Emerging Health Innovators (EHI)

ARPA-H-SOL-26-150

Technical - Frequently Asked Questions (FAQs) as of 10/22/2026

Questions for this ISO should be submitted to EHI2026@ARPA-H.gov . FAQs will be updated on a continual basis through February 03, 2027. Updated content will be highlighted in green.

Topic 3: Deep Brain Stimulation for Mechanistic Sleep Exploration (Deep Sleep)

1Q: Are implanted technologies required or can novel non-invasive/minimally-invasive techniques also be responsive to TA 3?

1A: We remain open to innovative solutions, so long as they are capable of accomplishing the stated goals on mapping the deep brain circuitry and mechanisms of sleep and arousal.

2Q: Could externally delivered sensory stimulation and synchronized behavioral or physiological measurements fall within scope as supporting tools in a DBS-based mechanistic sleep study, provided the study directly addresses the topic's objectives and is led by an eligible early-career investigator?

2A: Such approaches are in scope as supporting tools, provided they are part of a study that directly addresses the stated goals of mapping the deep brain circuitry and mechanisms of sleep and arousal.

3Q: How might preclinical research fit into this vision? I.e. mapping/testing these phenomena in mice/rats? The EHI Proposers Day slide jumps straight to clinical studies, so I am wondering where preclinical science fits. Would purely preclinical research not be appropriate? I am assuming some research plan that includes both preclinical (discovery) and clinical (therapeutic optimization) might be well received but unclear from the presentation how preclinical would be viewed from the program perspective. Thank you.

3A: For topic 3, preclinical research and animal model alone efforts are not in scope. Projects will need to reach deep into the brain to get at the circuitry and establish causality in humans.

4Q: I understand that topic 3 has a high emphasis on approaches that can be used in humans. However, given the project timeline, approval for testing new approaches for

intracranial DBS and recordings in humans is unlikely. I was hoping to hear from the program officer that a proposal can focus on validation in animal models (specifically non-human primates) with a very real path towards human clinical translation. My institution has the team and infrastructure for translation to humans, but I do not believe it would be feasible to propose in-human recordings within the project timeline.

4A: For topic 3, preclinical research and animal model alone efforts are not in scope. Projects will need to reach deep into the brain to get at the circuitry and establish causality in humans.

Topic 4: CLEAR-MIND — Restoring the Brain's Drainage and Immune Balance to Enable Healing After Injury

Q1: I am considering a submission to Topic 4, CLEAR-MIND. Could you clarify whether this topic *requires* a nonhuman preclinical research component? Page 9 encourages demonstrations in preclinical models and specifies an imaging-based drainage objective "in a preclinical model undergoing immune suppression."

A1: Yes. The CLEAR-MIND objectives and base-period outcomes are built around demonstrations in a nonhuman preclinical model. These include repeatable imaging of brain drainage and immune state in the same animals across at least 3 timepoints, validation of imaging against tissue analysis, and evidence that immune suppression reduces drainage after injury. Proposals should therefore include an in vivo preclinical component that can meet these outcomes.

Proposers are welcome to add complementary approaches that strengthen the work, such as human data, human tissue, in vitro systems, or organoid models. These should support and extend the in vivo preclinical studies, not replace them.

ARPA-H does not prescribe a specific injury model or immune-suppression model. Proposers may choose the models they believe best address the topic objectives and should explain why those models are relevant to the problem and how they will support measurable progress toward the stated outcomes.

Proposers should refer to the solicitation for complete topic requirements and evaluation criteria.

Topic 6: Protecting Patient Data in Life Science AI

Q1: For topic 6, Do we need to include preliminary data?

A1: Preliminary data is not required, but it can significantly strengthen a proposal. Preliminary data can help demonstrate the proposer's relevant experience and capabilities, while also providing evidence that the proposed research concept is credible and feasible. In the absence of preliminary data, R&D proposals should still be well substantiated through other supporting evidence, such as published literature, prior technical results, or sound scientific rationale. Preliminary data is not expected to have already achieved a solution to the EHI challenge; rather, it should help illustrate why the proposed path is plausible and why the underlying hypothesis is worth pursuing. If an author has sufficient data to claim all of the requirements of the EHI are solved, further discussion and engagement is appropriate to ensure ARPA-H investments are appropriately targeted.

Topic 7: Engineering DRT for Programmable DNA Synthesis as Emerging New Medical Countermeasures (MCM) Strategy

Q1: For topic 7, please explain why the scope is limited to DRTs. Are other classes of programmable RTs of interest?

A1: DRTs were selected because they offer a unique dual value proposition: first, as a novel natural system for investigating template-free synthesis; and second, as a potentially transformative pathway for addressing antimicrobial resistance, which is well aligned with the ARPA-H mission. While DRTs may not be the only programmable RTs of scientific interest within either of these objective areas individually, they are the only class the author has identified in the current literature that appears to span both. If proposers are aware of other programmable RT classes supported by substantiated publications or compelling preliminary data that address both objectives, the EHI author would be open to considering them.

Topic 12: Innovations in Biotransport to Support Long-Term Preservation of Tissues and Organs

Q1: What duration of preservation is considered long term for this proposal (Topic 12)?

A1: Topic 12 doesn't set a minimum preservation time. The topic is about biotransport: getting protective agents into and out of complex tissues inclusive of small blood vessels, efficiently and with low toxicity. It is not about reaching a specific shelf life. Many of the high-risk ideas this topic is looking for will be partial solutions. They won't achieve long-term preservation on their own, but they could unlock the capability needed for long-term

shelf life of complex biologics. These proposals don't need to show long-term preservation outcomes. For proposals that do offer a complete preservation solution, and include tests of long-term shelf life, they must show a significant advance over the current state of the art.

Topic 13: Organs-in-Action: Next-Generation Human Tissue Platforms for Longevity, Disease, and Therapy Discovery

Q1: For Topic 13 (Organs-in-Action), would the use of animal models that closely recapitulate human physiology and disease pathophysiology also be considered within the scope of the program, or is the topic strictly focused on human-derived models?

A1: Topic 13 is intended for human-derived systems only. Proposed models must be built from human cells, tissues, or other human biological material. Proposals that use animal models to build the model, even animal models that closely mimic human physiology or disease, are outside the scope of this topic.

Q2: Regarding Topic 13 (Organs-in-Action), could you please clarify whether stem-cell-based engineered approaches such as organoids are encouraged for this topic?

A2: Yes, stem-cell-based engineering approaches, including organoids, are in scope, but proposals should go further than standalone organoids. The topic is looking for more complex systems. As stated in the solicitation, "ARPA-H seeks next generation human platforms that leap beyond organoids and lab-on-chips in order to capture multicellular tissue-level organization, patient-relevant complexity (e.g., immune, stromal, neural, vascular components) and dynamic biochemical processes**."**

Topic 15: ICAT (In-Cavity Adjuvant Therapy): Implantable Systems for Local Cancer Control at the Resection Margin

Q1: For Topic 15, would it be appropriate to focus the two-year base period on localized drug delivery in one tumor indication, with sensing and closed-loop control in the optional third year, or would you expect earlier sensing integration and validation across multiple tumor types?

A1: Yes. Topic 15 spans two technical areas, and proposals addressing either area alone are responsive to the topic. Demonstration in a single tumor indication is also acceptable, and we are looking for approaches on how the architecture would generalize to other constrained margin sites. If sensing and closed-loop control is committed in an option

year, describe how it would integrate with the delivery system developed in the base. All proposals will be evaluated against the criteria stated in the solicitation.

Q2: How rigid are the proposed solution directions? For Topic 15, would a robotic/ sensing solution to improve margin resection during surgery with the goal of resecting all margins and reducing the reliance on adjuvant therapy be considered for this topic? Or are you only looking for implantable systems?

A2: Only implantable systems are in scope and improvement of surgery techniques that help a surgeon find and remove more disease during operation, including robotic approaches and intraoperative margin assessment, are out of scope.

Q3: Must the implant release a drug? Would a non-drug implant (thermal, electrical, radiation) be responsive?

A3: The Topic area does not specify a treatment modality; delivery medium and therapeutic payload are open to innovation. The requirements are functional: a cavity-conforming, radiotranslucent, biocompatible implant delivering therapy to the peri-cavity rim with a steep, tunable dose gradient, sustained delivery preferred over a single bolus. The solution must be appropriate for a confined space and preserve function through localized treatment rather than wide-margin resection. Submissions are evaluated on technical merit and innovativeness, and Section 2.2 excludes research that primarily results in evolutionary improvements to the existing state of practice. An approach with limited pre-existing scientific basis carries greater technical risk, which proposers should address directly.

Q4: Is a proposal addressing only one of the two areas (delivery or sensing) permissible, or is closed-loop coupling strongly preferred?

A4: A single proposal that addresses delivery alone, sensing alone, or both would be permissible. Should a submission advance only one area, the proposer should address how the missing capability could later be incorporated, or why it would not be necessary.

Topic 16: Causally-Grounded Alignment for Clinical Generative Artificial Intelligence Tools

Q1: Do surgical safeguards for physical AI and robotic tools fit in the scope of Topic 16?

A1: Surgical safeguards for physical AI and robotic tools do not align with the objectives and goals of Topic 16.