INNOVATIVE SOLUTIONS OPENING

FOR

COMPREHENSIVE ORGAN SYSTEM MODELING IN OUTER SPACE

COSMOS

HEALTH SCIENCE FUTURES (HSF)

ARPA-H-SOL-26-165

16 September 2026

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1 SOLICITATION SUMMARY INFORMATION

FEDERAL AGENCY: Advanced Research Projects Agency for Health (ARPA-H)

TITLE: Comprehensive Organ System Modeling in Outer Space (COSMOS)

ANNOUNCEMENT TYPE: Innovative Solutions Opening (ISO)

ISO SOLICITATION NUMBER: ARPA-H-SOL-26-165

ISO CONTACT: COSMOS@ARPA-H.GOV

ANTICIPATED AWARDS: Multiple Other Transaction (OTs) Agreements

DATES: (All times listed are Eastern Time)

Questions & Answers (Q&A) due date: October 1, 2026, 5pm ET
Full Proposals due date: October 7, 2026, 2pm ET
ISO closing date: October 7, 2026, 2pm ET

WHERE TO SUBMIT:

Proposals: https://solutions.arpa-h.gov/Submit-Proposal/
Questions: https://solutions.arpa-h.gov/Ask-A-Question/

Registration is required to submit documents via the ARPA-H Solution Submission Portal, which may take several business days. Plan to register well in advance of the submission deadline; late submissions resulting solely from delays with registration may not be considered.

ISO PURPOSE:

ARPA-H seeks proposals from all eligible entities (see Section 8, Eligibility Information) to accomplish the COSMOS goals as described in this solicitation package. Ultimately, ARPA-H intends to negotiate multiple OT Agreements with Proposers whose proposals are most advantageous to the government.

2 INTRODUCTION TO COSMOS

2.1 BACKGROUND

2.1.1 Executive Summary

Regenerative therapeutics, those that return healthy function to damaged or otherwise compromised tissues, are an aspirational goal at present. Currently, there are no targeted therapeutics to mitigate or reverse diseases of age in the heart, brain, uterus or kidney. Current approaches frequently require 10 to 15 years to move from discovery to approved therapy. This is in part because existing preclinical models do not adequately capture the biology of human aging- the central driver of many of these diseases.

Cellular senescence, where cells no longer divide but maintain most other processes, combined with direct damage may represent important components of aging. Microgravity in low Earth orbit (LEO) is believed to accelerate aging (or potentially senescence) over weeks rather than years, offering a unique research opportunity to investigate aging. However, that acceleration of aging has never been substantiated or experimentally validated. To meaningfully perform biotechnology and biomedical R&D in LEO, it is essential that we first understand whether accelerated aging takes place in LEO to justify the investment. Moreover, above a certain aging rate threshold, biomedical R&D in LEO may in fact be cheaper and faster than R&D on Earth, decreasing the time and costs currently hindering the drug development pipeline.

Comprehensive Organ System Modeling in Outer Space (COSMOS) centers on quantifying the Tissue Aging Rate in Space (TARIS) relative to the Tissue Aging Rate on Earth (TAROE) for human tissues affiliated with diseases that have the highest morbidity and mortality across multiple adult age groups. COSMOS will establish if there is an accelerated aging rate in LEO flight across four critical tissues—brain, cardiac, uterine, and kidney—using microphysiological systems (organs-on-chips) and organoids.

COSMOS will definitively prove or disprove if exposure to microgravity in LEO truly accelerates tissue aging across these four tissue types and across representative adult age brackets. Provided TARIS exceeds TAROE at a rate that exceeds the on Earth breakeven cost for new drug R&D, COSMOS will create a first-in-class platform for fully autonomous, high-throughput drug screening in LEO that would be more cost effective and faster than new drug R&D on Earth.

2.1.2 Current State of R&D in Low Earth Orbit:

Space based research has, until recently, been limited by the issue of reliable, repeatable access. The International Space Station (ISS) and the ISS National Lab have provided a platform for scientific research for decades, enabling proof-of-concept demonstrations of numerous space-based methods and biologic phenomena. The ISS will be decommissioned in ~2030, adding time pressure to the already limited availability of experimental locker space and ascent/descent payloads. A number of new entrants into the commercial space industry, also known as Commercial LEO Destinations or CLDs, are building a thriving, private sector market that promises to allow for a high cadence of LEO flights with plentiful R&D space on board, reducing

experimental costs and risk over time while opening the opportunity for further biotechnology R&D in space. These CLDs will range from fully crewed to fully autonomous, providing optionality and healthy market competition. With commercial space entities and commercial LEO destinations, it is now feasible to plan and execute experiments at the scale that can generate robust evidence in LEO and compel large biopharma entities to consider entering the arena.

2.2 AGE-RELATED DISEASE:

Age-related diseases—including neurodegenerative, cardiovascular, chronic kidney, and female reproductive conditions—are overwhelming our current healthcare and drug development systems, with no regenerative cures in sight. The following tissue types are affiliated with the highest morbidity and mortality rates Nationwide and deserve particular focus in the quest for regenerative therapies:

- Brain. Neurodegenerative diseases (ND) including Alzheimer's, Parkinson's and other dementias affect an estimated 8-11 million Americans (~200,000 deaths) and cost more than $435 billion dollars when considering direct and indirect costs[1].
- Heart. Cardiovascular diseases (CVD) including stroke, heart disease and arterial pathologies affect an estimated 127 million Americans (~843,000 deaths) and cost more than $400B in direct and indirect costs[1].
- Uterus. The uterus goes through a series of poorly understood changes across a lifespan. Organ-specific pathologies such as fibroids, the effects of polyendocrine metabolic ovarian syndrome, and abnormal bleeding conditions. Though difficult to define, estimates on healthcare and quality of life costs associated with non-fertility related reproductive ailments ballpark $17-35B annually with attributable deaths greater than 30,000 per year[2].
- Kidney. "Kidney disease" includes chronic kidney disease (often caused by diabetes, hypertension, and obesity), nephritis, nephrosis and other medium to long-term kidney conditions affect ~35 million Americans. Though the annual death rate is relatively lower than CVD (~55,000), the annual cost of Medicare-based dialysis alone is greater than $6.7 billion annually[3].

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[1] Centers for Disease Control (CDC) and Prevention. (2026c). About chronic diseases. https://www.cdc.gov/chronic-disease/about/index.html CDC. (2006). Dementia and its implications for public health. Preventing Chronic Disease, 3(2). https://www.cdc.gov/pcd/issues/2006/apr/05_0167.html

[2] Centers for Disease Control (CDC) and Prevention. (1987). Hysterectomies in the United States, 1965–84 (Series 13, No. 92). National Center for Health Statistics. https://www.cdc.gov/nchs/data/series/sr_13/sr13_092.pdf; CDC. (2025b, June 10). Cervical cancer statistics; CDC (2025c, August 15). Health and economic benefits of cervical cancer interventions https://www.cdc.gov/nccdphp/priorities/cervical-cancer.html. Nature Reviews Endocrinology, 18(5), 290–308. https://www.nature.com/articles/s41574-021-00629-4; Frontiers in Cell and Developmental Biology, 9. https://www.frontiersin.org/journals/cell-and-developmental-biology/articles/10.3389/fcell.2021.633180/full https://www.cdc.gov/cervical-cancer/statistics/index.html; De Corte, P., Klinghardt, M., von Stockum, S., & Heinemann, K. (2025). Time to diagnose endometriosis: Current status, challenges and regional characteristics—A systematic literature review. BJOG: An International Journal of Obstetrics and Gynaecology, 132(2), 118–130. https://pubmed.ncbi.nlm.nih.gov/39373298/

[3] Hassan, M.B. et al; Chronic kidney disease and cardiovascular risk: Pathophysiology and interventional approaches – systematic review. Medicine, 104(49), e46189. https://doi.org/10.1097/MD.0000000000046189; National Institute of Diabetes and Digestive and Kidney Diseases. (n.d.). Kidney disease statistics for the United States. https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease; United States Renal Data

2.2.1 Microphysiological Systems / Organs on Chips:

An organ-on-a-chip is a small microphysiological system (MPS) that recreates key functions of a specific organ using living cells. MPSs are three-dimensional microfluidic devices that incorporate living human cells to replicate the structural, mechanical, and biochemical conditions of specific tissues and organs *in vitro*. These controlled environments can mimic dynamic fluid flow, shear stress, and biochemical gradients more closely approximate *in vivo* conditions than conventional two-dimensional cell culture.

Due to their biological complexity and scale, robust microfluidic support is required to keep MPSs healthy. Engineering microfluidics for support of MPSs in LEO has been achieved on small scales (up to 16 MPSs), and many of the optimizations made for terrestrial studies are adaptable to LEO. Commercial service providers (CSP), in fact, now offer fully autonomous lab units compatible with commercial launch cargo parameters. In addition to the engineering advances needed, MPS technology continues to be refined, and MPSs of greater complexity featuring multiple organ systems working together are routinely produced. The field has developed to the point where the semi-mass or mass production of many MPSs is achievable on a predictable timeline. Leveraging the maturation of MPSs as a biological proxy for human tissues, they present a potential path to modeling aging in human tissues.

2.2.2 Regenerative Medicine:

Regenerative medicine refers to the science of repairing, replacing, or restoring the biological function of damaged tissues and organs. Currently, approaches include cellular therapies, biomaterials, gene editing, and tissue engineering. Rather than managing symptoms, its core aim is to address the underlying structural and functional deficits that arise from disease or injury. While regenerative medicine is agnostic to the reason that restoration is needed, it is not agnostic to the mechanisms of functional decay. "Aging" is biologically defined by a collection of changes to cells and tissues that include genomic instability, telomere attrition, epigenetic alterations, protein dysfunction (from translation through correct turnover), mitochondrial dysfunction, cellular senescence, and stem cell exhaustion. Individually (or more frequently in combinations) these changes degrade cell function and converge to impair the body's intrinsic capacity for tissue repair and homeostasis.

Age-related disease reflects, in part, a failure of endogenous repair mechanisms, and regenerative strategies offer a framework for restoring those mechanisms at the cellular and tissue levels. The loss of maintenance and renewal creates conditions favorable to chronic diseases such as neurodegeneration, cardiovascular diseases, and metabolic

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System. (2024). Healthcare expenditures for persons with CKD. Annual Data Report. https://usrds-adr.niddk.nih.gov/2024/chronic-kidney-disease/6-healthcare-expenditures-for-persons-with-ckd; National Institute of Diabetes and Digestive and Kidney Diseases. (n.d.). United States Renal Data System. https://www.niddk.nih.gov/about-niddk/strategic-plans-reports/usrds

syndromes. By design, regenerative therapies would encompass therapeutics that could intervene in multiple degradative cascades from the molecular to systemic scale. There are at least two paths to humans living longer healthier lives: finding ways to treat the changes caused by aging or preventing those changes in the first place. It is unclear which path may be more effective. The road to an answer starts with reliable and reproducible models of human aging.

2.2.3 Pharmaceutical Drug Screening:

Traditional drug candidate screening requires a broad assessment of potential therapeutics across a library of assets, lead asset selection and optimization, and validation within an animal model of disease. The preclinical stage alone can take more than 5 years, assuming relevant in vivo models have even been established. Adding to that potential time, the translation through small animal, large animal, and non-human primate models each offers an opportunity for failure. Recent FDA guidance (New Approach Methodologies (2026), Roadmap to Reducing Animal Testing in Preclinical Safety Studies (2025)) has incentivized a more streamlined process that relies heavily upon robust, in vitro tissue models of disease that would limit both animal and human testing. High fidelity, naturally aged models made from human cells could both shorten the lead development and pre-clinical timelines. The potential advantages of LEO remain unrealized, as no TARIS has been definitively established and no current platform exists for autonomous LEO-based pharmaceuticals, and, therefore, the value proposition for private industry remains unproven. Opening a LEO-based bioeconomy rests on demonstrating the utility, feasibility, and extensibility of a LEO-based pharmaceuticals platform which inspires pharmaceutical manufacturers to co-invest.

2.3 COSMOS OVERVIEW

Comprehensive Organ System Modeling in Outer Space (COSMOS) centers on quantifying Tissue Aging Rate in Space (TARIS) relative to Tissue Aging Rate on Earth (TAROE) for human tissues affiliated with diseases that have the highest morbidity and mortality across multiple adult age groups impacting four critical tissues—brain, heart, uterus, and kidney—using microphysiological systems (organs-on-chips) and organoids. Accelerating the drug discovery process via COSMOS will mean more treatments in the development pipeline can be screened faster and more cost effectively than on Earth, expediting both the pathway to patients and decreasing downstream pharmaceutical costs.

COSMOS will definitively prove or disprove if exposure to microgravity in LEO truly accelerates tissue aging across these four tissue types and across representative adult age brackets. Provided TARIS exceeds TAROE at a rate that exceeds the breakeven cost on Earth for new drug R&D, COSMOS will then create a first-in-class platform for fully autonomous, high-throughput drug screening in LEO that would be more cost effective and faster than new drug R&D on Earth.

COSMOS will not only accelerate the creation of best-in-class MPSs across the largest donor pool in history for tissues affiliated with the leading causes of death but will also

use that MPS platform for biopharmaceutical R&D at a scale never seen before. In turn, COSMOS will generate downstream pharmaceutical and private space interest and investment that can create a sustainable pathway for drug testing and, ultimately, development and clinical trials in space.

3 COSMOS DETAILS

3.1 COSMOS STRUCTURE AND TIMELINE

COSMOS includes two sequential phases. See Attachment C: COSMOS Schedule for more granular details of the schedule.

- Phase I is 27 months and includes establishing and validating an MPS system based on a selected target organ with the objective of definitively establishing the TARIS and TAROE in four tissues (heart, brain, uterus, and kidney) across a range of representative ages that cover all adult populations.
- PH II is 15 months. Phase II performers will use the MPSs or organoids (tissue and age range) in which the TARIS substantially exceeds TAROE to develop models of age-related pathology. These models will be used to justify LEO R&D for targeted, pro-regenerative drug testing on validated and unvalidated therapeutic assets in partnership with commercial biopharmaceutical partner(s) (CBPs). The objective is to demonstrate that MPSs can offer an in vitro high fidelity test bed for regenerative medicines that either directly counteract age-related tissue changes or prevent those tissue changes even as tissue ages.

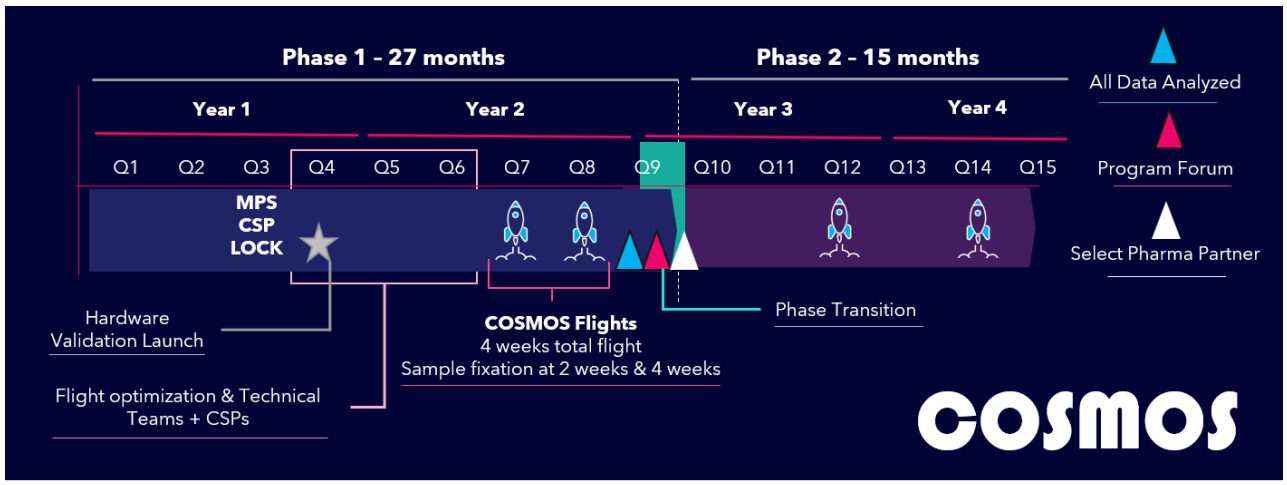

Figure 1 COSMOS schedule; for granular schedule see Attachment C

3.2 PHASE I DETAILS

During Phase I, proposers shall establish and validate an MPS system based on their selected target organ (each proposer can only select one organ). The MPS design, cell types, and interactions must recapitulate structures and functions that change with age. Phase I experiments consist of a terrestrial MPS set and a LEO MPS set. There will be two scheduled spaceflights for performers to fly their MPSs: one at month 19 and one at month 23. Each flight will remain in LEO for 4 total weeks but requires that fifty percent of

MPS tissues are preserved at 2 weeks in LEO, and the remainder at 4 weeks in LEO, prior to descent.

All experimentation in LEO will be fully autonomous, requiring no human input or interaction from launch through splashdown. All twinned LEO experiments performed on Earth will also be autonomous. This must be accounted for in each proposer's experimental design and plans. A Hardware Validation Launch will occur at Month 12 Ffter Contract (MAC) but will not involve MPSs or organoids as it is intended to ensure all non-biology logistics are in lockstep prior to the month 19 launch.

Each team must present a plan to develop MPSs at the scale required for the terrestrial arm, and a plan to develop no fewer than 384 single-donor MPSs that will mature in parallel (matched 192 LEO: 192 Terrestrial) and be delivered as a LEO payload by the established launch dates(s) for the LEO Twin Study (See Figure 2: Phase I Experimental Design requirements). The 'twin' in this instance refers to a set of MPSs derived from the same donor (n=384), constructed under the same protocols and conditions, and housed in autonomous laboratory housings. One of the sets will remain on earth (n=192), the other will launch and achieve flight for a specified amount of time (n=192). All MPSs will be preserved using identical technology and then analyzed for LEO-associated variances.

3.2.1 Phase I Launch Schedule

Phase I includes two (2) space launches tentatively scheduled for months 19 and 23. Both hardware for housing MPS systems and launch vehicles will be provided by ARPA-H selected Commercial Service Providers.

3.2.2 Phase I Results Showcase

Phase I culminates in a 3-month window where the ARPA-H team will convene a research forum (date to be determined, 25-27 MAC) where performer teams will share the completed results of their Phase I efforts including TARIS: TAROE modeling.

3.2.3 Phase I Commercialization Requirements

See Section 3.5

3.3 PHASE II DETAILS

Success in Phase II requires that each team have an established partnership (e.g., signed contractual agreement) with a commercial biopharmaceutical partner (CBP) that has drugs of interest applicable to the selected organ type and age brackets in which TARIS>TAROE.

3.3.1 Phase II: Establishing Rapid Drug Screening for Age-Related Diseases

Phase II performers will use the MPSs or organoids (tissue and age range) in which the TARIS substantially exceeds TAROE to develop models of age-related pathology. These models will be used to justify LEO R&D for targeted, pro-regenerative drug testing on validated and unvalidated therapeutic assets in partnership with CBP(s).

3.3.2 Phase II Launch Cadence

Phase II includes two (2) space launches tentatively scheduled for months 39 and 41. No less than 50% of MPS and drug combinations described in Table 1 (Section 4.2) must be launch capable simultaneously (e.g., 50% of the selected MPSs need to launch on the first launch and the remaining 50% need to fly on the second launch).

3.3.3 Phase II Results Showcase

The format and schedule of the end of program meeting will be established during Phase II, but the general intention is an all-COSMOS showcase of results of the second phase.

3.3.4 Drug Candidate Selection

Drug libraries licensed or acquired should have relevance to any biological variances discovered in the LEO Twin Study data of Phase I. Ideal libraries or candidates would target tissue/organ processes, mechanisms, or phenotypes known to contribute to pathology.

3.3.5 Phase II Commercialization Requirements

See Section 3.5

The following experimental design, technical, personnel, scale, and timing requirements must be met by a successful performer team.

3.4 PERFORMER REPORTING, EVALUATION AND PROGRESS MONITORING

To ensure success, each COSMOS phase will include regular performance evaluations, including (but not limited to) monthly, semi-annual, and annual progress reports. Specifics regarding deliverables will be stipulated in any award made under this solicitation.

In addition to the technical requirements associated with each phase, COSMOS also includes additional metrics designed to guide and monitor each Performer's progress towards biopharma partnerships and regulatory buy-in for sustained, post-program biopharma and biotechnology work in LEO (e.g., in vitro clinical trials, drug development, and continued drug screening).

Performer progress evaluation will be an ongoing process over the duration of COSMOS. Written deliverables, meetings, schedule and financial management, and achievement of milestones are some of the information that is integrated into progress evaluation. The ARPA-H model requires active performer management and a high degree of involvement by the PM and their technical team. Performers should expect regular interactions with the ARPA-H team. Further details will be available in any awards made under this solicitation.

3.4.1 Required Meetings

- Kickoff Meeting (Include in travel budget) - ARPA-H will convene a kickoff meeting at the beginning of COSMOS, after contract award. Details will be forthcoming, but the meeting is likely to be held at a TBD CONUS space launch facility.
- Scientific Reviews (Include in travel budget) – Semi-annual all-performer (technical and CSP) meetings with locations TBD to discuss progress, hurdles, key findings, etc. Current tentative schedule is for months 7,14, 21 (Phase I) and 34 (Phase II). Further details and a template for deliverables will be provided at kick-off.
- Site visits - At the discretion of the GOV team with the expectation key personnel are present at their prime location. ARPA-H will travel to you at a cadence TBD.
- MPS/Organoid and CSP Hardware/Flight Team Meetings: Regular touchpoints between MPS/Organoid teams and Commercial Service Partner Engineering teams are required. It is understood that the physical support of MPS for flight is complex and will require iteration and testing. Immediately following award, Performer teams must initiate material transfer agreements and data-sharing agreements to allow full cooperation on the design, build, and testing of autonomous experimental MPS support hardware and MPS design teams.
- Ad Hoc Meetings: At the program manager's discretion, additional meetings will be requested with Performer teams. These requests will be made in writing, listing the team members requested to attend.

3.5 REQUIRED COMMERCIAL BIOPHARMACEUTICAL PARTNERNERSHIPS ENGAGEMENT

- Phase I: By the end of Phase 1, each team must establish a signed, contractual commercial public-private partnership (PPP) with AT LEAST one Fortune 100 biopharmaceutical company to leverage the COSMOS platform for regenerative therapeutic R&D for all tissues where TARIS>TAROE to include: drug screening, in vitro clinical testing, etc. Selected partner must have:
    - Each team's partner(s) must: 1) have ≥3 drug candidates that are either approved for age-related disease in the selected tissue type or target aging-relevant molecular pathways in clinical testing and/or 2) have a panel of known and novel drug candidates relevant to the target tissue type. Drugs selected for screening must be relevant to aging and the target tissue and must include drugs with known mechanisms of action and/or drug candidates/leads.
    - Proposers must also propose the design, development plan, and substantiating evidence for MPSs of disease in only the ages and tissues demonstrating TARIS>TAROE. Those MPS-based models of disease will be what the CBP will use to screen validated and unvalidated therapeutics of interest in Phase II.
    - For each tissue and age group where TARIS>TAROE, the CBP must demonstrate how that rate translates to the discount on the downstream therapeutic MSRP. For instance, if 35-year-old uterine tissue demonstrates TARIS is 5x TAROE, the CBP must clearly demonstrate how that 5x accelerated rate will be recognized by patients benefiting from novel regenerative therapeutics.

Phase II: Technical teams (MPS/Organoids) will establish a commercial public-private partnership (PPP) with a Fortune 100 pharmaceutical company to leverage the

COSMOS platform for translational, regenerative therapeutic applications to include: drug screening, in vitro clinical testing, etc.

- Proposers and their CBP(s) shall use the MPSs in which the TARIS substantially exceeds TAROE to utilize LEO R&D for targeted, pro-regenerative drug testing in validated and unvalidated therapeutic assets. De minimis, proposer teams must secure access to a drug library relevant to the cell types, functions, and variance associated with the "accelerated aging" models developed in Phase I.
- Performer teams are expected to coordinate with the selected CBP to develop MPS models of disease relevant to the drugs being screened in LEO. Selected CBP must have three approved drugs which target aging-related pathways proof of concept of the COSMOS as well as a panel of experimental therapeutics for LEO-based drug screening.
- Phase II success includes the creation of a PPP pipeline to utilize the COSMOS platform.

4 MANDATORY EXPERIMENTAL DESIGN

Each performer team will produce the required number of MPS and organoids from the designated number of donors in each Phase. Each Phase has specific design requirements that are laid out on the following tables. Phase I details are in Section 4.1; Phase II details in Section 4.2.

4.1 PHASE I EXPERIMENTAL DESIGN

The parameters outlined in the infographic, text, and tables below are mandatory. Please ensure your final proposal package includes all the relevant experiments, justifications, and design requirements outlined in Tables 1-3 and sections 4.1 and 4.2.

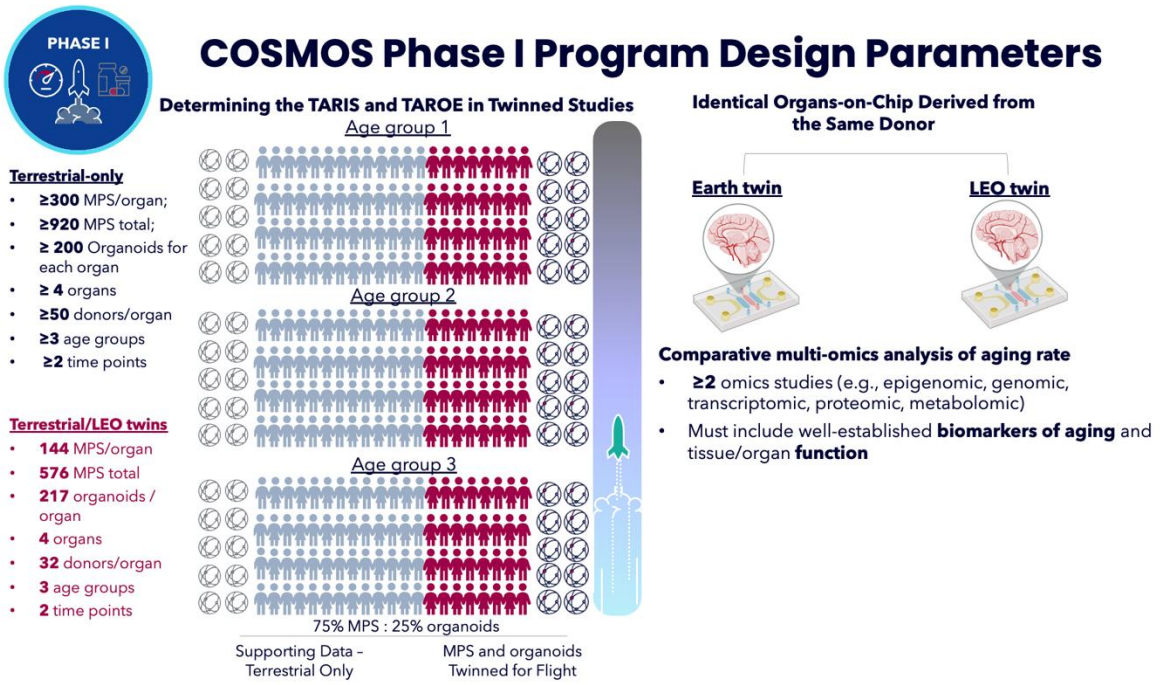

Figure 2: COSMOS Phase I Design Parameters – note these numbers address the entire period of performance; metric tables in Section 4.1.5

4.1.1 Experimental Age Brackets

All Phase I experiments must include cell/tissue donors in the following restricted age brackets: 30 years ± 2 years, 45 years ± 2 years, 60 years ± 2 years. These age brackets have been selected based on emerging evidence that our bodies age in a non-linear pattern, where a large change across the system occurs at relatively predictable timepoints (*Liu et al, Nature 2024*). An emerging model of aging is that there are non-linear accelerations in age in the mid-30's, mid-40's and mid-60s. Around age 30, most adults are past developmental maturation but have not generally hit the first major nonlinear aging shift seen in later adulthood. This makes it a useful reference/baseline state for adult biology.

The mid-40s are the first major adult aging inflection point. In women, this window also often overlaps with perimenopausal transition biology, which can strongly affect metabolism, inflammation, vascular risk, bone, and immune regulation. Midlife is when cardiovascular aging becomes more biologically apparent, with rising arterial stiffness, endothelial dysfunction, vascular inflammation, and subclinical atherosclerotic burden. The late transition point, the mid-60s, is when many aging hallmarks become more integrated at the organism level: immune remodeling, senescence burden, endocrine change, vascular stiffening, and reduced resilience.

4.1.2 Terrestrial Study

This arm of the study will act as a temporal and technical 'ground' for the LEO Twin study. The object is to run technical duplicates (2) for each donor for each relevant time point. For example, for kidney MPS from a 30 (+/-2 years) year-old, a total number of 4 MPSs are required. This must be replicated for each required age

bracket. The experimental timepoints can be determined by the performer, though the proposer should offer justification as to why timepoints were selected. This study does not require the use of the CSP-provided microfluidics housing.

4.1.3 LEO Twin Study

All MPSs for the LEO Twin study (both terrestrial and flight twin) will be housed for the experimental duration in a fully autonomous functional unit provided by a commercial service provider (to be determined by ARPA-H and relayed to selected performers). This arm of the study will determine if there is detectable variance between MPS on earth (at 2 and 4 weeks) and those in flight for the same time points (at 2 and 4 weeks). Each organ will be recapitulated in quadruplicate with 2 for flight and 2 on earth.

4.1.4 Commercial Service Providers (CSP)

The government will select and announce two commercial service providers who will work in collaboration with each performer team and will be responsible for flight hardware and logistics. These CSPs will be determined by the Government, and it is expected that selected performers will only work with and use the designated CSPs within COSMOS.

CSP-Hardware will provide experimental housing (with power, imaging, sample preservation, and microfluidic support) compatible with the CSP-Flight LEO platform. At the time of award, performer teams will immediately institute the required agreements with the CSP partners to allow for co-engineering, testing and integration of MPS systems and flight hardware. The ARPA-H technical team will work with performers to determine how many MPS from each team will launch on each launch.

4.1.5 Phase I Design Requirements

The following tables (Tables 1, 2, 3) outline the Experimental parameters, MPS requirements, and Computational modeling (Baseline, TARIS/TAROE) requirements.

Table 1: Phase I Mandatory Experimental Parameters

Per Team	Experimental Design
1 Tissue of Interest per team	Brain **OR** Heart **OR** Uterus **OR** Kidney *NOTE: Do NOT propose to more than one organ group per proposal*
Donor Ages	30+/- 2 yrs, 45+/- 2 yrs, **AND** 65 yrs+/- 2 yrs
Experimental Timepoints	Terrestrial: Performer determined; justify why these timepoint(s) were selected, how they will contribute to the TARIS model and support the maximum potential data extraction from the MPS and organoid LEO Twin: MPS fixation will occur at 2 weeks flight time and 4 weeks flight time

Experimental design	The experimental design of LEO and terrestrial components of the MPS twin study must be identical to facilitate direct comparison of aging rates. Terrestrial-only study must adhere to the twin study set up as much as practicable but will not require housing in CSP hardware
Tissue donors	• 32 healthy individuals for the LEO/Terrestrial MPS twin study • ≥50 healthy individuals for the supplemental terrestrial-only study for each age group Teams must ensure that the selected donors have sufficiently large tissue samples to generate the appropriate number of MPSs: ≥2 MPS/tissue sample for the terrestrial-only study and ≥4 MPS/tissue sample for the twin study
Terrestrial MPS total	[51 healthy donors] x [3 age group] x [technical duplicates] x [2 experimental time points] = 612 MPS for Phase I NOTE: NO fewer than 75% of the total numbers of the experimental units must be MPS; the use of organoids in some percentage is encouraged to act as a 'fail safe' for the MPS cohort
Terrestrial Organoids	A subset of 51 donors, distributed across age groups should contribute to ~500 organoids
LEO Twin MPS (Per team)	[32 donors] x [3 age groups] x [experimental duplicates (1 LEO:1 Terrestrial)] x [2 experimental time points] = 384 MPS for Phase I NOTE: NO fewer than 75% of the total numbers of the experimental units must be MPS; the use of organoids in some percentage is encouraged to act as a 'fail safe' for the MPS cohort
LEO Twin Organoids	Subset of 32 donors distributed across age groups should contribute to 217 organoids
Co-Engineering progress	Commercial service providers for flight hardware and experimental support systems will be selected by the Government under separate solicitation. Technical performers are expected to schedule regular meetings with hardware providers to support co-engineering of MPS support systems
Twin LEO MPS Design Lock	Design of MPS organ and required fluidics support must be design locked no later than 10 MAC
Co-Engineering Design Lock	MPS and support housing designs must be locked not later than 10 MAC
Phase I Exit Criteria	Only the tissue types and donor ages in which TARIS exceeds TAROE (such that it justifies further investment) will move into COSMOS Phase II

4.1.6 Mandatory Microphysiological Systems / Organs on Chips & Organoid Parameters

Table 2:	**MPS/Organoid Required Parameters**
Item	Requirements
MPS requirements	All MPSs must be derived from primary human cells, iPSC, or tissue samples from healthy donors. Proposers selecting iPSC *must* justify why that organ specifically requires iPSC over primary cells MPSs must recapitulate key features of the tissue/organ of interest as demonstrated by an analysis of the 3D microarchitecture, cell lineage identity and composition MPS cells, structure and maturation conditions must be selected to support the detection of age-related changes over time
MPS Model Fidelity	• MPSs recapitulating organs with specific basement or other critical, functional membranes must have robust physiologically relevant basement membranes • Proposers must offer justification for how both tissue age and tissue physiology is represented in the MPS
Organoids	A fraction of the experimental samples (≤25%, TBD by launch capacity) must be comprised of organoids
Donor Heterogeneity	To the maximum extent possible given time and budget, donor heterogeneity (outside of the age requirement) should follow American population demographics: • Sex: 50% female (for non-uterine tissues) • Race/Ethnicity: 56% Non-Hispanic (NH) White, 20.5% Hispanic or Latino of any race; 13.5% NH Black; 6.9% NH Asian; 4.9% multiracial (≥2 races); 2.1% American Indian & Alaskan Native; 0.3% Native Hawaiian/Pacific Islander
MPS In Flight Monitoring Requirements	MPSs must be optically clear to allow for real-time imaging/ monitoring of the viability of each MPS; further monitoring and testing integration should be described to satisfy the data targets requirement *NOTE: For LEO Twins, final testing, monitoring, -omics, and extraction processes will be determined and refined in partnership with the commercial service provider for hardware*
Preservation	MPS will be preserved at experimental timepoints (2 and 4 weeks of flight) by the method required to perform the multiomic analyses selected by the performer

Experimental Assessments	≥2 broad, quantitative and unbiased multi-omics approaches that allow a holistic analysis of tissue/organ function and integrity must be selected to assess LEO Twin samples
MPS chip & microfluidics design lock	LEO Twin Study MPS format and protocol must be locked no later than Month 10 in consultation with the Hardware Commercial Service Partner
Data Targets	≥2 broad, quantitative and unbiased multi-omics approaches that allow a holistic assessment of normal vs. pathological organ function must be selected Any available non-destructive orthogonal approaches for real time data capture prior to MPS preservation should be integrated and that data captured (up to the limit of the autonomous housings for the LEO Study arm) Approaches selected to monitor variance / potential aging for each organ must allow monitoring of ≥2 biomarkers for each of the following: 1) established and potential tissue agnostic and tissue-specific biomarkers of aging, 2) age-related biological pathways (e.g. stress, senescence, inflammation), and 3) tissue agnostic and tissue specific biomarkers of tissue integrity
Data Analysis	Performers must complete all data analysis within three months of landing

4.1.7 In Silico Aging Model

To establish if there is variance between healthy tissues on the ground and identical tissues in flight, proposers must offer a rational data capture and modeling strategy.

Table 3:	**In Silico Aging Model**
Item	Requirements
In Silico Aging Model	Performers will create an in silico model of aging as a pre-flight baseline for their tissue/organ using extant and open-source data • This model should serve as the grounding for MPS-derived data from the terrestrial experimental set, as well as for the future integration and comparison of data form the LEO twin set • Performers must: establish the data sources to be used, training and test data, integrated assumptions in the model build, describe the model and establish how it will be used to inform the TARIS/TAROE analyses • Performers may leverage extant models of aging for their specific organ provided they can justify the model selected, and

	clearly detail how new data will be added, or the model will be modified with TAROE and TARIS data • Using the in silico model of aging in the specific organ type, each team should put forth a list of prospective biopharma partners with relevant drug libraries for their organ
Final In Silico Aging Model	TARIS and TAROE data from month 19 and month 23 flights will be used to refine the In Silico Aging Model in the selected organ. This flight-optimized In Silico Aging Model will be presented at a specific date TBD between 22-24 MAC. Refined final models and results should seek to prove or disprove the "accelerated aging in space" hypothesis across each age bracket and tissue type.

4.2 PHASE II EXPERIMENTAL DESIGN

Each performer team selected for Phase II will generate testable disease model(s) using the organ and age bracket(s) (up to 2 brackets per performer team) that showed the greatest TARIS:TAROE ratio. The design parameters for Phase II are listed in Table 4.

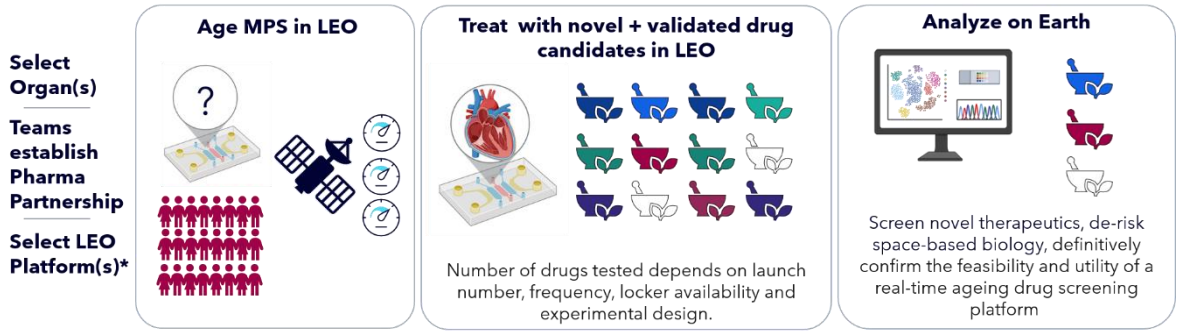

Figure 3: COSMOS Phase II

4.3 MPS-BASED DISEASE MODEL

Each performer team selected for Phase II will generate testable disease model(s) using the organ and age bracket(s) (up to 2 brackets per performer team) that showed the greatest TARIS:TAROE ratio. Technical details for Phase II MPS-based disease models are not required at time of proposal submission, however a generalized technical plan for no more than 2 models per organ team is required in the proposal. Model designs and specifics are not part of this current proposal beyond budgeting for the potential of 1-2 disease models per team. Technical description and justification of the MPS-based disease model will be finalized in the final quarter of Phase I (18 MAC). It is expected that disease models would be developed with specific pharmaceutical partner(s) in mind.

Table 4:	**Phase II Mandatory Experimental Design**
Item	Requirements

MPS-based disease model	The model must accurately represent the organ and its functions AND reproduce organ biology related to the drug library selected for Phase II
Pharmaceutical Library Requirement	Drugs selected for screening must be relevant to aging and the target tissue and must include both drugs with known mechanisms of action, a validated control drug, and drug candidates
Pharmaceutical Testing Design	Performers will develop a prospective drug testing strategy based on the hardware CSP parameters and biopharma requirements. This will be a COSMOS deliverable due at 6 MAC.
MPS Disease Model Scale Production	Selected performers must be capable of scaling MPS production for a single organ. Final number to be determined by selected Phase II commercial service providers
Co-Engineering Design Lock	MPS and support housing designs must be locked not later than 35 MAC.
MPS cell sourcing	• Performers must utilize donors from the age brackets showing the greatest TARIS:TAROE in collaboration with their commercial partners • Teams must ensure that the selected donors have sufficiently large tissue samples to generate the appropriate number of MPSs
Co-Engineering progress	Commercial service providers for flight hardware and experimental support systems will be selected by the Government under separate solicitation. Technical performers are expected to schedule regular meetings with hardware providers to support co-engineering of MPS support systems
LEO Launches	Phase II features 2 launches on a commercial service provider's hardware and flight vehicle; launches tentatively scheduled in months 37 and 39

5 COSMOS METRICS

To evaluate how effectively a proposed solution will achieve the stated objectives, the government hereby promulgates the following metrics that may serve as the basis for determination of satisfactory progress to warrant continued funding.

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

5.1 PHASE I METRICS

Table 5	**Phase I Success Metrics**
Metrics	Specifications
Phase I Deliverables	• Quantification of Tissue Aging Rate in Space (TARIS) using microphysiological systems (MPSs) (and potentially organoids as well) for target organ • Licensable data set comprising the Terrestrial Arm data and LEO Twin Data • Commercial CSP Hardware integration plan with MPSs for timely spaceflight • Baseline In Silico Aging Model pre-flight • Final In Silico Aging Model of tissue changes in LEO • Signed, contractual partnership and licensing agreement with AT LEAST one CBP that has drugs of interest that are applicable to the organ type with the greatest TARIS:TAROE
Commercial Biopharmaceutical Partnership (CBP)	• By the end of phase 1, each team must establish a signed, contractual commercial public-private partnership (PPP) with AT LEAST one Fortune 100 biopharmaceutical company to leverage the COSMOS platform for translational, regenerative therapeutic R&D for all tissues where TARIS>TAROE to include: drug screening, in vitro clinical testing, etc. Selected CBP must have: • ≥3 drug candidates that are either approved for age-related disease in the selected tissue type or target aging-relevant molecular pathways in clinical testing, • Have a panel of known and novel drug candidates relevant to the target tissue type. • Drug Screening: Drugs selected for screening must be relevant to aging and the target tissue and must include drugs with known mechanisms of action and drug candidates
Demonstrate TARIS > TAROE	Present data and evidence that there is or is not an accelerated, detectable variance between identical tissues from normo- versus microgravity
TARIS Model of Aging	In the event of a detectable variance between terrestrial and LEO-flown MPS, performers will leverage the alpha model and the data collected in Phase I to formulate a model of aging or age-like effects induced by flight in LEO
Phase II Disease Model and Scaling Plan	Credible plan to develop relevant disease model(s) within the selected organ based on state of the art, scale MPS production to

	occupy a to-be-determined number of payloads on a commercial service provider's autonomous LEO platform

5.2 PHASE II METRICS

Table 6	**Phase II Success Metrics**
Metrics	Specifications
Phase II Deliverables	• Credible, reproducible disease model(s) of tissues where TARIS > TAROE from Phase I successfully used in coordination with commercial partner(s) for novel drug screening • Demonstration of proof-of-concept high throughput drug testing using microgravity-leveraged MPS models of aging to identify drugs that can prevent and/or reverse age-related tissue dysfunction and/or disease • Commercial CSP Hardware integration with MPSs for timely spaceflight
Commercial Biopharmaceutical Partnership	• Proposers and their commercial biopharma partner(s) (CBPs) shall use the MPSs in which the TARIS substantially exceeds TAROE to utilize LEO R&D for targeted, pro-regenerative drug testing for at least three validated and unvalidated therapeutic assets. De minimis, proposer teams must secure access to a drug library relevant to the cell types, functions, and variance associated with the "accelerated aging" models developed in Phase I. • Successful collaboration with a CBP with three approved drugs which target aging-related pathways proof of concept of the COSMOS as well as a panel of experimental therapeutics for LEO-based drug screening. • For each tissue and age group showing TARIS>TAROE, the CBP must demonstrate how that rate translates to the discount on the downstream therapeutic MSRP. For instance, if 35-year-old uterine tissue demonstrates TARIS is 5x TAROE, the CBP must clearly demonstrate how that 5x accelerated rate will be recognized by patients benefiting from novel regenerative therapeutics. • Evidence of post-program investment from at least one of the team's CBP for continued use of the COSMOS platform in the commercial sector following contract conclusion

6 COSMOS TEAM REQUIREMENTS

Teams must present a plan to have a qualified team of expert advisors with adequate levels of effort and subject matter expertise to ensure the success of the effort.

Successful proposers and performer teams will be comprised of, at minimum, the following experts and specialists. Unless sufficiently justified otherwise, the government's assumption is that the Project Manager is full-time, and the other key personnel (KP) will be proposed for at least a minimum of a 0.5 full-time equivalent and cannot be the same person. KPs require Research Security Review (RSR). See Section 14.5 for RSR details.

Table 7	**Required Personnel**
Title	Description
Project Manager (KP)	Project manager must have a demonstrated history of managing large, complex, high budget, ARPA (or ARPA-like) research programs. Subject matter expertise is strongly preferred to ensure proper, reliable integration of multiple data streams into polished results and reporting deliverables
Principal Investigator (KP)	The experimental design and technical lead responsible for the overall design of the project.
Engineer(s)	Emphasis and extended experience in microfluidics support of MPS
Organ Specialist (KP)	Expert in structure, function, physiology of the target organ; clinical experience is highly desirable but not a requirement
Computational Biology Specialist (KP)	Required: Expertise in the in-silico modeling of the specific organ the team is supporting and the integration of high-resolution data into new models of aging and physiology. The specialist is integral to the MPS design process to ensure biologically informed MPS design to recapitulate relevant, contextual organ functions
Machine learning & other Modeling Expert	Conversant in the design, testing, optimization and expansion of ML-assisted models
Regulatory expertise	While COSMOS is not explicitly interested in meeting FDA requirements for MPS as in vitro testing models, MPS and MPS-based disease models should anticipate future development under GMP and GLP conditions. Expertise in achieving FDA regulatory standards is strongly recommended
IP Counsel	Given the unique nature of the data and IP generated within Phase I and the need for eventual partnership with at least one CBP, it is advised that teams have IP counsel to ensure commercial viability of PHI/II data/IP in accordance with the BIOSECURE Act
NO Trainees	ARPA-H contracts and awards are **not** conducive to graduate training. The aggressive timeline and strict performance standards are generally

	incompatible with the teaching/training component of PhD candidate's education. Trainees are discouraged.

KP = Key personnel

7 COSMOS DATA & DATA MANAGEMENT

Data Management and Sharing Plan (DMSP) (recommend NTE 2 pages); The DMSP shall include all information included in the 6-Element plan format recommended by the National Institutes of Health (to view the 6-Element suggested format visit https://grants.nih.gov/grants/forms/data-management-and-sharing-plan-format-page).

Note: this plan will not be specifically evaluated against Criteria 1-3 but will likely be used to give feedback for proposals that are selected for award negotiations. Data generated by COSMOS must be generated in such a way as to maintain commercial viability for the required, downstream CBP in Phase II while simultaneously adhering to all provisions within the BIOSECURE Act.

8 ELIGIBILITY INFORMATION

8.1 ELIGIBLE PROPOSERS

All responsible sources capable of satisfying the Government's needs may submit a proposal to this ISO. Specifically, universities, non-profit organizations, small businesses and other than small businesses are eligible and encouraged to propose to this ISO.

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

8.2 PROHIBITION OF PERFORMER PARTICIPATION FROM FEDERALLY FUNDED RESEARCH AND DEVELOPMENT CENTERS (FFRDCS) AND OTHER GOVERNMENT ENTITIES

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

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

If an FFRDC or Government entity has a unique research idea that is within the technology scope of this solicitation that they would like considered for funding; OR, if an FFRDC or Government entity, including a federal Government employee, is interested in working directly with the Government

team supporting the research described by this solicitation, contact COSMOS@arpa-h.gov.

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

8.2.1 Current professional support

Those individuals/entities currently providing contracted support services to ARPA-H have an organizational conflict of interest (OCI) that cannot be mitigated and thus are ineligible for award.

8.2.2 Non-U.S. Entities

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

8.3 SYSTEM FOR AWARD MANAGEMENT (SAM)

All proposers must have an active registration in SAM.gov for their proposal to be found conforming. Proposers must maintain an active registration in SAM.gov with current information at all times during which a proposal is under consideration or a current award from ARPA-H is held. Information on SAM.gov registration is available at SAM.gov.

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

9 PROPOSAL REQUIREMENTS

Proposals must conform to the requirements in this section as well as the experimental and technical requirements in Section 4. Proposal submissions are due by the date and time listed in Section 1. All proposal documents must be submitted in .pdf, .odx, .doc, or .docx, formats. All submissions must be written in English, and all pages must be formatted for printing on 8-1/2 by 11-inch paper with 0.75-inch margins and sans serif font size not smaller than 11 point. Font sizes of 8 or 10 point may be used for figures, tables, and charts only.

Proposers are encouraged to submit concise and concrete proposals. Specific examples of problems, approaches, or goals are preferred to qualitative generalities. Additional

information not explicitly called for in the Technical & Management Proposal must not be submitted but may be included as links in the bibliography. Any additional materials included in the proposal package will be considered for the reviewers' convenience only and not evaluated as part of the proposal.

Supporting and illustrative figures should be submitted as an additional attachment and should not exceed 3 pages. All figures should be of publication quality, with comprehensive labeling, legends, and description of any statistical testing in the legend.

Required for Submission:

Volume I: Technical Management Proposal (Attachments A.1, A.2)
- Supporting figures – Submit as separate attachment with the full proposal
- Task Description Document: Attachment A.2

Volume II: Cost Proposal and Budget
Cost Proposal Workbook: Attachment D
Milestone and Payment Table (Attachment A.3)
COSMOS Eligibility and Conformance Sheet (Attachment B)

9.1 PROPOSAL VOLUME I

Detailed instructions are available in Attachment A.1 (Volume 1 Model (Technical and Management Proposal).
It is STRONGLY recommended that when selecting sub-awardees and vendors, appropriate due diligence in line with the provisions of the BIOSECURE Act be made to ensure compliance with Article 7 of the Draft Other Transactions Agreement. All possible caution should be exercised to protect Intellectual Property (IP) developed under awards made from this solicitation.

Total text pages of Volume 1 may not exceed 14 as detailed in Attachment A.1: Volume I Technical & Management Proposal Model

The government will not consider pages in excess of the page count limitations, as described herein. Proposals with fewer than the maximum number of pages will not be penalized.

Not part of the page limit:
- The Technical Description Document and Milestone and Payment Table (Attachments A.2 & A.3); At time of submission only the Phase I TDD is required (Months 1-27)
- Supporting and illustrative figures: submitted as an additional attachment and should not exceed 3 pages. All figures should be of publication quality, with comprehensive labeling, legends, and description of any statistical testing in the legend.

9.2 PROPOSAL VOLUME II

Detailed instructions are embedded in the Excel workbook file accompanying this solicitation "COSMOS Cost Proposal Template (Attachment D). There is no maximum page count for Volume II. The Cost Proposal is comprised of the editable Excel Cost Proposal excel file and

associated supporting materials, ideally provided in a single attachment (e.g., Adobe pdf) led by a cover page. The cover page should include: proposal title, name of prime organization, prime organization's Unique Entity Identifier (UEI), total cost by phase, grand total requested; resource sharing (if any) by phase, grand total resource sharing, date of proposal submission and proposal validity period (minimum 120 days).

9.2.1 Cost Proposal Excel File

ARPA-H Standard Excel Cost Proposal Template (Attachment D) shall be submitted with all full proposals. All tabs and tables in the cost proposal template should be developed in an editable format with calculation formulas intact to allow traceability of the elements of the cost proposal. The cost proposal template must be used by the prime organization and all sub-performers at any tier. To be clear, each sub-performer must submit its own Cost Proposal Template with the same level of detail as the prime.

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

9.2.2 Cost and Pricing Data Support

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

ARPA-H recommends that proposers ensure that the vendors, manufacturers, and suppliers who may interact with the IP generated under COSMOS meet the requirements of the CHIPS and Science and BIOSECURE Acts. A complete list of subawardees and vendors who may access IP generated under COSMOS should be submitted at the time of proposal for the purposes of the RSR review.

Cost and pricing support may also facilitate a value analysis by the government through information other than detailed cost and pricing data.

9.3 TASK DESCRIPTION DOCUMENT (TDD)

Attachment A.2 [MS Word format] must be included as part of Volume 1.

9.4 MILESTONE AND PAYMENT TABLE MODEL

Attachment A.3 is a spreadsheet version of the TDD which can be used as a Milestone & Payments Table and be submitted separately from Volume I.

9.5 ATTACHMENT B COSMOS ELIGIBILITY AND CONFORMANCE SHEET

A completed sheet must be submitted with each proposal. Failure to submit this sheet may result in the proposal being deemed non-conforming.

9.6 ATTACHMENT C COSMOS SCHEDULE

Highly detailed schematic of the COSMOS schedule including planned meetings and events, launches, and results showcases.

10 SUBMISSION PROCESS

10.1 SUBMISSION PROCESS OVERVIEW

Submissions for COSMOS are as follows:

- ✓ Submit Full Proposals (Proposers must submit full proposals, in compliance with all required Attachments (including supporting figures) and experimental designs.)
- ✓ Submit a Milestone and Payment Table (Attachment A.3)
- ✓ Submit Attachment B: COSMOS Eligibility and Conformance Sheet

10.2 FULL PROPOSAL SUBMISSIONS

Full proposal submissions are due by the date listed in the ISO Summary Information Section in Section 1. See Attachment A.1 for the required Full Proposal format.
Attachment E: Administrative & National Policy Requirements Document Template OTs is required to be submitted for OT Full Proposals.

10.3 SUBMISSION INFORMATION

All submissions in response to this solicitation must be written in English and must be consistent with the content and formatting requirements of Attachment A (Full Proposal Content and Instructions.

Proposers are responsible for submitting all written submissions via the ARPA-H Solution Submission Portal and ensuring receipt by the date and time specified in the ISO. No other method of submission is permitted.

Questions may be submitted to the COSMOS inbox (COSMOS @ARPA-H.GOV)

NOTE: Registration is required to submit via the ARPA-H Solution Submission Portal and registration may take several business days to process. Plan to register well in advance of the proposal submission deadline as late submissions resulting from delays with registration may not be accepted or considered.

PROPRIETARY INFORMATION

- Proposers are responsible for identifying proprietary information in any submissions. Submissions containing proprietary information must have the cover page and each page containing such information clearly marked with a label such as "Proprietary."
- NOTE: "Confidential" is a classification marking used to control the dissemination of U.S. Government National Security Information as dictated in Executive Order 13526 and should not be used to identify proprietary business information.
- ARPA-H is responsible for handling submissions in accordance with applicable federal law, including the Freedom of Information Act (FOIA).

11 DOCUMENT DESCRIPTIONS

Proposal Section	Reference	Page Limit
COSMOS Solicitation		N/A
Technical & Management Proposal	Attachment A.1	14, Exclusive of bibliography and TDD
-	Summary Goals & Impact **Technical Plan** Management Plan	1 Page 1 Page **10 Pages** 2 Pages
Task Description Document (TDD)	Attachment A.2	Does Not Count Against Page Limit
Milestone & Payment Table	Attachment A.3	Does Not Count Against Page Limit
Eligibility and Conformance Certification Sheet	Attachment B	Does Not Count Against Page Limit
COSMOS Schedule	Attachment C	N/A
COSMOS Cost Proposal Workbook	Attachment D	No Page Limit
Administrative and National Policy Requirements	Attachment E	No Page Limit
Figures	Submitted by proposer, no template	3, Does Not Count Against Page Limit of Volume 1

12 SUBMISSION REVIEW AND EVALUATION PROCESSES

12.1 CONFORMING SUBMISSIONS

Conforming submissions contain all requirements detailed in this ISO. Submissions that fail to include required information may be deemed non-conforming and may be removed from further consideration and/or rejected without further review. A submission may be deemed non-conforming under this ISO if it fails to meet one or more of the following solicitation requirements:

- The proposed concept is applicable to COSMOS.
- The proposers meet the eligibility and conformance requirements.
- The submission meets the submission requirements.
- The submission meets the content and formatting requirements in the attached instructions.
- The submission must include all documents listed in Section 11.
- The proposer's concept has not already received funding or been selected for award negotiations for another funding opportunity (whether from ARPA-H or another Government agency).

Proposers will be notified of non-conforming determinations via email correspondence.

Please note that ARPA-H reserves the right, at its discretion, to reject as non-conforming proposals that it determines are duplicative of previously submitted solution summaries and proposals under this or other ARPA-H solicitations.

12.2 PROPOSAL REVIEW PROCESS

ARPA-H will conduct a scientific and technical review of each conforming full proposal, evaluating proposals on how well the submission meets the criteria stated in this ISO. At a minimum, proposers will be provided with notification of the Government's decision on whether the proposal was selected for negotiation of an award. Notification of the Government's decision will be provided to the primary technical point of contact included in the solutions tool.

12.3 EVALUATION CRITERIA FOR PROPOSALS

All proposals will be evaluated using the following evaluation criteria, listed in descending order of importance.

12.3.1 Criteria 1: Overall Scientific and Technical Merit

The proposed technical approach is innovative, feasible, and complete. The proposal identifies major technical risks, and planned mitigation efforts are clearly defined and feasible.

- Potential to transform biomedicine: The evaluation may take into consideration how and to what extent the proposed work creates a paradigm change in biomedicine
- Potential for future commercial applications: The evaluation may take into consideration the extent to which the proposed intellectual property (IP) rights structure and software components will potentially impact the ability to commercialize the technology and adhere to open-source solutions and/or standards.

12.3.2 Criteria 2: Proposer's Capabilities and/or Related Experience

The proposed technical team has the expertise and experience to accomplish the proposed tasks; the proposer's prior experience in similar efforts clearly demonstrates an ability to deliver products that meet the proposed technical performance within the proposed budget and schedule; the proposed team has the expertise to manage the cost and schedule and; similar efforts completed/ongoing by the proposer in this area are fully described, including identification of other Government entities.
In terms of capability, the Government shall assess the Volume 2 bio-sketches provided for the performer team members including the Principal Investigator, Project Manager, and any other key personnel (KP) on the project team as requested by ARPA-H.

12.3.3 Criteria 3: Assessment of Cost Reasonableness

All proposals will be evaluated to determine the reasonableness or value of the proposed price/cost to accomplish the work in the Technical Description Document (TDD). Analysis may be performed to ensure proposed costs are realistic for the proposed scientific and technical approach and capabilities/related experience. Costs should accurately reflect the technical goals and objectives of the solicitation; the

proposed costs must be consistent with the proposer's TDD and reflect a sufficient understanding of the costs and effort needed to successfully accomplish the proposed technical approach. The costs for the prime proposer and proposed sub-awardees should be substantiated by the details provided in the proposal (e.g., the type and number of labor hours proposed per task, the types and quantities of materials, equipment and fabrication costs, travel and any other applicable costs including the basis for the estimates).

It is expected the effort will leverage all available relevant prior research to obtain the maximum benefit from the available funding.

NOTE: Proposers are encouraged to propose the best technical solution. For example, proposers are discouraged from proposing low-risk ideas with minimum uncertainty or to staff the proposed effort with junior personnel to be more appealing from a budget perspective. ARPA-H seeks novel solutions that are reflective of the level of effort and risk proposed.

13 SELECTABLE OR NON-SELECTABLE DESIGNATION

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

13.1 SELECTABLE

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

13.2 NON-SELECTABLE

A proposal is considered non-selectable when the proposal has been evaluated by the government against the evaluation criteria listed in this ISO, and the positive aspects of the overall proposal do not outweigh its negative aspects. Any Proposal that lacks merit in relation to Criterion 1 will be deemed non-selectable overall.

13.2.1 Non-Selectable Criterion 1 Solutions

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

13.3 REVIEW AND EVALUATION TIMELINES

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

13.4 HANDLING COMPETITION SENSITIVE INFORMATION

It is the intent of ARPA-H to protect all proposals as competitive sensitive information and to disclose their contents only for the purpose of evaluation, and only to screened personnel for authorized reasons, in accordance with applicable federal laws and regulations, including FOIA. Restrictive notices notwithstanding, submissions may be handled by ARPA-H support contractors during the evaluation process for administrative purposes and/or to assist with technical evaluation.
ARPA-H support contractors are expressly prohibited from performing ARPA-H-sponsored technical research and are bound by appropriate non-disclosure agreements. Input on technical aspects of a proposal may be solicited by ARPA-H from non-government consultants/experts who are strictly bound by appropriate non-disclosure requirements. No submissions will be returned.

13.5 EVALUATION AND AWARD DISCLAIMERS

The government reserves the right to select for negotiation all, some, one, or none of the proposals received in response to this ISO. In the event the Government desires to award only portions of a proposal, negotiations will commence upon selection notification. The Government reserves the right to fund proposals with phases or options for continued work, as applicable.

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

The government Agreements Officer (AO) will have sole discretion to negotiate all terms and conditions with proposers.

14 POLICY REQUIREMENTS AND MISCELLANEOUS OTHER INFORMATION

14.1 CONTROLLED UNCLASSIFIED INFORMATION (CUI) ON NON-FEDERAL INFORMATION SYSTEMS

Information on Controlled Unclassified Information (CUI) identification, marking, protection, and control is incorporated herein and can be found at 32 CFR § 2002.

14.2 ORGANIZATIONAL CONFLICTS OF INTEREST (OCI)

The Proposer, through submission of a proposal, is required to identify and disclose all facts relevant to any potential OCI involving the Proposer, its organization, and/or any proposed team member (i.e. proposed subawardee). Along with the disclosure, the Proposer may be required to submit a mitigation plan, which is a description of the action the Proposer has taken to avoid, neutralize, or mitigate the stated OCI. The government may require the Proposer to provide additional information to assist the government in evaluating the OCI mitigation plan.
If the government determines the Proposer failed to fully disclose an OCI; or failed to provide the affirmation of ARPA-H support; or failed to reasonably provide additional

information requested by the government to assist in evaluating the proposer's OCI mitigation plan, the government may reject the proposal and withdraw it from consideration for award.

14.2.1 Agency Supplemental OCI Policy

ARPA-H restricts Performers from concurrently providing professional support services, including Advisory and Assistance Services or similar contracted support services, in addition to performing as an R&D technical Performer. Therefore, the Proposer must affirm whether it or any proposed team member (proposed subawardee, etc.) is providing professional support services to any ARPA-H office(s) under: (1) a current award or subaward; or (2) a past award or subaward that ended within one calendar year prior to the proposal's submission date.

If any professional support services are or were provided to any ARPA-H office(s), the proposal must include:

- The name of the ARPA-H office receiving the support,
- The prime contract number, and
- Identification of proposed team member (including any proposed subawardee) providing the support.

14.3 INTELLECTUAL PROPERTY

Proposers must provide a good faith representation that the proposer either owns or possesses the appropriate licensing rights to all IP that will be utilized for the proposed effort. ARPA-H strongly encourages IP rights to be aligned with open-source regimes. Further, it is desired that all non-commercial software (including source code), software documentation, and technical data generated and/or developed under the proposed project is provided as a deliverable to the Government. IP delivered to the Government should align with project or Program goals and should be aligned with the level of government funding provided to generate and/or develop the IP.

14.4 DATA AND DATA MANAGEMENT

Performer-generated data, IP, know-how, trade secrets, etc. must be generated in such a way as to maintain commercial viability for the required, downstream CBP in Phase II while simultaneously adhering to all provisions within the BIOSECURE Act. Project data should be stored in alignment with best practices for each data type.

14.5 RESEARCH SECURITY DISCLOSURES

- Conforming proposals selected for negotiation of a potential award will undergo a Research Security Review (RSR). The RSR involves a review of the proposer's disclosures made as part of the Administrative & National Policy Requirements document, and a validation and comparison of those disclosures utilizing publicly available information and commercially available information tools. Section 10631 of the CHIPS and Science Act of 2022 prohibits federal research agencies, such as ARPA-H, from providing R&D awards in response to any proposal in which a covered individual is participating in a Malign Foreign Talent Recruitment Program (MFTRP). It also requires federal agencies to require recipient institutions to prohibit covered

individuals participating in MFTRPs from working on projects supported by federal R&D awards.

- In accordance with NSPM-33, to receive federal funding, research organizations should identify and mitigate conflicts of commitment (COCs) and conflicts of interest (COIs). COCs and COIs involving foreign countries of concern (FCOCs), including the People's Republic of China, the Russian Federation, the Islamic Republic of Iran, and the Democratic People's Republic of Korea (also known as North Korea), will require risk mitigation plans. A research organization proposing in response to this ISO must provide research security disclosures as described in the Administrative & National Policy Requirements document and the Office of Science and Technology Policy-identified Common Forms. The Common Forms are required for all senior or key personnel.
- After a proposal is selected for negotiations of a potential award, ARPAH will conduct an RSR of each proposer and its senior or key personnel. The RSR is not part of the ARPA-H scientific merit review process. The RSR reviews include assessments of potential risks associated with covered individuals' disclosed or undisclosed participation in MFTRPs, funding received from FCOCs, collaboration with FCOC entities (including researchers and research institutions that have been identified on various entity lists), foreign ownership control or influence with regard to FCOCs identified in proposals, and the pursuit of foreign patents stemming from U.S. government funded research prior to obtaining U.S. patent protections.
- If ARPA-H determines the proposer failed to provide all requisite research security disclosures or failed to reasonably provide information requested by ARPA-H to assist in evaluating the proposer's disclosures and/or research security mitigations, ARPA-H may eliminate the proposal from award consideration. ARPA-H may also eliminate the proposal from award consideration if ARPA-H determines the proposer did not or cannot properly mitigate research security-related risks.

14.6 HUMAN SUBJECTS RESEARCH

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

The informed consent document utilized in HSR funded by ARPA-H must comply with all applicable laws, regulations, and policies, including but not limited to U.S. federal regulations protecting human subjects in research (45 CFR § 46, and, as applicable, 21

CFR § 50). The protocol package submitted to the IRB must contain evidence of completion of appropriate HSR training by all investigators and key personnel who will be involved in the design or conduct of the ARPA-H funded HSR. Funding cannot be used toward HSR until ALL approvals are granted.]

14.7 ELECTRONIC INVOICING AND PAYMENTS

Performers will be required to register in, and submit invoices for payment through, the Payment Management Services (PMS) https://pms.psc.gov.

14.8 GENOMIC DATA SHARING

A resulting award will include the requirement to comply with NIH's Genomic Data Sharing (GDS) Policy (NOT-OD-14-124). Information about the GDS policy can be found at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-24-157.html.

14.9 PROCUREMENT OF SYNTHETIC NUCLEIC ACIDS OR BENCHTOP SYNTHESIZERS

Beginning April 26, 2025, HHS funds may only be used to procure synthetic nucleic acids or benchtop nucleic acid synthesis equipment from sources adhering to the Office of Science and Technology Policy Framework for Nucleic Acid Synthesis Screening. HHS awardees are expected to adhere to the Office of Science and Technology Policy Framework for Nucleic Acid Synthesis Screening for HHS projects.]

14.10 DANGEROUS GAIN-OF-FUNCTION RESEARCH

HHS Funds may not be used to conduct any dangerous gain-of-function research, per the definition in Section 8 of Executive Order (E.O.) 14292 on Improving the Safety and Security of Biological Research. Further, per Section 3 of E.O. 14292, no HHS Funds may be used to fund life science research with foreign entities in countries of concern (e.g., China) pursuant to 42 U.S.C. 6627(c), or in other countries where there is not adequate oversight to ensure that the countries are compliant with United States oversight standards and policies.

ADDITIONAL LINKS

42 U.S.C. § 290c(g)(1)(D); https://uscode.house.gov/view.xhtml?req=granuleid:USC-prelim-title42-section290c&num=0&edition=prelim

ARPA-H's public website; https://arpa-h.gov/explore-funding/open-funding-opportunities

National Archives (CUI Registry); https://www.archives.gov/cui/registry/category-list

ARPA-H's Solution Submission Portal; https://solutions.arpa-h.gov/Ask-A-Question/

CHIPS and Science Act of 2022; https://www.govinfo.gov/content/pkg/PLAW-117publ167/pdf/PLAW-117publ167.pdf

50 U.S.C. § 3059; https://uscode.house.gov/view.xhtml?req=(title:50%20section:3059%20edition:prelim)

Controlled Unclassified Information on Non-Federal Information Systems; 32 CFR § 2002; https://www.ecfr.gov/current/title-32/subtitle-B/chapter-XX/part-2002

Human Subjects Research (HSR); 45 CFR § 46; https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46

Office of Human Research Protection Federal Wide Assurance; https://www.hhs.gov/ohrp/index.html

21 CFR § 56; https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-56

21 CFR § 50; https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-50

- Animal Subjects Research
    - Department of Agriculture rules that implement the Animal Welfare Act of 1966; https://www.nal.usda.gov/animal-health-and-welfare/animal-welfare-act
    - 7 U.S.C. § 2131-2159; https://www.govinfo.gov/content/pkg/USCODE-2015-title7/html/USCODE-2015-title7-chap54.htm
    - Public Health Service Policy on Humane Care and Use of Laboratory Animals; https://olaw.nih.gov/policies-laws/phs-policy.htm
- U.S. Government Principles for the Utilization and Care of Vertebrate Animals

- Used in Testing, Research, and Training; https://olaw.nih.gov/policies-laws/gov-principles.htm

- Guide for the Care and Use of Laboratory Animals: Eighth Edition, Copyright 2011, NAS; https://olaw.nih.gov/policies-laws/guide-care-use-lab-animals

- Worksheet for Applications Involving; Animals https://olaw.nih.gov/sites/default/files/VAChecklist.pdf

- Research Security Disclosures
  - National Security Policy Memorandum 33; https://www.nsf.gov/bfa/dias/policy/nspm-33-implementation-guidance

- Electronic Invoicing and Payments
  - Payment Management Services; https://pms.psc.gov/