA-H mission.**

Proposals are evaluated independently; they are not ranked or compared against each other during evaluation. Proposals may be deemed to be of merit and not selected for negotiations.

An award will be made to proposer(s) determined to be the most advantageous to the government, consistent with instructions and evaluation criteria, and based on availability of funding

ARPA-H reserves the right to incorporate into the resulting agreement(s) any aspect of the successful proposal(s) that is evaluated, relied upon, or otherwise considered in the ARPA-H's selection decision.

Non-conforming Proposal submissions may be removed from consideration. If a submission is determined to be non-conforming and will not advance for further consideration, the proposer will be notified via email. No additional feedback will be provided.

## 5.3 Use of Large Language Models (LLMs)

LLMs may be used to assist reviewers by extracting, summarizing, and drafting text. They do not substitute for human judgment. Reviewers remain responsible for all scores and recommendations and verify LLM output against the original submission.

## 5.4 Selection

After Proposal evaluations, ARPA-H will select proposers for negotiations. Proposers will be notified via email after their Proposal evaluation if they are selected or not selected for negotiations. Notifications will not occur until after all Proposals have been fully reviewed and evaluated. Those not selected are not eligible for negotiation. Selection for negotiations does not constitute an award. ARPA-H is not required to make any award under this ISO and reserves the right to select all, some, or none of the Proposals received. ARPA-H may select Proposals for full or partial funding. As such, a proposer's Proposal may be evaluated to be of merit but not selected for negotiations. Those not selected for negotiations will be notified via email.

# PART VI: GENERAL INFORMATION

## 6.1 Research Security

ARPA-H will conduct a Research Security Review (RSR) of all Proposals selected for negotiations. Teams selected for awards will be required to submit required documents provided with Proposal instructions.

## 6.2 Intellectual Property

ARPA-H will negotiate intellectual property and data rights as part of award negotiations. ARPA-H intends to negotiate terms that enable both government use and commercial transition of program outputs.

## 6.3 Publication and Dissemination

ARPA-H expects research results to be broadly publishable consistent with the fundamental research principles, subject to pre-publication review by ARPA-H. Performers are prohibited from using ARPA-H logos without written authorization from COMPASS.

## 6.4 Disclaimers

This ISO does not constitute a commitment by the U.S. Government to make an award, nor does it commit ARPA-H to pay any costs incurred in the preparation or submission of a Solution Summary or Full Proposal. ARPA-H reserves the right to cancel this ISO at any time.

## 6.5 Questions and Answers

Questions regarding this ISO must be submitted via the Solutions site Ask-A-Question (select SPECTRA in the dropdown). The Solutions site can be found at: solutions.arpa-h.gov/ask-a-question. Questions and responses of general applicability will be posted publicly. Please check posted answers before submitting a question; duplicate answers will not be provided. Questions sent via email may not be answered. The following types of questions will not be answered:

- Which Technical Area a given team or concept should address
- Whether a specific idea or approach falls within SPECTRA's scope
- Preferred or recommended teaming arrangements
- Requests for ARPA-H's position on topics beyond the requirements of this solicitation

# APPENDIX

**Alternative version of Figure 1:**

**Figure title**: *SPECTRA Program Structure and Technical Areas*

The SPECTRA Program Structure and Technical Areas flowchart shows the relationships among the program's four technical areas, shared infrastructure, data flows, and quality-of-life outcomes. The table below provides a detailed, accessible version of this information, including the relationships among the elements and the four quality-of-life outcomes measured and improved by TA4.

| TA/Element | Primary Function | Relationship With Other Elements |
|---|---|---|
| **TA1: Multifactor Analysis and Trajectory Identification** | Analyze | Receives real-world measurement and device data. Exchanges information with TA2 and TA4. |
| **TA2: Population-Scale Modeling and Data Integration** | Integrate | Receives shared infrastructure and serves TA1, TA3, and TA4. Exchanges information with TA1 and TA3. |
| **TA3: Precision Intervention and Trajectory Testing** | Act | Receives delivery and outcomes. Exchanges information with TA2 and TA4. |
| **TA4: Technologies for Communication, Quality of Life, and Embedded Assessment**<br>***New assessments from preconception to infancy to geriatrics, built for natural, everyday settings*** | Enable | Exchanges information with TA1 and TA3. Measures and improves quality-of-live outcomes through four outcome areas described below. |
| **Quality-of-Life Outcomes** | Measured and Improved by TA4 | Connects directly to four parallel outcome areas described below. |
| **Communication** | Intent-preserving expressive and receptive communication, including validated AAC. | One of four quality-of-life outcome areas measured and improved by TA4. |

| TA/Element | Primary Function | Relationship With Other Elements |
|---|---|---|
| **Behavior and Sleep** | Emotional and behavioral regulation and healthier, more consolidated sleep. | One of four quality-of-life outcome areas measured and improved by TA4. |
| **Sensory, Pain, GI** | Sensory regulation and relief from pain and gastrointestinal burden. | One of four quality-of-life outcome areas measured and improved by TA4. |
| **Independence** | Daily living function and autonomy across the full lifespan. | One of four quality-of-life outcome areas measured and improved by TA4. |

**Alternative version of Figure 2:**

**Figure title:** *SPECTRA Solicitation: ISO Posting and Solution Summary Windows*

The SPECTRA solicitation timeline shows the anticipated schedule for ISO postings or updates, preparation periods, submission portal openings, and solution summary deadlines for the TAs. Proposers have approximately four weeks from an ISO posting or TA-specific amendment to prepare their solution summaries. The submission portal opens two weeks before the solution summary deadline and remains open for 14 days.

The initial ISO is provided for TA4 and serves as a beginning framework for TAs 1–3. Subsequent amendments to the ISO, which add criteria for the TAs, are targeted at approximately six-week intervals. The amendment dates are approximate and subject to change.

**SPECTRA Solicitation Timeline:**

| TA | ISO Posting or Update | Preparation Period | Submission Portal Opens | Solution Summary Due |
|---|---|---|---|---|
| **TA4: Communication and Embedded Assessment** | Initial ISO posts Sept. 17, 2026 | Approximately 4 weeks | Oct. 4, 2026 | Oct. 18, 2026 |
| **TA1 and TA2: Trajectory Identification, Federated AI, and Data Integration** | ISO update targeted for late October 2026; target date Oct. 29, 2026 | Approximately 4 weeks | Nov. 18, 2026 | Dec. 2, 2026 |

| TA | ISO Posting or Update | Preparation Period | Submission Portal Opens | Solution Summary Due |
|---|---|---|---|---|
| **TA3: Precision Intervention and Trajectory Testing** | ISO update targeted for early December 2026; target date Dec. 10, 2026 | Approximately 4 weeks | Jan. 4, 2026 | Jan. 18, 2027 |