Broad Agency Announcement

CoasterChase

BIOLOGICAL TECHNOLOGIES OFFICE

HR001125S0014

June 26, 2025

This publication constitutes a Broad Agency Announcement (BAA) as contemplated in Federal Acquisition Regulation (FAR) 6.102(d)(2) and 35.016 and 2 CFR § 200.203. Any resultant award negotiations will follow all pertinent law and regulation, and any negotiations and/or awards for procurement contracts will use procedures under FAR 15.4, Contract Pricing, as specified in the BAA.

OVERVIEW INFORMATION:

- **Federal Agency Name** – Defense Advanced Research Projects Agency (DARPA), Biological Technologies Office
- **Funding Opportunity Title** – CoasterChase
- **Announcement Type –** Initial Announcement
- **Funding Opportunity Number –** HR001125S0014
- **Assistance Listing Number:** 12.910
- **Dates/Time - All Times are Eastern Time Zone (ET)**
    - Posting Date: June 26, 2025
    - Industry Day: **July 7, 2025**
    - Proposal Abstract Due Date: **July 24, 2025 at 4:00 pm**
    - Proposal Due Date: August 28, 2025
- **Anticipated individual awards** - DARPA anticipates multiple awards with a total program funding up to $25 Million, subject to the availability of funds. Proposed efforts should be appropriately scaled.

Types of instruments that may be awarded - Procurement Contract, Cooperative Agreement, Other Transaction Agreement for Research (OT-R), or Other Transaction Agreement for Prototype (OT-P).

- **NAICS Code**: 541714
- **Agency contact**

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SECTION I: FUNDING OPPORTUNITY DESCRIPTION

The Defense Advanced Research Projects Agency (DARPA) is soliciting innovative proposals that leverage a novel understanding of the enteric nervous system as well as emerging neuromodulation technologies to selectively target neurons in the small intestine and alter the body's stress response. The CoasterChase program aims to develop a multimodal, ingestible, sensing and stimulation platform for use in monitoring and modulating biomarkers of acute stress from within the small intestine. Proposed research should investigate innovative approaches that enable revolutionary advances in enteric neuromodulation and sensing, ingestible electronics, and modulation of the stress response. Specifically excluded is research that primarily results in evolutionary improvements to the existing state of practice.

Background:

Warfighters under stress make poor decisions with immediate and lasting consequences. Excessive stimulation of the nervous system under perceived threats can lead to long-term trauma in the warfighter such as post-traumatic stress disorder (PTSD). On the other end of the spectrum, a lack of activation of the "fight or flight" response can lead to a decrease in effective reactions to high-demand combat scenarios, ultimately resulting in poor performance. The CoasterChase program aims to 1) develop a dynamic platform to examine whether stimulation of enteric neurons in the small intestine can change circulating concentrations of neuropeptide Y (NPY) and cortisol in a way that modulates the stress response; and 2) explore, both acutely and chronically, the upper and lower bounds of cortisol and NPY concentration and their hypothesized relationship in response to enteric stimulation. Broader impact of the proposed work potentially includes overcoming deficits in memory formation and retention by optimizing the stress response[1,2], maintaining peak immunological defenses in the face of stress[3]; and regulating metabolism for optimal calorie conservation in a food-poor environment[3].

Distinct neuronal populations in the hypothalamus and the enteric nervous system release the NPY molecule, which has been implicated in stress resilience[4]. In the paraventricular nucleus (PVN) of the hypothalamus, NPY triggers the release of corticotropin releasing hormone (CRH). From there, CRH travels down the portal veins of the pituitary stalk to the pituitary proper, triggering the release of adrenocorticotropic hormone (ACTH). Finally, ACTH travels through the bloodstream to the kidneys, where it triggers the release of cortisol from the adrenal glands. This encompasses the hypothalamic-pituitary-adrenal (HPA) axis, which regulates the body's response to stress in all its gradations, and with all its consequences. Cortisol is the primary stress hormone in the body and is directly regulated by NPY production in the myenteric and

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[1] "The stressed hippocampus, synaptic plasticity and lost memories | Nature Reviews Neuroscience." Accessed: Mar. 13, 2025. [Online]. Available: https://www.nature.com/articles/nrn849.

[2] D. M. Diamond, A. M. Campbell, C. R. Park, J. Halonen, and P. R. Zoladz, "The Temporal Dynamics Model of Emotional Memory Processing: A Synthesis on the Neurobiological Basis of Stress-Induced Amnesia, Flashbulb and Traumatic Memories, and the Yerkes-Dodson Law," *Neural Plast.*, vol. 2007, no. 1, p. 060803, 2007, doi: 10.1155/2007/60803.

[3] J. A. Rusch, B. T. Layden, and L. R. Dugas, "Signalling cognition: the gut microbiota and hypothalamic-pituitary-adrenal axis," *Front. Endocrinol.*, vol. 14, Jun. 2023, doi: 10.3389/fendo.2023.1130689.

[4] Hirsch D and Zukowska Z. NPY and Stress 30 Years Later: The Peripheral View. Cell Mol Neurobiol. 2012 Jan 24;32(5):645–659. doi: 10.1007/s10571-011-9793-z.

sub-mucosal plexi of the enteric nervous system surrounding the small intestine. Notionally, controlling the enteric nervous system enables control over the systemic stress response that lies downstream of it.

Current state-of-the-art therapies (including cervical or trans-auricular vagus nerve stimulation, pharmaceutical approaches, and cognitive behavioral therapies) [5, 6, 7, 8, 9, 10, 11, 12] addressing the modulation of the HPA axis and its stress response lack specificity, are slow or variable to act, and are reactive rather than prophylactic. Furthermore, attempts to modulate the HPA axis's stress response - specifically through stimulating the production of signaling molecules central to this response (e.g. cortisol, NPY) - from within the enteric nervous system have not been recorded in the literature.

Program Description:

CoasterChase seeks to understand whether stimulating neurons in the enteric nervous system (specifically the small intestine) can modulate the warfighter stress response under extreme conditions, improving training recall and decision-making in the moment and mitigating the development of PTSD in the long term. To investigate this hypothesis, the CoasterChase program aims to develop and implement a novel platform for real-time monitoring and modulation of peripheral neuropeptides underlying responses to acute stress. Program efforts will entail the development of an ingestible system that persists in the small intestine for at least five days, detects changes in concentrations of stress-related biomarkers in the small intestine, and stimulates enteric neurons to release NPY, which has been implicated in stress resilience. *In vivo* animal work performed in CoasterChase will be designed to inform the ingestible platform design while providing new insight on the poorly understood enteric nervous system – such as its relation to behavioral and physiological biomarkers of stress. CoasterChase technologies and results are anticipated to provide a foundation for future device iterations, subject to future funding decisions. Simultaneously, CoasterChase will enable translation to a potential first-in-

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[5] Li S, Wang Y, Gao G, Guo X, Zhang Y, Zhang Z, Wang Y, Zhang J, Wang J, Li L, Yang Y, Rong P. Transcutaneous Auricular Vagus Nerve Stimulation at 20 Hz Improves Depression-Like Behaviors and Down-Regulates the Hyperactivity of HPA Axis in Chronic Unpredictable Mild Stress Model Rats. Front Neurosci. 2020 Jul 15.

[6] Evanson NK, Tasker JG, Hill MN, Hillard CJ, Herman JP. Fast feedback inhibition of the HPA axis by glucocorticoids is mediated by endocannabinoid signaling. Endocrinology. 2010 Oct

[7] O'Keane V, Dinan TG, Scott L, Corcoran C. Changes in hypothalamic-pituitary-adrenal axis measures after vagus nerve stimulation therapy in chronic depression. Biol Psychiatry. 2005 Dec 15

[8] Clayton AH, Lasser R, Parikh SV, Iosifescu DV, Jung J, Kotecha M, Forrestal F, Jonas J, Kanes SJ, Doherty J. Zuranolone for the Treatment of Adults With Major Depressive Disorder: A Randomized, Placebo-Controlled Phase 3 Trial. Am J Psychiatry. 2023 Sep 1

[9] Clayton AH, Lasser R, Parikh SV, Iosifescu DV, Jung J, Kotecha M, Forrestal F, Jonas J, Kanes SJ, Doherty J. Zuranolone for the Treatment of Adults With Major Depressive Disorder: A Randomized, Placebo-Controlled Phase 3 Trial. Am J Psychiatry. 2023 Sep 1

[10] Clevenger SS, Malhotra D, Dang J, Vanle B, IsHak WW. The role of selective serotonin reuptake inhibitors in preventing relapse of major depressive disorder. Ther Adv Psychopharmacol. 2018 Jan

[11] Packard AE, Egan AE, Ulrich-Lai YM. HPA Axis Interactions with Behavioral Systems. Compr Physiol. 2016 Sep 15

[12] de Jonge M, Bockting CLH, Kikkert MJ, van Dijk MK, van Schaik DJF, Peen J, Hollon SD, Dekker JJM. Preventive cognitive therapy versus care as usual in cognitive behavioral therapy responders: A randomized controlled trial. J Consult Clin Psychol. 2019 Jun

human study aimed at real-time tuning of the stress response in the warfighter to improve decision making under stress and possibly reduce the incidence of negative long-term effects such as PTSD. The CoasterChase program will address two equally important Functional Areas (FAs):

FA1 will explore the effects of modulating neuronal populations of the myenteric and sub-mucosal plexi within the small intestine (known to be central to the enteric nervous system)[13] with the goal of modulating the HPA axis and mitigating deleterious effects of acute stress in animal models.

FA2 will develop an ingestible platform to examine the hypothesis that stimulation of enteric neurons in the small intestine can change circulating peripheral concentrations of hormones such as NPY and cortisol to modulate the body's stress response in a controllable manner.

Program Structure and Scope:

CoasterChase is planned as a 24-month program with a 12-month Phase 1 Base Period and 12-month Phase 2 Option Period.

Phase 1 will explore the **acute** changes in cortisol and NPY localized in the small intestine, as well as in circulation, in response to dynamic stimulation, Phase 1 will also include the design and development of two ingestible platforms: one to modulate enteric neurons in the small intestine using multiple stimulus modalities, and the second to sense biomarkers of interest (e.g. cortisol and NPY). Additional biomarkers beyond those two may be considered, as well, given appropriate justification.

Phase 2 will comprise the integration of the ingestible platforms into a single capsule form factor, with parallel experiments to examine how the neuromodulation platform and paradigms developed in Phase 1 change the stress response at a behavioral/cognitive performance level in a large-animal model (excluding non-human primates/cats/dogs) chronically (over a longer period of time).

Performers will pursue experimental designs to examine how using this dynamic platform modulates the HPA axis and mitigates deleterious effects of acute stress in large-animal (barring non-human primate, cat, and dog) models (both acutely and chronically). At the completion of CoasterChase, DARPA anticipates transitioning the technology to one or more government partners to perform first-in-human studies to assess the ability to modulate the HPA axis from within the enteric nervous system across multiple test environments.

Performers will be conducting Animal Subjects Research (ASR) and must plan for initial approvals of experimental protocols by their Institutional Animal Care and Use Committee (IACUC) and secondary review by the U.S. Army Medical Research & Development Command's (USAMRDC) Animal Care and Use Review Office (ACURO). No ASR data collection can begin prior to ACURO approval. More information about DARPA regulations on ASR can be found at Human Subjects and Animal Subjects Research | DARPA.

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[13] Kulkarni S, Ganz J, Bayrer J, Becker L, Bogunovic M, Rao M. Advances in Enteric Neurobiology: The "Brain" in the Gut in Health and Disease. J Neurosci. 2018 Oct 31;38(44):9346-9354. doi: 10.1523/JNEUROSCI.1663-18.2018. PMID: 30381426; PMCID: PMC6209840.

Key Functional Areas:

CoasterChase performer teams will address both key FAs within each team, and will iteratively leverage progress in one FA to inform development of the other. These FAs, detailed below, are intended to demonstrate an ability to selectively neuromodulate the HPA axis from the enteric nervous system and evaluate the effects of this neuromodulation on behavioral outcomes following episodes of acute stress in large-animal models.

In order to explore enteric neuronal targets, their selective stimulation, and modulation of biomarkers of stress in FA1, performers will:

- explore the link between neuromodulation of the enteric nervous system (electrical and/or mechanical) and hormone production.
- provide quantifiable direct or indirect control the body's systemic stress response (for example as measured through cortisol) via enteric neuromodulation (for example of NPY release).
- develop methods to sense endocrine biomarkers of stress (for example from one or more of: cortisol, NPY, adrenocorticotropin hormone, corticotropin-releasing hormone, vasopressin, and so on) from within the small intestine lumen.
- measure off-target effects from stimulation of unintended enteric neuronal populations (for example those that release serotonin or GLP-1) to demonstrate both specificity and selectivity of the proposed neuromodulation approach.
- conduct acute *in vivo* behavioral studies that measure performance under stress (for example of one or more of: cognitive measures of attention, alertness, processing speed, response selection and inhibition, or working memory), with and without neuromodulation.
- conduct chronic (long-term) *in vivo* behavioral studies using the FA2 platform, and measure performance under stress, with and without neuromodulation.
- explore the relationship between neuromodulation and stress in populations with: 1) demographic differences (e.g. age, sex); 2) situational differences (variations in stress protocols); and 3) temporal differences (e.g. circadian rhythm).

In order to develop a dynamic platform capable of enteric biomarker sensing and stimulation in an ingestible, persistent form factor, FA2 performers will:

- explore the integration and miniaturization of neuromodulation and sensing technologies within a single ingestible form factor.
- develop a method of biomarker sensing for the biomarker identified in FA1 (for example NPY or cortisol).
- compare developed biomarker sensing to gold-standard approaches of sensing the same biomarker (for example from intravascular or interstitial approaches).
- identify and develop a minimum of two distinct stimulation modalities (both electrical and/or mechanical) to modulate the systemic stress response as described in FA1.

- integrate the two stimulation modalities onto a single, ingestible platform.
- design the platform such that stimulation can be simultaneously delivered over a physiologically relevant extent of the small intestine (i.e. show control of sufficient small intestine surface area to quantifiably modulate the systemic stress response).
- integrate biomarker sensing and neuromodulation into a single platform for closed-loop control.
- develop a closed-loop control algorithm leveraging the proposed sensing and neuromodulation approaches.
- constrain the integrated platform to meet the size, weight, and other metrics in Table 4.

Program Schedule:

CoasterChase is planned as a 24-month program with a 12-month Phase 1 Base Period and 12-month Phase 2 Option Period with two parallel functional areas (FAs). Continuation into Phase 2 is subject to performance and availability of funds. The schedule and structure of the program are shown below (Figure 1). A target start date of January 2026 may be assumed for planning purposes.

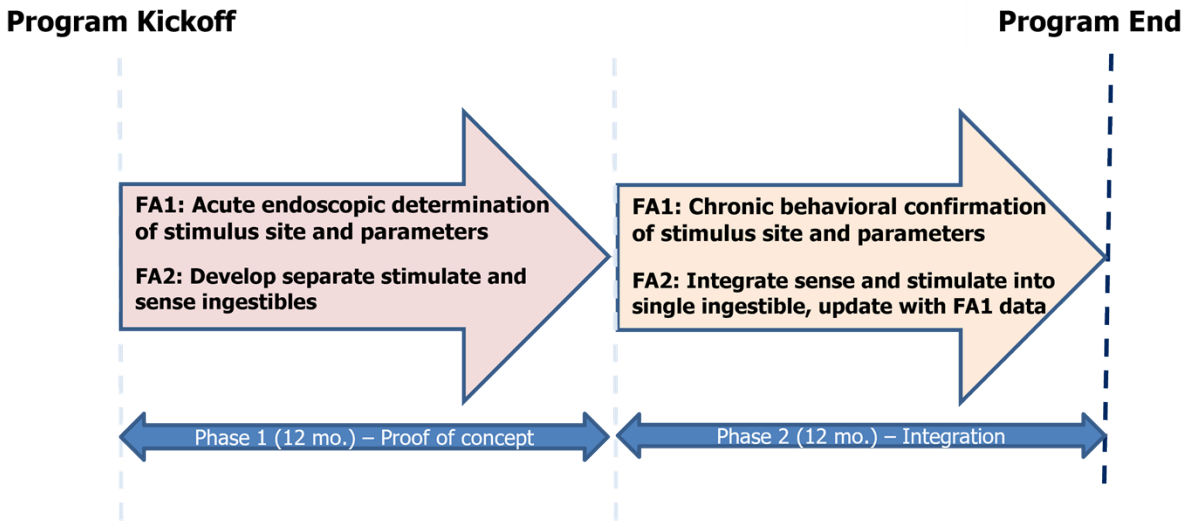

Figure 1. CoasterChase schedule and structure

CoasterChase Phase 1 will focus on exploring enteric targets and their selective stimulation, sensing subsequently produced biomarkers of HPA activation as they relate to the stress response, and the development of ingestible hardware for sensing and stimulation. Phase 2 will focus on refining and subsequently integrating the sensing and stimulating modalities onto a single ingestible platform and using this platform to perform large-animal (excluding non-human primates/cats/dogs) behavioral studies of HPA axis modulation.

It is expected that CoasterChase will require strong teaming efforts to successfully innovate and integrate multidisciplinary critical technologies necessary to meet all of the metrics of the program. Because several different technologies must ultimately work together to prototype an ingestible sensing and stimulation platform, all teams are strongly encouraged to identify a Project Manager/Integrator to serve as the primary point of contact to communicate with the

DARPA Program Manager and Contracting Officer's Representative, coordinate the effort across co-performers, vendors, and subcontractor teams, organize regular performer meetings or discussions, facilitate data sharing, and ensure timely completion of milestones and deliverables.

Program Milestones and Metrics

CoasterChase milestones and metrics are focused on understanding the effect of enteric neuromodulation on the stress response and developing a sensing/stimulating platform to allow for interrogation of these effects. The program's milestones, metrics, and deliverables are organized by functional area and phase into the following tables (1-4 below). Milestones are checkpoints within a task that mark the completion of a stage of said task. Metrics are measures of quantitative assessment used for assessing and tracking progress throughout the program. Deliverables are tangible products of the program development process as tasks progress.

As FA1 is highly exploratory and involves more fundamental science, FA1 program deliverables are tied to meeting milestones, which are less quantifiable than metrics. FA2, which is highly quantifiable due to the hardware development, has deliverables that are tied to meeting metrics. Performer progress will be measured against the milestones and metrics shown in the following tables.

Table 1 - FA1 Phase 1 Milestones and Deliverables

Program Month	Milestone	Deliverable(s)
0	Project kickoff meeting	• Briefing package to include team organization, technical approach, research goals, expected results, schedule, and risk mitigation strategies
2	Submitted animal use protocols (IACUC and ACURO)	• Milestone report detailing progress of acute studies • Copy of submitted IACUC and ACURO protocols
4	Identification and stimulation sensitivity results of targeted intestinal neurons for 2 stimulation modalities	• Milestone report detailing results of studies and progress towards goals **(should detail plan to incorporate findings into platform design)** • Quantitative results (data/charts/graphs) evaluating targeted neuron responses to stimulation
6	Acute, *in vivo* study of neuromodulation-stress relationship for segment of small intestine	• Milestone report detailing results of *in vivo* studies and progress towards goals **(should detail plan to incorporate findings into platform design)** • Input-output curve for neuromodulation-stress relationship as a function of stimulation dosage for 1 cm of small intestine (2 modalities)

11	Acute, *in vivo* study of neuromodulation-stress relationship for large portion of small intestine	• Milestone report detailing results of *in vivo* studies and progress towards goals (**should detail plan to incorporate findings into platform design)** • Input-output curve for neuromodulation-stress relationship as a function of stimulation dosage for up to 20 cm of small intestine (2 modalities) • Defined range of intestinal length activation needed to produce significant changes to targeted biomarker
12*	Finalized *in vivo* sensing (local and circulating) study of biomarker concentration dynamics as a function of stimulation	• Milestone report component detailing results of sensing studies (**should detail plan to incorporate findings into platform design)** • Circulating and local concentration dynamics for neuromodulation-stress relationship during stimulation
12*	Finalization of induced stress protocol and cognitive performance paradigm for chronic *in vivo* animal subject research	• Milestone report component detailing plan to use *in vivo* data to refine sensing and stimulating platform • Submission of proposed cognitive performance ASR to ACURO

*Milestones, metrics, and deliverables with the same program due date may be combined in reporting but are separated in the tables for visualization purposes.

Table 2 - FA2 Phase 1 Metrics and Deliverables

Program Month	Metrics	Deliverable(s)
3	Demonstrate ability to electrically stimulate within the following ranges: • 1 Hz – 10 kHz • 100 µA – 5 mA	• Metric report detailing progress on designing stimulation platform • Test results from benchtop stimulation circuitry with capability to meet electrical stimulation range in metric
5	Demonstrate ability to mechanically stimulate within the following ranges: • 1 Hz – 300 Hz • 2 µm - 20 µm *If proposers wish to use a different second modality, an appropriate range with literature/data justification for	• Milestone report component detailing progress on designing stimulation platform • Test results from benchtop stimulation circuitry with capability to meet mechanical stimulation range in metric

	that modality must be included in the proposal.	
5	Demonstrate ability to sense identified biomarkers with the following metrics: • 1 pg/mL sensitivity • 1- 100 pg range • 5 min. refresh rate	• Milestone report component detailing progress on designing sensing platform • Test results from benchtop sensing study with capability to meet metrics
10	Combine stimulation modalities into a single, ingestible capsule form factor	• Milestone report component detailing progress towards integration stimulation platform and meeting form factor • Demo of pill capsule stimulation platform
10	Conform sensing modality into a single, ingestible capsule form factor	• Milestone report component detailing progress towards encapsulating sensing platform and meeting form factor • Demo of pill capsule sensing platform
12	Fabricate multiple (> 4) stimulation and sensing capsules for chronic behavioral testing in Phase 2	• Milestone report component detailing fabrication and progress towards program goals • Circulating and local concentration dynamics for identified biomarkers during stimulation (to accompany the *in vivo* studies)

Table 3 – FA1 Phase 2 Milestones and Deliverables

Program Month	Milestone	Deliverable(s)
16	Completion of an *in vivo** study using the stimulation and sensing platforms (paired with gold-standard sampling of circulating biomarker(s)) to explore cognitive performance during neuromodulation	• Milestone report detailing cognitive performance scores across multiple stimulated biomarker concentrations • Plots/data/diagrams of cortisol vs. cognitive performance vs. stimulation
18	Completion of an *in vivo* study exploring cognitive performance as biomarker(s) are modulated, with the addition of: • 1 demographic variable (e.g. age, sex)	• Milestone report detailing cognitive performance scores across multiple stimulated biomarker concentrations • Plots/data/diagrams of cortisol vs. cognitive performance vs. stimulation
20	Completion of an *in vivo* study exploring cognitive performance as biomarker(s) are modulated, with the addition of:	• Milestone report detailing cognitive performance scores across multiple stimulated biomarker concentrations • Plots/data/diagrams of cortisol vs. cognitive performance vs. stimulation

	• 1 situational variable (e.g. water-restriction, predator-presence)	
22	Completion of an *in vivo* study exploring cognitive performance as biomarker(s) are modulated, with the addition of: • 1 innate variable (e.g. circadian rhythm)	• Milestone report detailing cognitive performance scores across multiple stimulated biomarker concentrations • Plots/data/diagrams of cortisol vs. cognitive performance vs. stimulation
23	Completion of an *in vivo* study exploring cognitive performance as biomarker(s) are modulated, with the addition of: • 2 or more demographic, situational, or innate variables.	• Milestone report detailing cognitive performance scores across multiple stimulated biomarker concentrations • Plots/data/diagrams of cortisol vs. cognitive performance vs. stimulation
24	Completion of persistence study in the small intestine for 5 days in large-animal model (see metrics in Table 4)	• Milestone report component describing results of persistence study • Submission of data/figures/plots summarizing the persistence study results
24	Participation in at least one informational pre-Investigational New Device (IDE) meeting with the U.S. Food and Drug Administration (FDA)	• Milestone report component detailing final results towards Phase 2 goals and milestones/deliverables. • Meeting minutes and report from the FDA informational meeting

*All *in vivo* behavioral experiments must be completed in a large-animal model (excluding non-human primates/cats/dogs) with a GI tract analogous to that of a human.

Table 4 – FA2 Phase 2 Metrics and Deliverables

Program Month	Metrics	Deliverable(s)
16	Demonstrate performance of sensing and stimulation platforms in simulated GI tract conditions: • Withstands ~1000 cycles/day at 50g/cm2 • Stable in gastric fluid facsimile (pH < 3.5) 1 day	• Metric report component detailing progress towards reaching performance goals • Test results (data/plots/figures) from benchtop testing to reach performance in simulated GI conditions as described in metric
20	Demonstrate maintenance of cortisol concentrations at the following values using stimulation: • Total cortisol: ± 10 % from desired operating point of 200-500 nmol/L	• Milestone report detailing experimental progress towards maintenance of cortisol concentration levels • Data/plots/figures demonstrating adherence of cortisol concentrations to those described in metric

	• Free cortisol: ± 10 % from desired operating point of 0-30 nmol/L	• Data/plots/figures of stimulation paradigms accompanying above
22	Complete integration of the capsule platform with 2 stimulation modalities and 1 sensing modality adhering to following parameters: • Diameter < 1.3 cm • Weight: < 5 g	• Milestone report detailing progress on integrating and encapsulating sensing/stimulating platform • Demo of fully integrated platform capsule
24	Demonstrate persistence of sensing and stimulation platform in chronic animal preparation: • Device persistent **in small intestine** for minimum 5 days	• Metric report detailing progress towards reaching persistence goals • Test results (data/plots/figures) from benchtop persistence testing to reach longitudinal metric
25	Demonstrate closed-loop control of the dynamic platform using sensing inputs to drive stimulation outputs	• Metric report component detailing progress towards reaching closed-loop control goals. • Test results (data/plots/figures) showing results from closed-loop control testing.

Meetings and Travel

To ensure the dissemination of program developments, CoasterChase will conduct annual Program Review meetings (for planning purposes assume those meetings will take place in Arlington, VA). Performers should anticipate at least one site visit during the period of performance by the DARPA Program Manager – during which they will have the opportunity to demonstrate progress on the technology and science as they finish contractual milestones and deliverables. Additionally, regular teleconference meetings will be scheduled with the government team for technical status reporting as well as identification of problems and risk mitigation.

Performers will be expected to provide, at a minimum, the following deliverables:

- Periodic progress reports, including both technical and financial updates. Technical updates can be the same as the presentations used for the monthly teleconferences – so long as the level of technical detail is high enough for the evaluation of progress against metrics and milestones.
- All deliverables listed in Tables 1-4.
- Other negotiated deliverables specific to the objectives of individual efforts. These may include registered reports; submissions of animal subject research protocols (e.g. IACUC and ACURO), publications, conference abstracts, design documents, modeling/simulation data and results, and summary figures.

Successful proposals will succinctly and explicitly explain:

- All fundamental hypotheses to be tested (e.g. enteric neuronal targets for NPY/stress biomarker production, selective enteric stimulation of said targets, biomarker correlation to stress response, etc...); these explanations must include underlying assumptions, expected outcomes, and strategies for risk mitigation.
- The basis (from the peer-reviewed literature) underlying how they will identify enteric neuronal targets, and address how their chosen stimulus modalities (minimum of two – electrical must be at least one of these) and paradigm designs will allow for selective control over these neuronal targets.
- Theoretical, physiological, and neuroscience basis for the proposed methods of neuromodulation using the stimulus modalities, including the underlying mechanisms and associated risks.
- The measurement and analysis of cortisol and NPY as they relate to one another in the context of the dynamic stress response (i.e., before, during, and following stress), as well as analysis of associations between the concentrations of these molecules in the small intestine vs. in circulation; if including further biomarkers, demonstrate a link between the modulation of these in the enteric nervous system and the stress response.
- The measurement and analysis of biomarkers to demonstrate a lack of off-target activation of unintended neuronal populations.
- Experimental design, including power analyses, for the ASR, including but not limited to the designs for the stress induction protocols, the cognitive performance studies, the cognitive performance studies introducing demographic, situational, and innate variables, and performance testing of the platform in environments analogous to conditions in the gastrointestinal tract (see Table 4 for metrics).
- Data analysis approaches corresponding to the proposed ASR experimental design.
- How the proposed methods are able to meet or exceed the program's metrics (include literature-backed explanations, data, calculations, and/or prior art).
- Specific plans, including cost, time estimates, and teaming composition to address the two key functional areas outlined in the program description.
- Identified risks to successful execution and fulfillment of program goals (using provided template format) and proposed strategies for mitigating these.
- Choice of large-animal model (excluding non-human primates/cats/dogs) and justify the selection of this animal model for the proposed studies, particularly in the context of translatability to humans. Multiple large animal models will be considered.
- Methodology to minimize confounding inputs from the environment, as well as consideration of sex- and age-related response differences to stress challenges.
- Plan to meet and/or exceed program metrics and milestones; these claims must be justified with literature-based explanations, data, and projections.

- How experimental approach is anticipated to lead to quantifiable changes in cognitive performance resulting from changes in HPA axis activation following acute stress.
- Anticipated impact of results on the understanding of the enteric nervous system; specifically, how the results will advance the field's knowledge of neuromodulation from within the gut and its relationship to the stress response.
- Anticipated design of closed-loop control circuit and how inputs from the sensing modality will be used to inform and modify stimulation outputs on the platform.
- How prior research was leveraged to maximize the impact and value of the requested funding.
- Demonstrate a thoughtful integration of existing research to avoid duplication and enhance effectiveness.

Successful proposals will not:

- Simply reiterate the justifications or background information provided in the BAA.
- Develop a platform that depends on surgical approaches to successfully localize the device in the small intestine.
- Include research in humans or non-human primates/cats/dogs.
- Include pharmacological approaches or approaches that require delivery of genetic material (e.g., optogenetic).
- Reflect cost strategies intended to artificially enhance competitiveness—such as minimizing technical risk, limiting innovation, or relying primarily on junior personnel.

Proposals that only address one FA or do not propose an integrated sensing and stimulation platform will be deemed non-conforming and not considered for further review.

SECTION II: EVALUATION CRITERIA

Proposals will be evaluated using the following criteria listed in **descending order of importance**. Overall Scientific and Technical Merit; Team Capabilities and Expertise; Potential Contribution and Relevance to the DARPA Mission; Cost Realism and Schedule.

- **Overall Scientific and Technical Merit**: The proposed technical approach is innovative, feasible, achievable, and complete. The proposed technical team has the expertise and experience to accomplish the proposed tasks. 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.
- **Team Capabilities and Expertise**: Proposal clearly outlines program structure to address integration of both FAs. Proposal identifies a lead integrator with a proven track record of managing and integrating disparate technologies and research. 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 sponsors.
- **Potential Contribution and Relevance to the DARPA Mission**: The potential contributions of the proposed effort bolster the national security technology base and support DARPA's mission to make pivotal early technology investments that create or prevent technological surprise.

  Cost Realism and Schedule: The proposed costs are realistic for the technical and management approach and accurately reflect the technical goals and objectives of the solicitation. The proposed costs are consistent with the proposer's Statement of Work and reflect a sufficient understanding of the costs and level of effort needed to successfully accomplish the proposed technical approach. The costs for the prime proposer and proposed sub-awardees are substantiated by the details provided in the proposal (e.g., the type and number of labor hours proposed per task, the types and quantities of materials, equipment and fabrication costs, travel and any other applicable costs and the basis for the estimates).

  Unless otherwise specified in this announcement, for additional information on how DARPA reviews and evaluates proposals through the Scientific Review Process, please visit: HYPERLINK "https://www.darpa.mil/work-with-us/proposer-instructions" \o "https://www.darpa.mil/work-with-us/proposer-instructions" \t "_blank" Proposer Instructions: General Terms and Conditions.

SECTION III: SUBMISSION INFORMATION

- This announcement allows for multiple award instrument types to be awarded to include Procurement Contracts, Other Transaction Agreement for Research (OT-R), Other Transaction Agreement for Prototype (OT-P), or Cooperative Agreements. Some award instrument types have specific cost-sharing requirements. The following websites are incorporated by reference and contain additional information regarding overall proposer instructions, general terms and conditions, and each specific award instrument type.

  Proposers must review the following links:

  - **Proposer Instructions: General Terms and Conditions**: https://www.darpa.mil/work-with-us/proposer-instructions
  - **Procurement Contracts**: https://www.darpa.mil/work-with-us/procurement-contracts
  - **Cooperative Agreements**: https://www.darpa.mil/work-with-us/grant-cooperative-agreements
  - **Other Transactions**: https://www.darpa.mil/work-with-us/other-transaction-agreements

  - This announcement contains an abstract phase. Abstracts are strongly encouraged but not required. Abstracts are due **July 24, 2025 at 4:00 p.m.** as stated in the Overview section. Additional instructions for abstract submission are contained within **Attachments A and B**.

  - Full proposals are due: August 28, 2025 at 4:00 PM as stated in the Overview section. **Attachments B, C, D, E, and F** contain specific instructions and templates and constitute a full proposal submission.

- **BAA Attachments**:
  - **(required) Attachment A**: Abstract Instructions and Template
  - **(required) Attachment B**: Proposal Summary Slide Template
  - **(required) Attachment C**: Proposal Instructions and Volume I Template (Technical and Management)
  - **(required) Attachment D**: Proposal Instructions and Volume II Template (Cost)
  - **(required) Attachment E**: Streamlined Cost Proposal Spreadsheet
  - **(required) Attachment F**: Risk Assessment Matrix Instructions and Template

SECTION IV: SPECIAL CONSIDERATIONS

- This announcement, stated attachments, and websites incorporated by reference constitute the entire solicitation. In the event of a discrepancy between the announcement, attachments, or websites, the announcement takes precedence.
- **Notwithstanding any prior Department of Defense (DoD) guidance or memoranda regarding indirect cost rate limitations, a resultant cooperative agreement award will be issued in compliance with the Temporary Restraining Order (TRO) entered on June 17, 2025, in *Association of American Universities v. Department of Defense*, No. 25-cv-11740 (D. Mass.). Accordingly, the indirect cost rate applied to a resultant cooperative agreement award will reflect the institution's current negotiated rate and does not incorporate the 15% indirect cost rate cap outlined in the Department's memoranda dated May 14, 2025. However, if the TRO is lifted, dissolved, or otherwise modified by court order, and such order permits the implementation of the Rate Cap Policy, the policies of the memos (Rate Cap Policy Memo dated May 14, 2025 and OUSD (R&E's) Implementation Memo dated June 12 2025) will be applicable for the entirety of the resultant cooperative agreement award.**
- As of the date of publication of this solicitation, all proposal submissions are anticipated to be unclassified.
- All responsible sources capable of satisfying the Government's needs, including both U.S. and non-U.S. sources, may submit a proposal that shall be considered by DARPA. Historically Black Colleges and Universities, Small Businesses, Small Disadvantaged Businesses and Minority Institutions are encouraged to submit proposals and join others in submitting proposals; however, no portion of this announcement will be set aside for these organizations' participation due to the impracticality of reserving discrete or severable areas of this research for exclusive competition among these entities. Non-U.S. organizations and/or individuals 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.
- DARPA encourages technical solutions from all responsible sources capable of satisfying the government's needs. To ensure fair competition across the ecosystem, DARPA prohibits contractors/performers from concurrently providing Systems Engineering Technical Assistance (SETA), Advisory and Assistance Services (A&AS), or similar support services and being a technical performer, unless the DARPA Deputy Director grants a written waiver. DARPA extends this prohibition to University-Affiliated Research Centers (UARCs) and Federally Funded Research and Development Centers (FFRDCs) including National Labs, who as a result of their specialized expertise and areas of competencies, are able to accomplish integral tasks that cannot be met by government or contractor resources. Therefore, these entities are highly discouraged from proposing against this solicitation as award to a UARC or FFRDC will only be made by exception. UARCs and FFRDCs interested in this solicitation, either as a prime or a subcontractor, should contact the Agency Point of Contact (POC) listed in the Overview section prior to the proposal (or abstract) due date to discuss potential participation as part of the government team or eligibility as a technical performer.

- As of the date of publication of this solicitation, the Government expects that program goals as described herein may be met by proposers intending to perform fundamental research and does not anticipate applying publication restrictions of any kind to individual awards for fundamental research that may result from this solicitation. Notwithstanding this statement of expectation, the Government is not prohibited from considering and selecting research proposals that, while perhaps not qualifying as fundamental research under the foregoing definition, still meet the solicitation criteria for submissions. If proposals are selected for award that offer other than a fundamental research solution, the Government will either work with the proposer to modify the proposed statement of work to bring the research back into line with fundamental research or else the proposer will agree to restrictions in order to receive an award. For additional information on fundamental research, please visit Proposer Instructions: General Terms and Conditions.
- Proposers should indicate in their proposal whether they believe the scope of the research included in their proposal is fundamental or not. While proposers should clearly explain the intended results of their research, the Government shall have sole discretion to determine whether the proposed research shall be considered fundamental and to select the award instrument type. Appropriate language will be included in resultant awards for non-fundamental research to prescribe publication requirements and other restrictions, as appropriate. This language can be found at http://www.darpa.mil/work-with-us/additional-baa.
- For certain research projects, it may be possible that although the research to be performed by a potential awardee is non-fundamental research, its proposed sub-awardee's effort may be fundamental research. It is also possible that the research performed by a potential awardee is fundamental research while its proposed sub-awardee's effort may be non-fundamental research. In all cases, it is the potential awardee's responsibility to explain in its proposal which proposed efforts are fundamental research and why the proposed efforts should be considered fundamental research.
- DARPA's Fundamental Research Risk-Based Security Review Process (formerly CFIP) is an adaptive risk management security program designed to help protect the critical technology and performer intellectual property associated with DARPA's research projects by identifying the possible vectors of undue foreign influence. DARPA will create risk assessments of all proposed senior/key personnel selected for negotiation of a fundamental research grant or cooperative agreement award. The DARPA risk assessment process will be conducted separately from the DARPA scientific review process and adjudicated prior to final award. For additional information on this process, please visit Proposer Instructions: Grants/Cooperative Agreements.
- Proposals could potentially include Human Subjects Research (HSR) and/or Animal Use. Proposers that anticipate involving human subjects or animals in the proposed research must comply with the approval procedures detailed at https://www.darpa.mil/work-with-us/humanresearch to include providing the information specified therein as required for proposal submission.
- The APEX Accelerators program, formerly known as the Procurement Technical Assistance Program (PTAP), focuses on building strong, sustainable, and resilient U.S. supply chains by

assisting a wide range of businesses that pursue and perform under contracts with the DoD, other federal agencies, state and local governments, and government prime contractors. See www.apexaccelerators.us/ for more information.

APEX Accelerators helps businesses:
o Complete registration with a wide range of databases necessary for them to participate in the government marketplace (e.g., SAM).
o Identify which agencies and offices may need their products or services and how to connect with buying agencies and offices.
o Determine whether they are ready for government opportunities and how to position themselves to succeed.
o Navigate solicitations and potential funding opportunities.
o Receive notifications of government contract opportunities on a regular basis.
o Network with buying officers, prime contractors, and other businesses.
o Resolve performance issues and prepare for audit, only if the service is needed, after receiving an award.

- Project Spectrum is a nonprofit effort funded by the DoD Office of Small Business Programs to help educate the Defense Industrial Base (DIB) on compliance. Project Spectrum is vendor-neutral and available to assist businesses with their cybersecurity and compliance needs. Their mission is to improve cybersecurity readiness, resilience, and compliance for small/medium-sized businesses and the federal manufacturing supply chain. Project Spectrum events and programs will enhance awareness of cybersecurity threats within the manufacturing, research and development, and knowledge-based services sectors of the industrial base. Project Spectrum will leverage strategic partnerships within and outside of the DoD to accelerate the overall cybersecurity compliance of the DIB.

  www.projectspectrum.io is a web portal that will provide resources such as individualized dashboards, a marketplace, and Pilot Program to help accelerate cybersecurity compliance.

- DARPAConnect offers free resources to potential performers to help them navigate DARPA, including “Understanding DARPA Award Vehicles and Solicitations”, “Making the Most of Proposers Days”, and “Tips for DARPA Proposal Success”. Join DARPAConnect at www.DARPAConnect.us to leverage on-demand learning and networking resources.

- DARPA has streamlined our Broad Agency Announcements and is interested in your feedback on this new format. Please send any comments to DARPAsolicitations@darpa.mil.