



In-Space Production Applications: Tissue Engineering and Biomanufacturing

ISS National Lab Research Announcement (NLRA) 2023-2

Instructions to Offerors

Center for Advancement of Science in Space, Inc.

6905 N. Wickham Road, Suite 500, Melbourne, FL 32940

Issuance Date: October 3, 2022

End Date of Step 1: Concept Summary submission period: November 29, 2022

Due Date for Step 2: Full Proposal submission: February 28, 2023*

(* by invitation only)

Note: For any updates regarding submission deadlines, please visit www.issnationallab.org/research-on-the-iss/solicitations/nlra2023-2. For general questions related to this research announcement, please email ispa@ISSNationalLab.org.

CONTENTS

I. SUMMARY	1
II. DESCRIPTION OF RESEARCH	1
Background	2
ISS National Lab Implementation Partners, Facilities, and Capabilities	2
Relevant ISS Facilities	2
Research and Technology Development Objectives and Priorities.....	3
III. SUBMISSION AND SELECTION PROCESS	4
Step 1: Concept Summary Submission	4
Step 2: Full Proposal Submission.....	5
Award Information.....	5
IV. PROPOSAL PREPARATION AND CONTENT	6
Offeror Qualifications.....	6
V. PROPOSAL EVALUATION AND SELECTION	6
VI. CONTRACTING AND COMPLIANCE	7
Appendix A: Technology Readiness Level Descriptions	8

I. SUMMARY

Since 2000, the International Space Station (ISS) has enabled humans to live and work in space, supporting research and technology development that is not possible anywhere on Earth. Since its designation in 2005, the ISS National Laboratory has expanded access to this orbiting laboratory to research communities from U.S. academic institutions, government agencies, and the private sector. ISS National Lab-sponsored research seeks scientific discovery and technology advancement on the ISS that directly benefit humanity by increasing fundamental knowledge, scientific application, education outreach, or workforce development, and demand creation for sustainable, scalable innovation and production in low Earth orbit (LEO).

As managers of this national laboratory in partnership with NASA, the Center for the Advancement of Science in Space, Inc. (CASIS) awards access to funding and resources on the ISS via competitive grant solicitations to support non-exploration science and technology development as well as science, technology, engineering, and mathematics (STEM) education initiatives from U.S.-based institutions.

As a U.S. taxpayer-funded organization, CASIS only contracts with U.S. Persons, as defined by the Code of Federal Regulations at 22 CFR §120.15. Submitted proposals must be compliant with all U.S. Export Administration Regulations (EAR) and International Traffic in Arms Regulations (ITAR). This document will assist offerors in the development of concepts and proposals to leverage the ISS for applied research and technology development and demonstration.

II. DESCRIPTION OF RESEARCH

This ISS National Lab Research Announcement (NLRA) is soliciting proposals that seek to demonstrate space-based biomanufacturing activities in microgravity. In-space biomanufacturing applications refers to LEO-based applied R&D microgravity regenerative medicine applications seeking to demonstrate space-based manufacturing and production activities that enable new business growth and capital investment, represent scalable and sustainable market opportunities, and produce reoccurring value with the potential to generate demand for and revenue from access to space. Research concepts are desired for which space-based testing can uniquely enable technical solutions to known or new science and engineering challenges and the creation of new products and business opportunities. The objective is to use the unique ISS environment to develop, test, or mature products and processes that have a demonstrated potential to produce near-term, positive economic impact.

The ISS National Lab enables scientific research and technology demonstration within a persistent microgravity environment in orbit. When gravity is no longer a dominant physical force, myriad effects on physical and biological systems and chemical and biological processes are induced. In some cases, these unique effects may enable the discovery of new phenomena that can be leveraged to improve existing or create new technologies. Technology demonstrations utilizing the extreme conditions of the space environment in LEO may be conducted using facilities within the crewed habitat of the ISS or on external facilities attached to the ISS, including platforms for materials exposure testing. Offerors' proposals may also seek to develop new ISS National Lab facilities for in-space biomanufacturing applications.

Background

The ISS National Lab offers the opportunity to conduct months-long experiments in persistent microgravity, where gravity-driven physical forces are negligible. Research results have been shown to uncover new practical insights and tangible benefits to multiple cross-cutting science and engineering fields and areas of industrial application.

The ISS National Lab supports a variety of facilities and hardware to exploit the extreme LEO environment for development and testing of new materials, devices, and subsystems. Such testing provides a mechanism for rapid failure mode analysis, thereby accelerating the qualification and commercial readiness of these new devices and products. Additional information is also provided in NASA's [ISS Researcher's Guide Series](#).

ISS National Lab Implementation Partners, Facilities, and Capabilities

Offerors should be familiar with capabilities of flight hardware for in-orbit studies that are relevant to their proposed scientific and technical objectives. Existing flight hardware can be referenced on NASA's [Space Station Research Explorer website](#).

The ISS National Lab partners with a variety of Implementation Partners—organizations that provide research, engineering, and technical services, and in some cases, operate and maintain commercial payload facilities on the ISS—to support and facilitate flight projects. For details about these providers and their specific hardware/services, visit our [Implementation Partner database](#). Where applicable, the ISS National Lab encourages contact between offerors and Implementation Partners prior to the submission of a Step 1 concept in order to obtain accurate and current information required for budget and schedule estimates. If requested, the ISS National Lab can facilitate contacts between Implementation Partners and offerors. Proposals to utilize commercial facilities owned and operated solely by international partners on the ISS will not be considered for this research announcement.

Relevant ISS Facilities

Facilities and services to support cell culture and cell- and tissue-based research and technology development are available on the ISS. Some of these facilities are described below. These and other facilities and services may be provided by NASA or Implementation Partners. For a listing of ISS facilities provided by NASA, please consult the NASA [ISS Researcher's Guide Series](#), including [“A Researcher's Guide to Cellular Biology.”](#) Information on commercial facilities and services for cell science in microgravity is available from organizations listed in the [Implementation Partner database](#).

As a fully functioning laboratory, the ISS National Lab supports a variety of multipurpose facilities to leverage microgravity conditions to advance life science research. The ISS platform includes microscopes, centrifuges, and freezers (to keep specimens cold before, during, or after use). In-orbit technologies include multipurpose facilities, tools, and systems for biology and human physiology, hardware for multiple methods of macromolecular crystal growth, and even nucleic acid sequencing technologies. Specific examples of life science facilities include, but are not limited to, the following:

- [BioFabrication Facility \(BFF\)](#): This platform will enhance bioprinting capabilities available on the space station. The system will be capable of culturing a defined heterogeneous cell population to bioprint tissues and organs that can then be implanted into patients.

- [*Advanced Space Experiment Processor \(ADSEP\)*](#): This platform is a thermally controlled single-middeck-locker equivalent that accommodates up to three cassette-based experiments that can be independently operated. Its companion hardware consists of a collection of several experiment cassettes, each doubly or triply contained, that accommodate experiments in cell technology, model organisms, multiphase fluids, solution chemistry, separation science, microencapsulation, and crystal growth.
- [*Multi-use Variable-gravity Platform Validation \(MVP\)*](#): This platform enables experiments that examine how organisms respond to artificial gravity (up to 2 g) in the space environment.
- [*Space Automated Bioproduct Laboratory \(SABL\)*](#): This platform supports a variety of investigations in the life, physical, and materials sciences, with a focus on supporting research of biological systems and processes.
- *Imaging systems*: These include but are not limited to multiple, commercial off-the-shelf light imaging microscope facilities and spectrophotometers.
- [*Nanoracks CubeLab Modules*](#), [*Space Tango TangoLabs*](#), [*Lamont Aerospace facilities*](#), and [*ICECUBES facilities*](#): These platforms enable a broad range of experiments that examine how biological and physical systems respond to microgravity—with applications in tissue engineering, regenerative medicine, pharmaceutical development, biofuels, and other sectors.
- [*Life Science Glovebox \(LSG\)*](#): This platform is a sealed work area that accommodates life science and technology investigations in a “workbench” type environment. Due to its larger size design, two crew members can work in the LSG simultaneously.

A listing and description of current or soon-to-be available facilities for life sciences investigations on the ISS can be browsed using [NASA’s Space Station Research Explorer](#) web tool. Offerors are encouraged to seek out additional information on the facilities from their operators. The ISS also offers virtually uninterrupted worldwide data and communication capabilities to support research in both the external and internal environments of the station.

Research and Technology Development Objectives and Priorities

ISS National Lab applied research and technology development is intended to validate technological advancements and rapidly advance the development of new Earth- or space-based products to bring value to our nation and drive a robust, sustainable, and scalable LEO economy. These objectives will be achieved by successfully executing flight experiments utilizing microgravity or the extreme conditions in LEO.

This solicitation focuses on proposals within the areas of regenerative medicine, tissue engineering, and biomanufacturing. This topic includes, but is not limited to, projects that demonstrate the following: the benefits of stem cell expansion and/or stem cell research in microgravity for therapeutic application(s) on Earth; an organoid culture system or multicellular culture system to model human disease and/or test therapeutics for the treatment of disease on Earth; or a system for the in-space biofabrication (e.g., additive manufacturing) of human tissue or other biocompatible material for regenerative medicine application(s) on Earth. Proposals seeking to advance the TRL of potentially high-science return initiatives well-suited to address limitations presented by ground-based (i.e., gravity-impacted) processes are of particular interest for this solicitation.

In-space biomanufacturing applications is a strategic focus area to promote LEO-based applied R&D projects in microgravity for regenerative medicine applications seeking to demonstrate space-based

manufacturing and production processes. In 2021, CASIS co-hosted a Biomanufacturing in Space Symposium to identify and prioritize opportunities for LEO commercialization in the area of biomanufacturing. Papers resulting from the symposium may be accessed at www.preprints.org/manuscript/202108.0044 and <https://doi.org/10.1016/j.stemcr.2021.12.001>.

Proposals must include a statement defining how the scientific or technical aims will benefit from execution in space and why the proposed investigation can only be performed in space. Offerors should explore the literature for prior research on the ISS, space shuttle, MIR, and Skylab that may help improve their experimental design and deliver novel, high-impact results.

Responsive proposals must describe milestones for successful space-based experiments and the projected timeline to mature the technology or advance a product toward a viable market offering. Technologies proposed for testing should generally be beyond basic concept validation and instead focus on seeking technological maturity through development and/or demonstration in the space environment. Desirable flight experiments will target raising the TRL from 4 or higher to 6 or higher (see Appendix A for a description of TRL). Ideally, projects will deliver a biological product that will benefit from being produced in space, a proof of concept for the manufacture of a biological product in microgravity, or a key result that will lead to a biological product with improved performance that can be produced in space.

The ISS National Lab strongly recommends obtaining and submitting letters of support from commercial partners and/or potential users of new technologies or products to demonstrate feasibility or commercial interest, when applicable.

Projects that may require multiple flights to the ISS will be accepted for submission. However, offerors seeking multiple flight opportunities must provide an estimate of the projected number of flights required and include sufficient detail in their concept to justify the expected R&D outcome of each flight or phase of the project leading to a complete solution.

III. SUBMISSION AND SELECTION PROCESS

This research announcement will follow a two-step proposal submission process. Before being invited to submit a full proposal, all interested investigators must first complete and submit for review a Step 1: Concept Summary. The purpose of the Step 1 summary is to provide information for an initial evaluation of the concept for operational feasibility, scientific or technological scope, compliance, and alignment with the scope of the research announcement prior to submission of a full proposal.

Step 1: Concept Summary Submission

- Concept summaries must use the template provided on the research announcement webpage.
- Concept summaries may be submitted and will be received, evaluated, and potentially approved continuously during the research announcement open period. No concepts will be accepted after the Step 1 close date for a given cycle. Offerors may revise and resubmit the concept to a later cycle.
- A CASIS internal review team with representatives from science, business, operations, and compliance will evaluate each concept summary. Approved concept summaries will be invited to submit a full proposal.
- Concepts approved based on Step 1 evaluation will proceed to Step 2 by invitation only.
- Concepts not invited to submit a Step 2: Full proposal will receive feedback.

Step 2: Full Proposal Submission

- The process for developing full proposals is outlined below and set forth in greater detail within the Proposal Instructions published on the research announcement webpage.
- Full proposals will be evaluated in accordance with proposal evaluation documents provided as attachments.
- At the end of Step 2, the proposals recommended for selection will be presented for final determination to the CASIS chief executive officer, who is the selecting official.

Further details and requirements for the concept summary and full proposal submission, including instructions and templates, can be found in the Proposal Instructions document available on the research announcement webpage at www.issnationalallab.org/research-on-the-iss/solicitations/nlra2023-2.

Award Information

CASIS may award a funded or unfunded agreement for a selected proposal. All awarded proposals will receive ISS National Lab sponsorship of ISS resource utilization, payload launch to the ISS, in-orbit ISS crew time, data return, and payload return, if required. Grant funding is not available for purely ground-based efforts not leading to flight research.

Funds Availability: The obligation of CASIS to make an award is contingent upon the availability of funds from which payment can be made. The number of grants awarded and the amount of grant funding for each award will depend on the number of meritorious applications received and favorably reviewed.

Funding for this Research Announcement: Total set aside funding for this research announcement is approximately \$1,000,000 with an expectation to make three to five awards. CASIS funding is to be allocated to support project development costs (both direct and indirect costs) and mission integration and operations (Implementation Partner) costs. It is anticipated that CASIS will execute task orders and/or subcontracts directly with the Implementation Partner on behalf of the awarded principal investigator. CASIS reserves the right to refuse award of grant if no meritorious offers are received.

Indirect Cost Rates: CASIS will allow any previously approved federal indirect cost rate that has been negotiated between the grantee and a U.S. government agency. If no such rate has been negotiated with a U.S. government agency, CASIS shall apply a *de minimis* indirect rate of ten percent (10%) for those seeking indirect costs in a grant award. Also, CASIS will allow a grantee to voluntarily waive indirect costs or charge less than the full *de minimis* indirect cost rate should they choose to do so.

All proposal submissions seeking funding from CASIS are subject to this policy. All grantees are required to provide satisfactory written evidence in or accompanying their proposal submission of a previously approved federal indirect rate. Such evidence shall demonstrate the existence of an approved federally recognized indirect cost rate negotiated between the grantee and a U.S. government agency. In the absence of this evidence, CASIS will apply the *de minimis* indirect cost rate stated above.

Notice of Award: For selected proposals, a CASIS officer will contact the principal investigator named in the proposal. Offerors have the right to be informed of the major factor(s) that led to the acceptance or rejection of their proposal.

Period of Performance: It is anticipated that the period of performance will be no longer than three (3) years from date of award.

CASIS assumes no liability (including bid and proposal costs) for cancelling this research announcement or for any entity's failure to receive notice of cancellation.

IV. PROPOSAL PREPARATION AND CONTENT

The Step 1: Concept Summary instructions and the Step 2: Full Proposal submission guidelines can be found in the Proposal Instructions available on the ISS National Lab research announcement webpage.

Before submission of a Step 1: Concept Summary, offerors are encouraged to identify and begin working with an Implementation Partner—organizations that work with the ISS National Lab to provide services related to payload development. There are two ways to identify an Implementation Partner:

- Visit www.issnationallab.org/implementation-partners to browse, select, and contact an Implementation Partner.
- Email the ISS National Lab Payload Operations team at Ops@ISSNationalLab.org for guidance.

Offerors are strongly encouraged to discuss any aspects of their experiment that they deem significant beyond its standard description with their Implementation Partner.

- **Before finalizing proposals, offerors are strongly encouraged to consult with the ISS National Lab Payload Operations team (Ops@ISSNationalLab.org)** for feedback regarding feasibility and compliance with flight requirements and capabilities. Please include reference to NLRA 2023-2 in the subject line and note that questions and answers will be posted on the ISS National Lab website. Offerors are also encouraged to work with an Implementation Partner.

Offeror Qualifications

Proposals must be submitted by a principal investigator or an authorized official of the proposing organization. Any individual business entity or institution capable of executing the proposed research may submit a proposal. However, CASIS will **ONLY** consider proposals from U.S. persons (business and individual), as defined by the Code of Federal Regulations (22 CFR §120.15).

V. PROPOSAL EVALUATION AND SELECTION

Proposals will be evaluated under the ISS National Lab's review and selection criteria for its In-Space Production Applications line of business. The proposal evaluation factors are scientific and technical merit, business and economic merit, funding and resource commitment, implementation and commercialization feasibility, and operations and ISS utilization. Each factor is numerically weighted and scored. Project cost is not scored but is a factor in the final selection. All proposals submitted must include an expressed commercial purpose or intent. Proposals that are determined to better fit other CASIS research announcements will be redirected to those areas.

Please note that CASIS will not accept or consider proposals submitted by NASA or NASA civil servants.

The proposal review is guided by an overall assessment of expected project impact upon successful completion of proposed objectives. CASIS has overall responsibility for conducting and facilitating reviews, presenting information for final determination, and ensuring compliance with CASIS-defined

processes. For further information on the proposal evaluation and selection process, including the relative importance of each evaluation factor, refer to the ISS National Lab Proposal Evaluator Instructions in the information package linked to the research announcement webpage.

VI. CONTRACTING AND COMPLIANCE

Offerors and their sponsoring organizations shall be U.S. Persons, as defined by the Code of Federal Regulations ([CFR](#)), and must be compliant with Export Administration Regulations (EAR) and International Traffic in Arms Regulations (ITAR).

Award recipients will be required to enter into a User Agreement or Grant Agreement with CASIS. As a nonprofit corporation doing business with the federal government via a Cooperative Agreement with NASA, CASIS is contractually bound, and bound by federal procurement law and regulations, to flow down to award recipients various contractual obligations that are in the CASIS Cooperative Agreement with NASA. The obligations are regulated in part by the Federal Acquisition Regulations (FAR), 48 C.F.R., as well as NASA-specific regulations. Mandatory clauses are non-negotiable and cannot be removed from CASIS User Agreements or Grant Agreements. If an award recipient does not desire to or cannot comply with mandatory flow down clauses, the awardee should not accept the award opportunity. These terms and conditions from the NASA Cooperative Agreement will apply to all Grant Agreements (funded) and User Agreements (unfunded). The documents listing the mandatory flow down provisions contained in a User Agreement and Grant Agreement are provided as part of the Step 1 and Step 2 zipped documents made available to offerors via the CASIS web page for this research announcement.

Appendix A: Technology Readiness Level Descriptions

Actual system “flight proven” through successful mission operations	TRL 9	COMMERCIALIZATION <ul style="list-style-type: none"> Product manufacturing Product sales <ul style="list-style-type: none"> Roll out for real-world application/deployment
Actual system completed and “flight qualified” through test and demonstration (ground or space)	TRL 8	
System prototype demonstration in a space environment	TRL 7	TRIALS/SCALE-UP <ul style="list-style-type: none"> Regulatory approval/certification Business analysis Market testing <ul style="list-style-type: none"> Testing on subjects/commercial target Manufacturing development/scale-up
System/subsystem model or prototype demonstration in a relevant environment (ground or space)	TRL 6	
Component and/or breadboard validation in a relevant environment	TRL 5	DESIGN/PRODUCT REFINEMENT <ul style="list-style-type: none"> New Applications, Product Improvements, and Line Extensions (NAPILEX; existing products) Product development/testing in advanced models Production development/optimization Product design/market research Business/market definition
Component and/or breadboard validation in a laboratory environment	TRL 4	
Analytical and experimental critical function and/or characteristic proof-of-concept	TRL 3	DISCOVERY/BASIC RESEARCH <ul style="list-style-type: none"> Testing in validated early models (optimization to candidate) Science development (model development/market understanding) Fundamental research <ul style="list-style-type: none"> Research leading to understanding of natural phenomena Screening and testing in basic models to identify the target
Technology concept and/or application formulated	TRL 2	
Basic principles observed and reported	TRL 1	