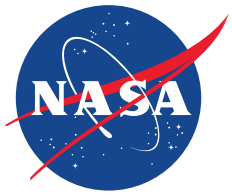

A Strategy for the Future of the International Space Station (ISS) National Laboratory (ISSNL) and Commercial Low-Earth Orbit (LEO) Development

For nearly 20 years, the United States has had at least one of its citizens continuously living and working in space in orbit around Earth. New commercial technologies and capabilities, including future commercial human spaceflight to the International Space Station (ISS), signal a new era. Accordingly, NASA has recognized it is also time to begin a new era in its management of the ISS National Laboratory (ISSNL).

The origin of the ISSNL dates to the National Aeronautics and Space Administration (NASA) Authorization Act of 2005. Congress designated "the U.S. segment of the ISS as a national laboratory," directed the Administrator "to seek to increase the utilization of the ISS by other federal entities and the private sector," and allowed, but did not require, the Administrator to contract with a nongovernmental entity to operate the new national laboratory. From the moment the bill was signed into law, the entire U.S. segment of the space station has been a designated National Laboratory, which NASA managed directly from 2005 until 2011. In the NASA Authorization Act of 2010, Congress directed NASA to enter into a cooperative agreement with a not-for-profit entity to manage the ISSNL. This direction was realized in 2011 when NASA entered into a 10-year cooperative agreement with the Center for the Advancement of Science in Space (CASIS). In July 2017, NASA extended this cooperative agreement with CASIS to September 2024.

In 2019, as NASA was approaching the 10th year of this cooperative agreement, NASA Administrator Jim Bridenstine directed an external review of the ISSNL, managed by CASIS, and engaged an Independent Review Team (IRT). The IRT delivered its resulting final report to NASA in February 2020, and the Agency has carefully reviewed the team's findings and recommendations. NASA thanks and acknowledges the IRT for its thorough efforts to deliver a balanced assessment of the ISSNL and expresses sincere gratitude to the IRT chairperson, Dr. Elizabeth Cantwell, for her leadership.

The IRT's report recognizes the enormity of the ISSNL's mission, the progress made to date, and that the underlying set of expectations and predicted futures for both the ISSNL and the space station itself have evolved dramatically since 2011. As such, the IRT concludes that changes are needed to ensure maximum benefit of this time-limited resource.

The IRT's findings also criticize both CASIS's performance and NASA's management of the ISSNL cooperative agreement. The IRT makes a strong case that the ISSNL management model established in 2011 has become inflexible and needs to respond to the changing landscape of ISS utilization. Since 2011, the changes for ISS have included:

- Full utilization of the resources available for research on the station;
- Establishment at NASA of the Division of Space Life and Physical Sciences Research and Applications (SLPSRA) (within the Human Exploration and Operations (HEO) mission directorate) to conduct basic and applied science in space. Priorities are guided by the 2011 Decadal Survey for Life and Physical Sciences Research at NASA and continue previous work of the Office of Biological and Physical Research;
- Dramatic growth of the commercial space industry with companies now attracting their own customers; and
- NASA's development of its strategy to enable a robust commercial low-Earth orbit economy.

These developments have resulted in confusion about the role of CASIS, and it was apparent to both NASA and the CASIS Board of Directors that a new operating model was needed to ensure American citizens realize the highest return on their investment in the ISS for the remainder of its operational lifetime.

NASA's forward plan is based on the IRT's findings and recommendations, many of which validate changes for which NASA and CASIS had already planned before the initiation of the Independent Review:

1. NASA and the CASIS Board of Directors are re-examining and adjusting the roles and composition of both the Board of Directors and the organization's executive leadership consistent with the IRT's recommendations and prior planning by NASA and CASIS.

2. In line with the IRT's recommendations and prior planning by NASA and CASIS, CASIS is establishing an ISSNL User Advisory Committee (UAC) to provide user input and perspective about how the ISSNL resources should be managed; such feedback will be provided to CASIS. The UAC will consist of members from organizations that have formal agreements with NASA or CASIS to utilize the ISSNL and existing NASA and other governmental agencies sponsoring ISS research.

3. In cooperation with the UAC, NASA and CASIS will create transparent project and program evaluation and prioritization processes. These processes will be applied to every payload requesting ISSNL resources, conforming with the IRT's recommendations.

4. To ensure NASA is speaking with one voice, in accordance with the IRT's recommendations, the ISSNL budget, strategy, and NASA liaison function will be

managed at NASA under the direction of an ISSNL Program Executive. The ISS Program Office at NASA's Johnson Space Center (JSC) will manage and integrate overall ISSNL resource allocations through the Program Science Control Board (PSCB) in coordination with the ISSNL Program Executive.

5. NASA's Program Executive will manage the ISSNL through the Cooperative Agreement with CASIS by updating strategic priorities on an annual basis, in line with the IRT's recommendations. The strategic priorities will define resource use for specific types of activities (e.g., basic science investigations, scalable industrial space applications, commercial facility usage, and education and outreach).

6. NASA and CASIS (with input from the UAC to CASIS), will manage prioritization and allocation of ISSNL resources (i.e., 50% of the total NASA portion of the U.S. Orbital Segment (USOS) resources, especially crew time) to meet the strategic priorities, in line with the IRT's recommendations. NASA will provide guidelines for sub-allocations to areas in competition for ISSNL resources such as upmass and downmass, crew time, and cold stowage. These areas include but are not limited to:

a. Commercialization projects focused on enabling sustainable, scalable commercial applications with the ability to generate non-NASA revenue;
b. Commercially-sourced investigations using hardware owned and operated by commercial companies with facilities on the ISS;
c. Fundamental research into the physical and life sciences as sponsored by NASA or other governmental agencies (OGA), and by non-governmental entities;
d. Early technology readiness level (TRL) demonstrations not critical to the NASA exploration mission with sufficient spaceflight justification and regardless of sponsor; and
e. Science, Technology, Engineering, and Mathematics (STEM) education and outreach projects. This new era in NASA's management of the ISSNL also presents an opportunity for the Agency to take new steps in NASA's efforts to accelerate a thriving commercial economy in low-Earth orbit. NASA appreciates the IRT's input into potential areas of R&D that could lead to a thriving commercial low-Earth orbit economy. The new priority on space industrialization, indicated by allocation areas (a) and (b) above, will serve to implement a core component of NASA's plan for commercial development in low-Earth orbit – the demand stimulation of sustainable, scalable, commercial applications of low-Earth orbit – and provide new impetus and focused resources. To this end, NASA will work with CASIS as described above to identify strategies and roadmaps to focus efforts toward the evolution of promising industrial programs, including development of criteria for on- and off-ramp of these programs from subsidized ISSNL resources.

NASA's renewed commitment to the management of the ISS as a National Laboratory also has provided new focus for another core component of NASA's five-part Plan for Commercial LEO Development to achieve a robust low-Earth orbit economy. NASA intends to maintain continuous human spaceflight capabilities in low-Earth orbit,

and therefore expects to operate the ISS until new commercial habitable platform(s) are available and can support the Agency's needs as one of many customers. Looking to the future, NASA will study the viability of establishing a low-Earth orbit National Laboratory that would acquire services from at least one new space station, and which would be operated in a manner similar to a traditional national laboratory.

NASA is grateful for the ongoing support of the CASIS Board of Directors and CASIS employees, who remain critical to the management of this important national effort. NASA also appreciates the CASIS team's dedication and commitment to the mission of the ISSNL. NASA is committed to the continuation and expansion of its legacy of human spaceflight and scientific and engineering leadership in low-Earth orbit and is excited and optimistic about this new phase for the ISSNL.

International Space Station (ISS) Cooperative Agreement
Independent Review Team

FINAL REPORT TO NASA

Delivered February 4, 2020

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Executive Summary

The International Space Station (ISS) represents one of mankind's most remarkable engineering feats, providing a platform for advancing fundamental knowledge and translation of these insights into potential benefits for exploration, national security, industrial competitiveness, and a range of broader societal benefits.

As a platform for scientific investigation and research, the ISS plays a vital role in advancing NASA's long-term, deep space exploration goals. Because of its proximity in low Earth orbit (LEO) and its microgravity environment, the ISS provides a unique, relatively accessible setting for scientific research, including the study and potential mitigation of a variety of human health risks on long-term exploration missions.

The NASA Authorization Act of 2010 (P. L. 111-267) required NASA to pursue additional international, commercial, and intergovernmental partnership arrangements to enhance the overall sustainability of the ISS and directed that an independent body be established to serve as the designated agent to manage the ISS National Laboratory (ISSNL). The act specifically required NASA to enter into a cooperative agreement (CA) with an appropriate not-for-profit organization to manage the activities of the ISSNL for non-NASA utilization of the ISS research capabilities and available facilities. The act also guaranteed National Laboratory managed experiments access to a minimum 50% of U.S. research capacity and crew time.

In August 2011, NASA awarded a 10-year, $136 million CA to Center for the Advancement of Science in Space (CASIS) to manage the ISSNL. In July 2017, NASA extended the CASIS CA to September 2024, increasing its total cost to $196 million.

The Independent Review Team (IRT) found that the ISSNL was created at a specific time for a specific purpose to address potential shortfalls in ISS utilization. However, the underlying set of expectations and predicted futures have evolved dramatically in the intervening 15 years. There are now entities using the ISS beyond the scope originally envisioned for the ISSNL as well as competition between NASA and the ISSNL for crew time, critical on-orbit facilities and "credit" for research results.

The IRT does not find that the ISSNL is a National Laboratory in any sense other than its legislative designation. To preclude the ISSNL from conducting work for its sponsor meets neither the spirit nor intent of a National Laboratory. There are four overarching issues with the current approach to managing the ISSNL: 1) The CASIS business structure does not reflect the typical structure or function of other non-profit organizations; 2) There is no routine and credible user community integration; 3) Oversight by the Federal sponsor has been poorly managed; and 4) Entry and exit procedures to/from the ISSNL are poorly defined.

While the authorizing legislation and CA have shifted significantly over the years, the IRT could not find that the CA fully met the intent of the authorizing legislation and it was clear that the CA never embodied the flexibility needed to meet a natural shift in intent, pursuant to changes in the ISS mission. While the CA mechanism can be used in a very flexible manner, it appears that NASA has increasingly revised the CA with CASIS to become less flexible, more prescriptive, and more demanding. Therefore, the CA with CASIS has not optimized a balance between scientific research and commercialization, and the relationship between NASA-funding scientific research and the ISSNL has not been cooperative. Both this lack of flexibility and the ill-defined mission of the ISSNL have harmed NASA and CASIS, resulting in unprofessional behavior on the part of NASA, and un-business like behavior on the part of CASIS. This was the result of long-standing neglect of the proper approaches needed by CASIS to run a viable 501(c)(3), and by NASA as the Federal agency providing sole funding to this entity to oversee and manage the

relationship. Further, the separate and distinct roles of Board and User Advisory Committee have been conflated.

The IRT found that CASIS lacks a purpose-driven mission statement. Consequently, priorities shift between research and commercialization. NASA and CASIS must define how these are to be allocated against the many needs of research, applied efforts, commercialization of products and stimulation of LEO commercialization. NASA has used CASIS and its results mainly for public relations and has played an insufficient role in driving what CASIS does. CASIS has been left to define and re-define success based on a "many voices" approach from NASA that has driven inflexible and potentially damaging board and operational behaviors. Changes in NASA personnel in the NASA-ISSNL liaison role, with accompanying high variability in strategic guidance has exacerbated this problem.

The CASIS model for project selection is outdated. The selection criteria for funding ISS investigations appear to place considerable importance upon social aspects of ISS projects and insufficient value on commercialization and progressive improvement of scientific knowledge. The process being used by CASIS for project selection is opaque. It involves their own staff, supplemented by several outside "experts" using a dubious economic graph tool. This methodology is unlike that of other major funds-granting agencies and does not appear to be well understood by NASA, the Implementation Partners, or the awardees. NASA has never taken full ownership of understanding and approving these methods. This lack of transparency has been tolerated throughout the life of CASIS resulting in an insular board which has been allowed to take a far too granular role in managing the operations of the entity.

NASA must recognize that the definition of success for CASIS has shifted as the Nation's goals for the ISS and LEO Commercialization have shifted. The value of access to the ISS is unparalleled and can result in a great deal of excellent research. Commercialization is a long game and partners are willing to play, but as commercial activities increase in value, the "voice of the user" becomes increasingly important. The 50% resource allocation has been interpreted and managed holistically, rather than the resource level, meaning that some assets potentially critical to NASA's needs were completely unavailable due to the allocation entirely to CASIS. The limiting factor of access to crew time needs to be acknowledged and managed at the outset of every partnership/agreement. Only recently has CASIS assigned a portion of the ISSNL portfolio to "programs, not projects," with an eye toward the longer-term optimization of industrial and manufacturing processes in LEO that might have future commercial value, and it is unclear what (beyond a desire to get in front of this very review) motivated this shift in portfolio allocation.

Consolidated Findings and Recommendations

Findings

Finding 1.1: The ISS National Laboratory was created as a broad-based research facility, but NASA reduced ISS research in 2004-2005 to focus on human health and safety. Congress did not want to lose the broad research facility for activities in LEO and the SLPSRA Division of HEOMD did not exist at the time of the original legislation. Consequently, there is now a NASA division tasked with enabling research activities that potentially overlap with the ISSNL. Both SLPSRA and CASIS perceive that they often operate in competition with one another for crew time, critical on-orbit facilities and "credit" for research results.

Finding 1.2: ISSNL was created at a specific time for a specific purpose to address potential shortfalls in ISS utilization. This problem no longer exists; the ISSNL has a robust portfolio of activities. However, the underlying set of expectations and predicted futures have evolved dramatically in the intervening 15 years – to include commercial LEO, new NASA and US perspectives and priorities on commercializing space, visions for human exploration and expansion of potential platforms upon which to conduct science.

Finding 1.3: There are now entities using the ISS beyond the scope originally envisioned for the ISSNL. The IRT heard from commercial stakeholders and Implementation Partners that this is a challenge and that they have little way to make their needs and desires heard.

Finding 1.4: There is confusion regarding the scope and purpose of the authorizing legislation among stakeholders and how it is represented in the CA between NASA and CASIS. There are slight to large differences in interpretations of what the ISSNL is supposed to do, many different definitions of the mission of the ISSNL, and no shared vision.

Finding 1.5. The functions of the ISSNL liaison and the INLAC have been implemented differently than the original intent of authorization language. It is not clear that this implementation has been fulfilled the critical need for oversight and stakeholder engagement

Finding 2.1: National Laboratories within the U.S. do not provide useful models for NASA to compare and consider when looking at the future of the ISSNL. ISSNL is unique in its mandated focus on non-NASA research and its secondary focus on non-research activities.

Finding 2.2: There is dysfunction in the Board Structure and Board-CEO dynamic. The previous board structure was inappropriate for the business structure; a 15 person board for a 60 person organization is excessive. Typically, 501(c)(3) organizations do not employ compensative boards. Rather, boards should be motivated by mission, not personal interest. It is not clear that CASIS corporate bylaws have been fully reconciled with changes to the CA.

Finding 2.3: The separate and distinct roles of Board and User Advisory Committee have been conflated. As noted in GAO-15-397, "NASA has still not staffed an Advisory Committee with which CASIS is required to interact."

Finding 2.4: The lack of operating structures typical for a startup or oversight structures typical for a Federally Funded Research and Development Center (FFRDC) has placed CASIS in the role of commercialization sponsor on the ISS. While this role does not meet the broader vision

outlined in 2005 and 2008 congressional authorization language, it is in keeping with the "one of many" construct presented in the NASA Transition Authorization Act of 2017.

Finding 2.5: CASIS's Value Impact Model does not address allocation of resources when meritorious projects exceed the capacity of the ISSNL. Furthermore, CASIS does not appear to have a mechanism in place to sunset projects because of success (program is ready to function independent of ISSNL, such as a purpose-built commercial platform) or failure (unsuccessful startup).

Finding 3.1: CASIS lacks a purpose-driven mission statement. Consequently, priorities shift between research and commercialization with neither NASA or stakeholder input There is a need to balance scientific research and commercialization against NASA-defined priorities. There is a definitive and very finite set of assets available. NASA and CASIS must define how these are to be allocated against the many needs of research, applied efforts, commercialization of products and stimulation of LEO commercialization.

Finding 3.2: The CASIS model for project selection is outdated. It needs to reflect not only quality but commercial promise. Lack of reliable access to ISS appears to be a major problem. Commercially, time is money. CASIS has developed an elaborate, in-house methodology for selection of US-sourced ISS science experiments. The selection criteria for funding ISS investigations appear to place considerable importance upon social aspects of ISS projects and insufficient value on commercialization and progressive improvement of scientific knowledge.

Finding 3.3: The process being used by CASIS for project selection is opaque. It involves their own staff, supplemented by several outside "experts" using a dubious economic graph tool. This methodology is unlike that of other major funds-granting agencies and does not appear to be well understood by NASA, the Implementation Partners, or the awardees.

Finding 3.4: Functionally, the relationship between NASA and CASIS appears to be devolving to the management (M&O) function specified in section 2.1.3 of the CA. It provides free access and utilization of instrumentation and facilities. NASA has driven CASIS to add the stimulus function to create its own R&D portfolio to meet metrics that are tied to utilization (e.g., number of PIs, publications) rather than to purpose.

Finding 3.5: Since its inception through FY18, CASIS has received approximately $109M through its CA with NASA. CASIS reports more than $180M of additional economic activity for the ISSNL[1], which includes cost sharing from universities and companies for their programs and projects on the ISS, Implementation Partners investments to support ISSNL projects, contributions from other government agencies to stimulate research using the ISSNL, and private investment.

Finding 3.6: NASA has internal confusion regarding the delineation of basic or applied "research," "industrialization," and "commercialization."

Finding 3.7: Meaningful long-term investment by the commercial sector (or other federal agencies) to develop a LEO economy will require a more proactive dialog between NASA, the ISSNL operator and interested commercial parties to realign ISSNL resource allocation to promote translational R&D on a larger scale. This will also allow the ISSNL operator to adopt more stringent performance criteria by the private sector in assessment of technical feasibility

[1] The IRT did not have access to all of the information necessary to fact check this statement.

and readiness for downstream prototyping and rigorous analysis of the anticipated cost and time to reach go/no go decisions to commit large scale resources to achieve commercialization.

Finding C.1: Stimulating industrial activities in LEO will require more reliable access over the long-term.

Finding C.2: ISS alone is not sufficient to stimulate the commercial market.
As a growing number of commercial space companies are providing low-cost and frequent access to suborbital and orbital space for humans and research payloads, it is important to fully utilize these capabilities to effectively stimulate the commercial market.

Finding C.3: Industrial R&D in microgravity is just one R&D tool for those companies - those multitude of tools compete for resources with each other inside companies. Proponents of using ISS need to be cognitive of the other R&D tools (e.g. Artificial Intelligence, etc.) to see if they can successfully compete within the company for resources by creating superior products in a cost-effective manner.

Finding C.4: The market timeframe for viable market needs reliability of access and clear IP terms. Smaller companies may not have the resources to reach out to new customers in microgravity. Larger companies need to see NASA as a partner in the longer game.

Finding C.5: The high cost and high risk of space missions, the imperative for comprehensive assessment of health risks for crew members and any prospect of evolution of self-sustaining commercial activities, will require a coherent systems-based, end-to-end approach involving diverse stakeholders that span the full spectrum from basic research discovery conducted by NASA, academia and industry to prototyping development of cost-effective commercial products and creation of new markets for space-based manufacturing.

Finding C.6: There is a lack of an integration mechanism (like IDIQ) to address strategic and operational barriers faced by companies and Implementation Partners to increase the reliability of access to space-based facilities.

Finding C.7: There is still significant need for low TRL R&D with a goal to reduce basic science findings to improved practice in the marketplace (manufacturing, clinical practice, etc.) Bifurcating the authority without clear joint planning, common NASA oversight and the development of a broad and integrated use community has had limited success. Conversely, SLPSRA has been stymied from similar issues, such as lack of funding, operational resources, and prioritization that has limited its capacity to execute.

Finding C.8: Restricting the ISSNL to non-NASA research may have reduced the Agency's ability to stimulate disruptive research that improves astronaut health and safety.

Finding C.9: The requirement for CASIS to design and implement a STEM education program using ISSNL resources, while laudable in intent, adds to the challenge of productive allocation of scarce ISSNL resources.

Finding C.10: The biopharmaceutical, diagnostic and biomedical device industries are among the most highly regulated segments of the advanced technology economy. These regulatory policies will likely also apply to these product classes manufactured in space.

Finding C.11: Any commercial LEO effort to produce proteins and living cells, tissues and organs, whether for down-transfer for use in terrestrial healthcare or exclusive use in space habitats to sustain astronaut health will likely be subject to significant regulatory oversight.

Recommendations

Recommendation 2.1: A normal business structure must be imposed or otherwise adopted immediately. Our reasoning is as follows:

- The ISSNL resource is too important and time-constrained to hold hostage to poor operational management
- Current management contractor has failed to deliver sufficient oversight (as originally intended to be embodied in the INLAC)
- Development of perverse and non-functional operating structure
- Lack of transparency in prioritization of critical resource allocation
- Inability of current ISSNL management to increasingly serve the growing and complex environment of commercializing LEO

Recommendation 2.2: At a minimum, CASIS should seat a new board which understands its role (e.g. fiduciary, leadership selection), select a new CEO, and allow true CEO leadership. Business development and sourcing of new users should be the function of the CEO, not the board.

Recommendation 2.3: The changes in the statement of Board Responsibilities in the most recent CA should be maintained. The IRT endorses NASA's decision to remove the paragraph setting marketing and research solicitation as responsibilities of individual Directors.

Recommendation 2.4: Any management contract for the ISSNL, with approval by NASA, should create and utilize criteria to evaluate projects and programs that adhere to principles of transparency in evaluation. In addition to science, the "value impact" of proposals should be evaluated by multiple external experts knowledgeable in the specific fields of research being proposed. These experts are located in major research universities, companies and special purpose institutes (e.g. RAND) in this country and aboard. Moving the value impact assessment to external review will increase transparency and improve community understanding of the process, as well reduce the internal management load.

Recommendation 2.5: Conflict resolution within the ISSNL operating structure needs to be built for scenarios that include the full continuum of conflicts that may arise with CASIS's external users - to include both Implementation Partners and SLPSRA. Both CASIS and NASA should play a role in this process, working through the ISSNL Liaison.

Recommendation 2.6: CASIS needs to develop policies for programs to on-ramp and off-ramp the ISSNL. In addition, CASIS should create a policy to effectively on-ramp R&D from SLPSRA and off ramp R&D to Implementation Partners. CASIS should consider the well-vetted Technology Readiness Level (TRL) model, with a potential entry point of TRL 4 and exit point of TRL 7.

Recommendation 2.7: We strongly recommend that the NASA liaison be the single point of contact between NASA and the operator of the ISSNL at a relatively high level – perhaps even reporting to the Administrator until the overall NASA culture has more fully embraced a unified

approach to operating the ISSNL in and developed a more unified view of the ISSNL mission in today's LEO economy.

Recommendation 2.8: The conduct and prioritization of basic research by SLPSRA within NASA were not productively coordinated with CASIS to identify potential commercialization opportunities and support CASIS outreach to potential industry partners.

Recommendation 2.9: Consistent with 2008 congressional authorization language, the INLAC construct should be established as a User Advisory Committee to include NASA, other federal agencies, Implementation Partners, and commercial users, that enables joint planning, information sharing and broad community input for both trouble-shooting and the creation and development of new opportunities. The User Advisory Committee could incorporate a Technical Interchange Meeting (TIM) format for information exchange across all elements of the ISSNL stakeholders. This function must be convened by the ISSNL operator, but completely independent of the CASIS Board. The NASA-CASIS liaison should serve on the INLAC in a non-voting *ex officio* role.

Recommendation 3.1: The CA should be greatly simplified so that it is a flexible instrument that allows annual input by NASA (defining the "what"), easily measures annual performance of CASIS' management of the ISSNL (the "how"), and a regular cadence of formal exchanges with the ISSNL user community. This revision should create brighter lines between CASIS and the basic research component of NASA, with significantly greater communication and joint planning between the two. When evaluating research that could accelerate space exploration and/or health and safety of astronauts, CASIS and NASA should have a defined and transparent process for joint scientific and value-impact assessment.

Recommendation 3.2: CASIS use of funding and access to do research, even if it is designed to ultimately be marketable, is in conflict with every model of successful commercialization. Low TRL activity will not attract commercial sponsorship. De-conflicting SLPSRA activity, the National Laboratory agenda, and the LEO commercialization agenda should be undertaken immediately, with consideration of the full R&D continuum – i.e. both R&D (SLPSRA), industrial development (ISSNL) and commercialization (Implementation Partners).

Recommendation 3.3: If NASA desires the ISSNL to operate as a National Laboratory in the traditional sense that advances NASA's primary missions of exploration, science and astronaut health, then NASA should commission a study to consider, at a minimum:

- Optimizing NASA management and oversight of both SLPSRA and the ISSNL to eliminate the current limitations of the authorizing language (i.e. for the ISSNL to do only non-NASA work);
- Vastly strengthening NASA oversight to assure that its primary mission is satisfied, with mechanisms that allow NASA to pivot responsibilities tasked to ISSNL based on NASA needs (reviewed annually, at a minimum)
- Potential duplication of services

Recommendation C.1: The ISSNL has the opportunity to maximize the utilization of the ISS as an "industrial incubator in LEO." However, even with regular, reliable up-and-down mass to the ISS, a lack of access to regular, reliable flight opportunities on a variety of platforms (i.e, free flyers, suborbital platforms, etc.) will stymie the progress of commercialization in LEO.

Recommendation C.2: Future considerations should be given to how the commercialization of LEO mandate expands beyond the concept of an industrial incubator to additional platforms.

We acknowledge that such activities are beyond the current scope of ISSNL authorization language. NASA can and should stimulate broad discussion among all stakeholders to develop a model for cross-platform (i.e., free flyers and suborbital platforms, etc.) considerations spanning the entire panorama of basic research to applied research to product development.

Recommendation C.3: The Government can help stimulate the commercialization of LEO by conducting a study or workshop on what would be necessary to have robust trans-atmospheric and orbital supply chain processes that support LEO industrialization. This should look at the complete system of potential platforms, policies, procedures and practices to be used by any commercial entity whether they are operating platforms or production processes and could include ISSNL as an option.

Recommendation C.4: With respect to commercialization activities, NASA should consider a more active approach that allows development of a clear set of steps leading from early science work to full product production and distribution. This will necessitate definition of progressive levels of required privacy and proprietary ownership of IP for their product(s).

Recommendation C.5: If NASA repositions the ISSNL as an industrial incubator in LEO, it should evaluate how the ISSNL can be used to support translational research that furthers the Agency's exploration goals.

Independent Review Team Introduction & Methodology

The IRT studied the CASIS organization over the period of September-December 2019. Utilizing in-person and virtual interviews and analysis, the IRT primarily focused on two features: 1) management structures within the CASIS organization; and 2) NASA oversight to insure that CASIS was meeting the goals set forth by its sponsor and congressional authorization language.

Throughout the study period, the IRT held biweekly teleconferences to review material and interview personnel. The IRT also met three times in person:

07 Oct 2019 in Washington, DC
21 Oct 2019 in Washington, DC
29 Oct 2019 in Florida with CASIS leadership

A total of 34 interviews were conducted with 47 people including CASIS leadership, board members, and program managers; NASA leadership, liaisons, and ISS program managers; ISSNL Implementation Partners[2] and users; and congressional and executive branch staff.

The IRT reviewed thousands of pages of documents, including authorizing language, external reviews of CASIS and ISS research, and research products from the ISSNL. From this information, the IRT formed an initial set of impressions that were discussed, reviewed, and formulated into a set of findings and recommendations contained in this report.

The team extends its sincerest gratitude to those individuals who shared their insights.

[2] https://www.issnationallab.org/implementation-partners/

Chapter I: Historical Context & Shifting Priorities

International Space Station Overview

The International Space Station (ISS) represents one of mankind's most remarkable engineering feats, providing a platform for advancing fundamental knowledge and translation of these insights into potential benefits for exploration, national security, US industrial competitiveness and a range of broader benefits for society. At its inception, the ISS was developed as a unique site for basic and applied scientific studies in low Earth orbit (LEO). The United States has invested an estimated over $100 billion in the construction, maintenance and operation of the ISS with an annual operating budget of approximately $3 billion.

Because of its proximity in LEO and its microgravity environment, the ISS provides a unique, relatively accessible setting for scientific research, including the study and potential mitigation of a variety of human health risks on long-term exploration missions. There are currently 16 multi-purpose diagnostic instruments plus 32 highly versatile small volume express racks on-board ISS, as well as 11 instruments on the exterior of ISS. Topics of investigation span physical and biological sciences with topics related to low gravity phenomena and the impacts of low gravity on humans, small mammals, plants and cells. In materials science, combinations of metals and other compounds are being investigated to increase understanding of, and pave the way to utilize, unusual electrical and mechanical systems. These experiments open doors to new and important knowledge of the behavior of physical and biological materials in microgravity – information that is impossible to obtain in terrestrial laboratories.

At the present time, half of the resources allocated to the United States for scientific and medical studies is allocated to internal programs of NASA. The remaining resources are apportioned to the ISS National Laboratory (ISSNL), and legislatively required to be used for non-NASA, U.S. scientific projects. To understand the creation of the ISSNL, it is instructive to first review the history of the ISS and how priorities have evolved over the past two decades.

The 1990s

The launch of the first module to ISS, the Zarya Control Module, occurred in November 1998. At that time, a Memorandum of Understanding (MOU) between NASA and Roscosmos described eight functions for ISS:

1. a laboratory in space, for the conduct of science and applications and the development of new technologies;
2. a permanent observatory in high-inclination orbit, from which to observe Earth, the Solar System and the rest of the Universe;
3. a transportation node where payloads and vehicles are stationed, assembled, processed and deployed to their destination;
4. a servicing capability from which payloads and vehicles are maintained, repaired, replenished and refurbished;
5. an assembly capability from which large space structures and systems are assembled and verified;
6. a research and technology capability in space, where the unique space environment enhances commercial opportunities and encourages commercial investment in space;
7. a storage depot for consumables, payloads and spares; and
8. a staging base for possible future missions, such as a permanent lunar base, a human mission to Mars, robotic planetary probes, a human mission to survey the asteroids, and a scientific and communications facility in geosynchronous orbit.

2000-2005

In the decade after the MOU was signed, the scope and capabilities of the ISS were repeatedly downsized due to cost growth and schedule delays. By 2001, NASA had downsized the number of goals for the ISS to three: 1) conducting world-class research; 2) establishing a permanent human presence in space; and 3) and accommodation of all international partner elements. Following the announcement of the Vision for Space Exploration (VSE) in 2004, NASA further reduced the scope and capabilities of its ISS research plans to only that which supported the VSE and planned to end operational support for the ISS in 2016. By 2005, the agency had narrowed the scope of ISS research and the goals were reduced to one - a laboratory for world-class research.

Concerned that the ISS's function as a national, broad-based research laboratory was being eroded, Congress took several legislative actions to bolster this role. The NASA Authorization Act of 2005 (P. L. 109-155) and accompanying conference report (H. Rept. 109-354) reaffirmed Congress' support for "the research potential of the ISS beyond its contribution to long-duration human spaceflight in support of the Vision for Space Exploration[.]" After overcoming years of challenges and debate to maintain support for development of the ISS, the act recognized that the "ISS ha[d] been supported by the Congress in large part due to its promise and potential as a unique international laboratory facility capable of hosting a wide range of scientific research that can only be undertaken in a microgravity environment."

While Congress supported NASA's plan to refocus its ISS research activities on meeting the requirements of the VSE, it did not intend to do so at the expense of the ISS' broader scientific research community and opportunities.[3] To preserve the ISS' potential as a broad-based research facility, the act included provisions that required NASA to carry out a microgravity research program, and specified that ISS research be directed toward a range of science disciplines not directly related to supporting the VSE. The act designated the US segment of the ISS as a National Laboratory and directed the NASA Administrator, "to seek to increase ISS utilization by other federal entities and the private sector through partnerships, cost-sharing agreements, and other arrangements that would supplement NASA funding of the ISS."

By designating the ISS as a National Laboratory, Congress intended to provide the means of ensuring the broadest possible use of the ISS for scientific research, while enabling NASA to focus its ISS-supported research on meeting VSE requirements. The NASA Administrator was allowed to enter into a contract with a non-government entity to operate the ISSNL. The act also required NASA to submit a research plan for utilization of the ISS.

In response to the 2005 Authorization Act, NASA conducted a zero-based review of its ISS research needs and determined that most life and physical sciences research was not highly relevant to achieving the goals of the VSE.[4] As a result of the review, NASA significantly reduced its basic biological and physical sciences research program budget, its funded Principal Investigators, and the number of research experiments and capabilities.[5] It has taken more than

[3] S. Rept. 109-108

[4] National Research Council. 2011. Recapturing a Future for Space Exploration: Life and Physical Sciences Research for a New Era. Washington, DC: The National Academies Press. https://doi.org/10.17226/13048.

[5] In 2001, NASA's basic life and physical sciences research budget was $410 million (in FY 2016 dollars) and supported 1,014 tasks. By 2010, it was $210 million and supported 364 tasks. Between 2004-2010, NASA's basic biology and physical sciences program suffered severe cuts in terms of number of PIs; Space Biology lost 75% and Physical Sciences lost 85% of their PI workforce. See "A Midterm Assessment of Implementation of the Decadal

a decade for these research communities to recover from these decisions and nearly 15 years after these decisions were made, research funded today is at a fraction of its pre-VSE levels.

2005-2010

The NASA Authorization Act of 2008 (P. L. 110-422) and accompanying conference report (H. Rept. 110-702) provided additional guidance that shaped the ISSNL. Congress reaffirmed its support for, "the full productive use of the ISS to support fundamental research, applied research, and other non-NASA federally funded research." Congress further noted that NASA had "cut funding for ISS research activities and canceled research facilities that had been completed or in development to support research on the ISS." Based on these cuts, NASA did not plan to utilize the full capabilities of the ISS.

Concerned by this trend in ISS research and the rate of progress on the National Laboratory, Congress directed NASA, "to reinvigorate the research community and the pipeline of experiments to be conducted on the ISS." Consequently, in the FY 2008 Omnibus Appropriations Act (P. L. 110-161) Congress directed the agency conduct a decadal survey to establish priorities in life and physical science research in microgravity and partial gravity. With the ISS nearing completion and a growing number of potential new users, Congress recognized NASA's need "to take immediate action in preparing for the full utilization of the ISS." As a result, the act required NASA to "have a plan in place for managing the utilization of the Space Station to support its internal research requirements, those of NASA-funded researchers, and those of the ISS National Laboratory."

The act also required that NASA establish an ISS National Laboratory Advisory Committee (INLAC). Congress directed the INLAC to " monitor, assess, and make recommendations regarding effective utilization of the ISS as a national laboratory and platform for research, … and submit a report containing these assessments and recommendations at least annually to the NASA Administrator."

In light of the ISS-related provisions in the 2005 and 2008 NASA Authorization Acts, the Government Accountability Office (GAO) conducted a review of the research use of the ISS[6]. The GAO noted in its report that NASA had been researching the possibility of developing a management body with both internal and external elements, similar to other national laboratories. The GAO stated that there were no direct analogs to the ISSNL, but identified three common management practices at other national laboratories and large scientific institutions that could be benefit the management of the ISS research, namely:

1) centralized management body;
2) in-house scientific and technical expertise; and
3) robust user outreach

Among its seven recommendations, the GAO recommended that NASA "[e]stablish a body that centrally oversees U.S. ISS research decision making, including the selection of all U.S. research to be conducted on board and ensuring that all U.S. research is meritorious and valid." NASA concurred with this recommendation, adding that the agency, "may be able to leverage existing agreements with management bodies to provide for a faster solution, or leverage the scientific and technical expertise of other sponsoring federal agencies (such as NIH) that have

Survey on Life and Physical Sciences Research at NASA", https://sites.nationalacademies.org/SSB/CompletedProjects/SSB_174910.

[6] GAO-10-9: International Space Station: Significant Challenges May Limit Onboard Research

experience in conducting peer-reviewed research in areas pertinent to their missions." Establishing an internal, centralized management body was therefore NASA's preferred response.

In 2009, the White House directed NASA to convene the Review of U.S. Human Space Flight Plans Committee to review U.S. human spaceflight plans and programs. The Committee recognized that the return on investment to both the United States and the international partners would be significantly enhanced by an extension of the ISS' life.[7] Among a number of significant changes in mission direction for NASA, the President's FY 2011 budget request included an extension of the ISS from 2015 through at least 2020. While NASA instituted a centralized management function within the agency to help coordinate research activities for the extension of the ISS, the ISSNL function was not clearly defined.

The NASA Authorization Act of 2010 (P. L. 111-267) and accompanying conference report (S. Rept. 111-278), extended ISS operations and supported the "full and complete utilization of the ISS through at least 2020." In what appears to be the first concerted policy effort to make NASA one of many ISS customers, Congress required "NASA to pursue additional international, commercial, and intergovernmental partnership arrangements to enhance the overall sustainability of the ISS and seek means to reduce or offset U.S. operating costs associated with the ISS." Congress continued to reaffirm its support for NASA to "maximize the returns from the ISS with respect to scientific and technological research and development, advancement of space exploration, and international collaboration." To enable that goal, Congress directed NASA "to increase the innovative use of the ISS national laboratory authority and to seek greater international and domestic collaboration."

The act noted that due to the previous changes in NASA's mission and research priorities, "an independent body should be established to serve as the designated agent to manage the ISS national laboratory." The act required NASA "to enter into a cooperative agreement with an appropriate not-for-profit organization to manage the activities of the ISS national laboratory for non-NASA utilization of the ISS research capabilities and available facilities." Congress recognized it as "essential to the effective and successful implementation of a broad-based research agenda that the independent national laboratory entity be allocated a fixed amount of the available capacity aboard the ISS for its management and use." The not-for-profit was required to plan non-NASA research activities on the ISSNL, develop guidelines and selection criteria for non-NASA research, coordinate transportation requirements for ISSNL research, and develop scientific outreach and education. Other research objectives or responsibilities were expressly prohibited. The act also guaranteed "national laboratory managed experiments access to a minimum 50% of U.S. research capacity and crew time."

The NASA Administrator was required to designate an official from the Space Operations Mission Directorate to act as a liaison with the not-for-profit entity for the purposes of cooperation and consultation. The liaison was given authority to grant exceptions to the ISSNL allocation for proposed experiments considered essential for purposes of preparing for exploration beyond LEO.

[7] Review of U.S. Human Space Flight Plans Committee: Seeking a Human Space Flight Program Worthy of a Great Nation. https://www.nasa.gov/pdf/396093main_HSF_Cmte_FinalReport.pdf

Initial funding was to be provided to help support seven functions:

1. Planning research activities;
2. Development and implementation of ISSNL activities;
3. Reviewing recommendations from the INLAC "regarding agreements with non-NASA departments and agencies of the United States Government, academic institutions and consortia, and commercial entities leading to the utilization of the ISSNL facilities"
4. Coordination of transportation activities to and from the ISS for ISSNL purposes;
5. Cooperation with NASA, other federal and state departments and agencies, and commercial entities for non-exploration-related research payload ground support facilities supporting ISSNL;
6. Development and implementation of scientific outreach and education activities designed to ensure effective utilization of ISS research capabilities; and,
7. Other matters related to the ISSNL utilization that the Administrator deemed appropriate

2011-Present

In 2011, NASA established the Division of Space Life and Physical Sciences Research and Applications (SLPSRA) at the recommendation of National Research Council[8] and restored a scientific home for life and microgravity sciences programs that had been nearly eliminated by the VSE. SLPRSA is currently part of NASA's Human Exploration and Operations Mission Directorate (HEOMD)[9]. SLPSRA provides administrative oversight of NASA's Life and Physical Sciences Research and is a programmatic base for an integrated research agenda, program leadership and program execution under a single management structure. SLPSRA currently administers NASA's Human Research (HRP), Fundamental Space Biology (FSB), and Physical Sciences (PS) Programs.

The establishment of a centralized research function within NASA fulfilled the recommendations of the 2009 GAO report. At the same time, an independent body had been created to manage the ISSNL, fulfilling the obligations of the 2010 NASA Authorization Act. An understanding had therefore been established by 2011 that CASIS would manage non-NASA research on the ISS and that HEOMD would manage NASA research.

The NASA Transition Authorization Act of 2017 (P. L. 115-10) made no fundamental changes to ISSNL organizational and operational structure. Rather, Congress affirmed that United States investment and access to low-Earth orbit remains paramount to maximum utilization and continued success of the ISSNL. It established that, "one of the primary objectives of the ISS program shall be to pursue a research program that advances knowledge and provides other benefits to the Nation" and committed the United States "to support full and complete utilization of the ISS through at least 2024."

P.L. 115-10 directed the NASA Administrator, in coordination with CASIS, ISS partners, the scientific user community, and the commercial space sector, to "develop a plan to transition in a step-wise approach from the current regime that relies heavily on NASA sponsorship to a regime where NASA could be one of many customers of a low-Earth orbit non-governmental human space flight enterprise." In furtherance of this policy, NASA was directed to pursue international, commercial, and intragovernmental means to maximize ISS logistics supply, maintenance, and operational capabilities, reduce risk to ISS systems sustainability, and offset

[8] National Research Council. 2011. Recapturing a Future for Space Exploration: Life and Physical Sciences Research for a New Era. Washington, DC: The National Academies Press. https://doi.org/10.17226/13048.
[9] For information on SLPSRA's vision and mission, see: https://www.nasa.gov/content/slpsra-overview.

and minimized United States operations costs relating to the ISS. Notably, the transition plan required a report to outline, among other things, the steps NASA is taking to stimulate and facilitate commercial demand and supply of products and services in low-Earth orbit; and, "an identification of barriers preventing the commercialization of low-Earth orbit, including issues relating to policy, regulations, commercial intellectual property, data, and confidentiality, that could inhibit the use of the ISS as a commercial incubator."

Thus, P.L. 115-10 restored an emphasis on the sixth goal originally stated in the NASA-Roscosmos MOU of 1998. At that time, NASA commented that the "highest measure of success for CASIS in developing the market is to identify users and match them with commercial service providers to enable a business-to-business transaction that does not require any CASIS funding or user agreement".

NASA and CASIS are now embarking on a program of adapting ISS and yet-to-be-built LEO platforms for commercial and terrestrial consumer products – what was described to the IRT as "LEO industrialization." Recent strategic plans prepared by the CASIS Board of Directors (March 2019), the CEO (June 2019) and the FY2020 Implementation Plan (September 2019) outline actions to optimize ISSNL resource allocation, expand applied research and support industry partners to accelerate the industrialization of LEO and catalyze new markets for sustainable commercial demand. The FY 2020 Consolidated Appropriations Act (P.L. 116-93) provides $15M to initiate the development of several new LEO facilities devoted to commercial product research and manufacturing. Discussions are also underway within NASA relative to revision of priorities for use of ISS technical and astronaut resources.

Chapter I Findings

Finding 1.1: The ISS National Laboratory was created as a broad-based research facility, but NASA reduced ISS research in 2004-2005 to focus on human health and safety. Congress did not want to lose the broad research facility for activities in LEO and the SLPSRA Division of HEOMD did not exist at the time of the original legislation. Consequently, there is now a NASA division tasked with enabling research activities that potentially overlap with the ISSNL. Both SLPSRA and CASIS perceive that they often operate in competition with one another for crew time, critical on-orbit facilities, and "credit" for research results.

Finding 1.2: ISSNL was created at a specific time for a specific purpose to address potential shortfalls in ISS utilization. This problem no longer exists; the ISSNL has a robust portfolio of activities. However, the underlying set of expectations and predicted futures have evolved dramatically in the intervening 15 years – to include commercial LEO, new NASA and US perspectives and priorities on commercializing space, visions for human exploration and expansion of potential platforms upon which to conduct science.

Finding 1.3: There are now entities using the ISS beyond the scope originally envisioned for the ISSNL. The IRT heard from commercial stakeholders and Implementation Partners that this is a challenge and that they have little way to make their needs and desires heard.

Finding 1.4: There is confusion regarding the scope and purpose of the authorizing legislation among stakeholders and how it is represented in the CA between NASA and CASIS. There are slight to large differences in interpretations of what the ISSNL is supposed to do, many different definitions of the mission of the ISSNL, and no shared vision.

Finding 1.5. The functions of the ISSNL liaison and the INLAC have been implemented differently than the original intent of authorization language. It is not clear that this implementation has been successful.

Chapter II: CASIS Business Structure and ISSNL Operations

Formation of CASIS

In 2010, NASA selected ProOrbis, LLC to conduct a 90-day independent study to develop an organizational model for managing the ISSNL and identify strategies to maximize the value of the U.S. Government's investment in the ISS. ProOrbis approached the study by 1) identifying the valuable uses of the unique ISS environment (tangible and intangible); 2) analyzing the capabilities of the ISS and its supply chain (payload development, transportation, labs, funding, etc.); 3) identifying the missing capabilities that are preventing value creating utilization; and 4) designing the optimal enterprise to deliver those capabilities. ProOrbis provided NASA with an organizational model that outlined a variety of strategies that, if adopted, would enable NASA to increase the number of researchers and commercial firms using ISSNL, raise funds from outside entities, and increase the likelihood of developing commercial applications that would result in jobs or produce financial gains.

Consistent with the NASA Authorization Act of 2008, ProOrbis recommended that NASA award management of the National Laboratory to a nonprofit organization through a CA. Indeed, the 2010 Authorization Act obligated NASA to use a CA. The INLAC function would be fulfilled through a "User Advisory Committee" comprised of organizations utilizing the ISS. The NASA liaison as specified in the 2008 Authorization Act was not included in the ProOrbis model, but a NASA liaison operating at the policy level was included.

Central to the study was the recommendation for a values-based prioritization scheme, which has been implemented as a value-impact assessment that considers economic, innovation, and social impact in addition to scientific merit and technical feasibility.

In August 2011, NASA awarded a 10-year, $136 million CA to CASIS to manage the ISSNL. In July 2017, NASA extended the CA to September 2024, increasing its total cost to $196 million. As of 2019, CASIS business development efforts have generated more than $180 million in external funding.

Approximately 50% of research resources (i.e. power, volume, equipment, crew time) on ISS are designated as the ISS National Laboratory (ISSNL). Per NASA's CA with CASIS, all ISSNL research is supposed to be non-NASA related. To date, almost 300 separate science and technology projects have been identified by CASIS and more than 140 experiments have been conducted aboard the ISS.

It is important to note that prior to the formation of the ISSNL, commercial entities had no clear access point within NASA to propose, let alone conduct, research aboard the ISS. The maturation of the space sector offers NASA new opportunities to assign the operator of the ISSNL a stronger role in stimulating a US presence in a vision for a fully commercial business model on the ISS.

Management of the ISSNL

The IRT does not find that the ISSNL is a National Laboratory in any sense other than its legislative designation. For instance, to preclude the ISSNL from conducting work for its sponsor meets neither the spirit nor intent of a National Laboratory. All other National Laboratories are established to conduct research for its sponsoring agency on behalf of the Federal Government and the Nation. On the ISS today, this role is served by SLPSRA.

Our review identified four overarching issues with the current CASIS approach to managing the ISSNL:

1. The CASIS business structure does not reflect the typical structure or function of other non-profit organizations.
2. There is no routine and credible user community integration.
3. Oversight by the Federal sponsor has been poorly managed.
4. Entry and exit procedures to/from the ISSNL are poorly defined.

Issue #1: The CASIS business structure does not reflect the typical structure or function of other non-profit organizations.

The corporate structure of CASIS is that of a typical Florida not-for-profit corporation, including a Board of Directors approved by NASA, centralized management, and two product divisions. One of these divisions is focused on promoting STEM education across the United States using the ISS as an icon of interesting advanced technologies. The second division is focused on assisting non-NASA users in the use of the technical facilities of ISS. The overall goal is twofold: 1) advancement of material and biological sciences, and 2) space science product commercialization.

The IRT observed that NASA has placed an unusual, peculiar responsibility on the shoulders on CASIS Board of Directors. Not only do Directors oversee the management, finances and well-being of the company, they are charged in both the original CA and the company's charter with personal responsibility for leading the marketing of CASIS at the highest levels accessible to the individual Directors. The leadership of this activity lies within the Directors and in the organization chart of the company; no indication was given that CASIS management need be informed about activities of the Board in its pursuit of new business relationships.

The IRT also noted that to recompense Directors for their marketing efforts and board responsibilities, prior to 2019, their compensation for 20% effort (8 hr/wk) was set at ~$40,000 per year[10]. Said a different way, CASIS paid the equivalent of 2.2 Full Time Equivalents (FTEs) who are not under the direction of the CEO to solicit new projects at an annual salary of $200K each. This level is much higher than would be normal for a 501(c)(3) organization receiving government funding of only $15M/year. It is more than a rhetorical question to ask whether a marketing staff of 4 FTE reporting directly to the CEO and receiving an annual salary of $110K (same cost) would have better serve CASIS.

This question highlights another serious flaw in NASA's stipulation for Directors to engage in marketing activities, namely that the placement of responsibility for marketing with the Board weakens the powers of the CEO with respect to management of the company. The IRT believes this decision has had a significant adverse impact on the unity of operation of CASIS, as well as its economic progress[11].

[10] Compensation for CASIS Board Members ended in 2019.
[11] For comparison, a list of typical Board responsibilities can be reviewed at https://nonprofitquarterly.org/nonprofit-board-governance-responsibilities-basic-guide/.

Issue #2: There is no routine and credible user community integration.

The IRT identified a number of communication mismatches between NASA and CASIS, as well as between CASIS and the Implementation Partners, that have resulted from over a decade of lack of clarity from NASA (many voices), lack of flexible realization of CASIS's CA and inappropriate Board intrusion on the part of the CASIS 501(c)(3).

The original intent of authorizing language was to mitigate these problems through the yet-to-be-formed INLAC. GAO 15-397 included the recommendation, "In order for NASA to fully implement the NASA Authorization Act of 2008 and for CASIS to fulfill its responsibility as outlined in the cooperative agreement directs the Associate Administrator for the Human Exploration and operations Mission Directorate to fully staff the INLAC." Although CASIS partially concurred with this recommendation, they asserted that the CASIS Board "effectively fulfills the intent of the INLAC charter by providing recommendations regarding effective utilization of the ISS as a national laboratory and platform for research." This assertion ignores the fact that the INLAC was intended to represent the user community. An INLAC, as originally chartered, would be a critical entity to examine the restructuring of the CASIS CA because it would begin with deep knowledge of the opportunities and threats to expand the use of the ISSNL.

The NASA Authorization Act of 2008 also made clear that the INLAC could be used by Congress to assure that the ISSNL was functioning as intended. It is therefore the IRT's opinion that Congress, not NASA or CASIS, holds the authority to modify or eliminate the INLAC. As a corollary, the Board of Directors holds no authority to report to Congress. The *de facto* designation of Board to serve the INLAC role has therefore created further confusion with regard to Congressional oversight.

To summarize, the functions of Board and INLAC are not the same – the Board serves CASIS under the CA, and the INLAC serves both the CEO and the government through its NASA sponsor.

Issue #3: Oversight by the Federal sponsor has been poorly managed.

NASA has not treated CASIS as an independent organization. NASA's interactions have occurred at all levels of the CASIS organization and at multiple levels within the agency. Communications have not been through a single designated individual and interactions at multiple levels appear to the IRT to have been inappropriate, somewhat obviating the independent relationship with appropriate funding agency oversight of what is to be achieved. It is not appropriate for the "many voices" of NASA to have so many contacts; the sponsor must exercise the discipline to work through the CEO of the organization, not the Board. In particular, we note that the primary role of a Board of Directors is to advise the CEO, not the funding agency.

Lacking a clear vision and an unadulterated chain of command, NASA has often used CASIS and its activities for public relations and has played an insufficient role in managing the complex relationships between SLPSRA, commercial partners, National Laboratory participants, and international partners on the ISS. CASIS has been left to define and re-define success based on a "many voices" approach from NASA that has driven inflexible and potentially damaging board and operational behaviors. Changes in the NASA-ISSNL liaison role, with accompanying high variability in strategic guidance, have only exacerbated this problem.

In this context, the IRT concluded that the conduct and prioritization of basic research by SLPSRA within NASA were not productively coordinated with CASIS to identify potential commercialization opportunities and support CASIS outreach to attract industry partners.

<u>Issue #4:</u> Entry and exit procedures to/from the ISSNL are poorly defined.

Increasing utilization of the ISS – the most expensive, complex, and long-lasting taxpayer-funded initiative in LEO – was clearly the intent of congressional authorization language. In 2015, CASIS reached a watershed moment, reporting that full utilization had been achieved for one of its allocations (crew time). This event is largely explained by CASIS adjusting its portfolio to include rodent research, which is notoriously crew-intensive. It also highlighted the now obvious fact that CASIS cannot continue to acquire and support projects for the ISSNL.

However, there appears to be no systematic procedure in place to assure Implementation Partners continued access to ISS resources. The problem is amplified with commercial success, especially when Implementation Partners develop their own hardware that depends on ISS resources such as power. In at least one case, a separate resource allocation was negotiated by allotting 5% of ISS resources from NASA (not ISSNL) to the implementation partner. While it was a thoughtful response to a growing problem, it was a reactive decision and is not sustainable. To accelerate the growth of the commercial LEO ecosystem, access to the ISSNL cannot be indefinite and options to relocate commercial manufacturing or research to other platforms must become viable.

As ISSNL resources become more constrained, the question that must be answered is whether the imbalance between resources and demand is growing because there are too many projects entering the ISSNL, too few leaving, or some combination of both. Other facilities in the federal government gauge a Technology Readiness Level (TRL) 4 as the threshold to attract private capital, major manufacturers, and stakeholders to bring a technology to the marketplace. CASIS does not appear to make such determinations about its portfolio, although they appear to have the necessary resources and expertise to do so. Given the cost of operating a supply chain that includes LEO, it seems pragmatic that CASIS employ more conservative TRL thresholds than ground-based facilities.

When one visits the CASIS website, there is almost no discussion of the breadth of factors that will be used in making a fly/no fly decision. The IRT was told that two or three CASIS employees plus two outside consultants make the decisions as to value, potential, and ultimately award. The ISS unequivocally offers qualified US scientists and technologists' access to common-use, high end tools for the benefit of discovery of new science and technology. The idea that four or five individuals in a small startup company are adequately qualified to judge a growing log of diverse proposals to make an ISS fly/no fly decision is not consistent with how such decisions affecting the development of new scientific or product knowledge should be made.

Chapter II Findings

Finding 2.1: National Laboratories within the US do not provide useful models for NASA to compare and consider when looking at the future of the ISSNL. ISSNL is unique in its mandated focus on non-NASA research and its secondary focus on non-research activities.

Finding 2.2: There is dysfunction in the Board Structure and Board-CEO dynamic. The previous board structure was inappropriate for the business structure; a 15 person board for a 60 person organization is excessive. Typically, 501(c)(3) organizations do not employ compensative boards. Rather, boards should be motivated by mission, not personal interest. It is not clear that CASIS corporate bylaws have been fully reconciled with changes to the CA.

Finding 2.3: The separate and distinct roles of Board and User Advisory Committee have been conflated. As noted in GAO-15-397, "NASA has still not staffed an Advisory Committee with which CASIS is required to interact."

Finding 2.4: The lack of operating structures typical for a startup or oversight structures typical for a Federally Funded Research and Development Center (FFRDC) has placed CASIS in the role of commercialization sponsor on the ISS. While this role does not meet the broader vision outlined in 2005 and 2008 congressional authorization language, it is in keeping with the "one of many" construct presented in the NASA Transition Authorization Act of 2017.

Finding 2.5: CASIS's Value Impact Model does not address allocation of resources when meritorious projects exceed the capacity of the ISSNL. Furthermore, CASIS does not appear to have a mechanism in place to sunset projects because of success (program is ready to function independent of ISSNL, such as a purpose-built commercial platform) or failure (unsuccessful startup).

Chapter II Recommendations

Recommendation 2.1: A normal business structure must be imposed or otherwise adopted immediately. Our reasoning is as follows:

- The ISSNL resource is too important and time-constrained to hold hostage to poor operational management
- Current management contractor has failed to deliver sufficient oversight (as originally intended to be embodied in the INLAC)
- Development of perverse and non-functional operating structure
- Lack of transparency in prioritization of critical resource allocation
- Inability of current ISSNL management to increasingly serve the growing and complex environment of commercializing LEO

Recommendation 2.2: At a minimum, CASIS should seat a new board which understands its role (e.g. fiduciary, leadership selection), select a new CEO, and allow true CEO leadership. Business development and sourcing of new users should be the function of the CEO, not the board.

Recommendation 2.3: The changes in the statement of Board Responsibilities in the most recent CA should be maintained. The IRT endorses NASA's decision to remove the paragraph setting marketing and research solicitation as responsibilities of individual Directors.

Recommendation 2.4: Any management contract for the ISSNL, with approval by NASA, should create and utilize criteria to evaluate projects and programs that adhere to principles of transparency in evaluation. In addition to science, the "value impact" of proposals should be evaluated by multiple external experts knowledgeable in the specific fields of research being proposed. These experts are located in major research universities, companies and special purpose institutes (e.g. RAND) in this country and aboard. Moving the value impact assessment to external review will increase transparency and improve community understanding of the process, as well reduce the internal management load.

Recommendation 2.5: Conflict resolution within the ISSNL operating structure needs to be built for scenarios that include the full continuum of conflicts that may arise with CASIS's external users - to include both Implementation Partners and SLPSRA. Both CASIS and NASA should play a role in this process, working through the ISSNL Liaison.

Recommendation 2.6: CASIS needs to develop policies for programs to on-ramp and off-ramp the ISSNL. In addition, CASIS should create a policy to effectively on-ramp R&D from SLPSRA and off ramp R&D to Implementation Partners. CASIS should consider the well-vetted Technology Readiness Level (TRL) model, with a potential entry point of TRL 4 and exit point of TRL 7.

Recommendation 2.7: We strongly recommend that the NASA liaison be the single point of contact between NASA and the operator of the ISSNL at a relatively high level – perhaps even reporting to the Administrator until the overall NASA culture has more fully embraced a unified approach to operating the ISSNL in and developed a more unified view of the ISSNL mission in today's LEO economy.

Recommendation 2.8: The conduct and prioritization of basic research by SLPSRA within NASA were not productively coordinated with CASIS to identify potential commercialization opportunities and support CASIS outreach to potential industry partners.

Recommendation 2.9: Consistent with 2008 congressional authorization language, the INLAC construct should be established as a User Advisory Committee to include NASA, other federal agencies, Implementation Partners, and commercial users, that enables joint planning, information sharing and broad community input for both trouble-shooting and the creation and development of new opportunities. The User Advisory Committee could incorporate a Technical Interchange Meeting (TIM) format for information exchange across all elements of the ISSNL stakeholders. This function must be convened by the ISSNL operator, but completely independent of the CASIS Board. The NASA-CASIS liaison should serve on the INLAC in a non-voting *ex officio* role.

Chapter III: Management Options for Consideration

Cooperative Agreement Challenges

While the CA mechanism can be used in a very flexible manner to address challenges, it appears that NASA has increasingly revised the CA with CASIS to become less flexible, more prescriptive, and more demanding. In concert with an evolving policy landscape, CASIS has regularly shifted its balance of scientific research and commercialization. The IRT sees four root causes:

1. Scientific leadership and management between HEO/SLPSRA and CASIS/ISSNL have not been cooperative.
2. The methods used by CASIS to determine value (whether scientific or commercial) lack transparency, and NASA has never taken full ownership of understanding and approving these methods. This lack of transparency has been tolerated throughout the life of CASIS and has resulted in an insular board which has been allowed to take a far too granular role in managing the operations of the entity.
3. CASIS has suffered from staff vacancies, particularly in its Science and Technology unit and its Commercial Innovation and Sponsored Programs unit. There have not been enough people complete the entire scope of work.
4. ISSNL lacks purpose-driven mission. ISSNL is defined as a place to go, not a goal to achieve.

ISSNL as a Science and Technology-Driven Multi-User System

Much has changed since 2011 when CASIS was tasked with "maximizing the value of the ISSNL by facilitating and prioritizing increased access to a broad base of users including commercial entities, other government agencies, and educational institutions." Over the intervening timespan, NASA and the ISSNL have worked to address the objective of creating broad, non-traditional, multi-industrial sector interest in investing in LEO operations, and by some measures, successes have been achieved. As of 2019, companies such as Anheuser-Busch, Sanofi, LambdaVision, Airbus, and Teledyne Brown Engineering have engaged in investigating the benefits of microgravity aboard the ISS.

Three parameters are ubiquitous in the science and technology landscape, both in the conduct of basic research and the downstream translation into commercial success, namely: 1) the dependency on multidisciplinary expertise; 2) the need for effective integration of multiple stakeholders at different stages in the discovery to product continuum; and 3) scalable production. CASIS has largely failed to address these requirements in the allocation of ISSNL resources and to strike an optimum balance between basic research and the translational R&D required for commercial prototyping. This task is also complicated by political pressures to demonstrate that of a viable commercial space economy is achievable.

In defining the appropriate balance between support of fundamental scientific knowledge and commercial initiatives, the CASIS mission has suffered from a lack of internal technical expertise necessary for in-depth examination of proposals coming from both upstream and downstream constituencies for access to the ISSNL. The expertise needed for informed analysis and prioritization of proposals coming from these two constituencies differs substantially. For large corporations with internal R&D resources that span the full spectrum basic research to advanced product development, the requisite knowledge exists internally to ensure that rigorous, systems-based, end-to-end approaches are used to assess technical feasibility, cost and projected timelines for industrialization. Many organizations refresh this knowledge through strong partnerships with the nation's research universities. This broad knowledge base has not been available to CASIS. Even without the management and board

governance issues highlighted earlier in this report, the limited budget and personnel resources available to CASIS has resulted in ineffective coordination with upstream basic science partners (i.e. SLPSRA and academia) and frustration of downstream corporate partners.

Models for Successfully Leveraging Government Investment in Unique U.S. Capabilities

Despite its designation as a National Laboratory, comparison of the ISSNL with the Department of Energy (DOE) National Laboratory facilities reveals clear differences in utilization and resource allocation. All twenty-seven DOE user facilities in the Office of Science list science, not commercialization, as their core mission. With one or two exceptions, they are managed by a university or university consortium in partnership with experienced, large management organizations, such as Battelle, Honeywell, and Blue. In no case is a DOE user facility managed by a small business, startup entity, or 501(c)(3).

The IRT identified several examples of multi-user science and technology programs that might provide instructive precedents to the future refinement of CASIS operations. The current ISSNL operating model may be usefully compared with a single-purpose User Facility at a National Laboratory (https://sc.osti.gov/User-Facilities) or the first asset in a multi-asset laboratory structure, such as the University National Oceanographic Laboratory System (https://www.unols.org/), or even a Manufacturing Innovation Institute (https://www.manufacturingusa.com/). Table 1 provides a comparison of these models to ISSNL and Appendix B provides greater information on each.

Several features are common to the exemplars, but are weak or absent in ISSNL:

- Clearly defined, narrowly focused, purposeful mission
- Managed by a large, experienced organization
- Member of a larger network of comparable facility operators
- Clear commitment of funds by commercial and academic partners prior to government investment
- High-quality cadre of in-house experts supplemented by robust engagement with a relevant academic community. Strong university ties are evident.

Table 1. Relevant examples of Government-Industry-Academic Partnerships to promote excellence in science, technology and commercialization*				
	R/V Marcus Langseth	**Building Technologies Research and Integration Center (BTRIC) at Oak Ridge National Lab**	**Advanced Regenerative Manufacturing Institute/BiofabUSA**	**ISS National Laboratory**
Established	2007	1993	2017	2011
Ownership	NSF	DoE	DoD	NASA
Operated by	Lamont–Doherty Earth Observatory; a research unit of Columbia University	University of Tennessee-Battelle for the DoE	DEKA Research and Development Corp	Center for Advancement of Science in Space
Annual budget (FY2018)	$15M federal		$16M federal $43M nonfederal	$15M NASA $4M non NASA
Award mechanism	Cooperative agreement		Cooperative agreement	Cooperative agreement
Focus	Research (multichannel seismic data, including 3-D surveys)	Industrial R&D (improve the efficiency in major areas of building energy use)	Commercialization (tissue growth and engineering)	Research, industrialization, and manufacturing on the ISS
Management Construct	FFRDC	FFRDC	Manufacturing Innovation Institute (MII)	ProOrbis Reference Model
Member of a facility network?	Yes	Yes	Yes	No
User advisory board	Yes	Yes	Yes	No
TRL/MRL	n/a	1-4	4-7	Not determined

*For detailed information of Government-Industry-Academic Partnerships mentioned in Table 1 see Appendix B

Building a LEO Commercial Economy and the Role of the ISSNL

At the present time, no commercial products from large U.S. or foreign companies are manufactured aboard ISSNL or any other space platform. This reflects the novelty, complexity, and cost of creating and operating a space-based manufacturing complex. Scalable commercial production in space requires robust processes related to the safety, transport and storage of raw materials, QA/QC testing of products and reliable schedules for transport of products to and from Earth.

A change in allocation of ISSNL resources to be more focused on industrialization, commercial product development and commercial use will have a substantial impact on the quality and quantity of non-governmental scientific work currently done aboard ISS. Accelerating the industrialization of LEO and catalyzing new markets for sustainable commercial demand will require a significant shift in strategic and operational priorities in resource allocation for use of the ISSNL. Given the high cost and high risk of space missions and imperative for comprehensive assessment of crew health risks, evolution of self-sustaining commercial

activities will require a coherent systems-based, end-to-end approach involving diverse stakeholders spanning the full spectrum of interests. Additional information for consideration is provided in Appendix C.

Transition from Individual ISSNL Projects to Focused Programmatic Thematic Areas

The historical focus of ISS resource allocation by CASIS has been to meet a NASA mandate for full utilization of the ISS for NASA to fulfill its Congressional obligation that the ISS be used for activities in basic science, commerce and STEM education. The breadth of this mandate has resulted in a disparate and somewhat ad hoc ensemble of projects being flown on the ISS, many of which represent single (one-off) studies of unknown value.

The designations ‘projects’ and ‘programs’ are typically used loosely and interchangeably in discussions about both basic science and commercial activities. Historically ‘projects’ has been used to refer to any activity flown on the ISS, irrespective of its goals. In contrast, the designation ‘program’ is now being adopted by CASIS to refer to ‘thematic’ areas of more focused scientific activity deemed to have a higher potential for eventual commercialization and build new markets for space commerce.

This transition to a thematic program-driven strategy should logically translate into more directed R&D efforts to promote more translational R&D and provide the continuity from basic research to translational activities needed to generate a more sustainable pipeline of commercialization candidates. Since many of the topics in the proposed thematic programs are still in their relative infancy it is important to emphasize that progress will require continued dedication of ISS resources to support basic research as the engine for the creation of translational assets and iterative refinement.

Without a major strategic shift in realignment of priorities in ISS resource allocation to support commercialization, the quest to develop a vibrant commercial LEO economy will be difficult to achieve. This includes the infusion of additional funding to support basic research in the targeted programmatic thematic areas with commercial potential and streamlining of multiple operational and logistical issues related to flight schedules and payloads. Given the short remaining life of the ISS, implementation of these reforms must become an urgent priority.

Chapter III Findings

Finding 3.1: CASIS lacks a purpose-driven mission statement. Consequently, priorities shift between research and commercialization. There is a need to balance scientific research and commercialization against NASA-defined priorities. There is a definitive and very finite set of assets available. NASA and CASIS must define how these are to be allocated against the many needs of research, applied efforts, commercialization of products and stimulation of LEO commercialization.

Finding 3.2: The CASIS model for project selection is outdated. It needs to reflect not only quality but commercial promise. Lack of reliable access to ISS appears to be a major problem. Commercially, time is money. CASIS has developed an elaborate, in-house methodology for selection of US-sourced ISS science experiments. The selection criteria for funding ISS investigations appear to place considerable importance upon social aspects of ISS projects and insufficient value on commercialization and progressive improvement of scientific knowledge.

Finding 3.3: The process being used by CASIS for project selection is opaque. It involves their own staff, supplemented by several outside "experts" using a dubious economic graph tool. This methodology is unlike that of other major funds-granting agencies and does not appear to be well understood by NASA, the integration partners, or the awardees.

Finding 3.4: Functionally, the relationship between NASA and CASIS appears to be devolving to the management and operations function specified in section 2.1.3 of the CA. It provides free access and utilization of instrumentation and facilities. NASA has driven CASIS to add the stimulus function to create its own R&D portfolio to meet metrics that are tied to utilization (e.g., number of PIs, publications) rather than to purpose.

Finding 3.5: Since its inception through FY18, CASIS has received approximately $109M through its CA with NASA. CASIS reports more than $180M of additional economic activity for the ISSNL[12], which includes cost sharing from universities and companies for their programs and projects on the ISS, Implementation Partners investments to support ISSNL projects, contributions from other government agencies to stimulate research using the ISSNL, and private investment.

Finding 3.6: NASA has internal confusion regarding the delineation of basic or applied "research," "industrialization," and "commercialization."

Finding 3.7 Meaningful long-term investment by the commercial sector (or other federal agencies) to develop a LEO economy will require a more proactive dialog between NASA, the ISSNL operator and interested commercial parties to realign ISSNL resource allocation to promote translational R&D on a larger scale. This will also allow the ISSNL operator to adopt more stringent performance criteria by the private sector in assessment of technical feasibility and readiness for downstream prototyping and rigorous analysis of the anticipated cost and time to reach go/no go decisions to commit large scale resources to achieve commercialization.

[12] The IRT did not have access to all of the information necessary to fact check this statement.

Chapter III Recommendations

Recommendation 3.1: The CA should be greatly simplified so that it is a flexible instrument that allows annual input by NASA (defining the "what"), easily measures annual performance of the ISSNL management contractor (the "how"), and a regular cadence of formal exchanges with the ISSNL user community. This revision should create brighter lines between CASIS and the basic research component of NASA, with significantly greater communication and joint planning between the two. When evaluating research that could accelerate space exploration and/or health and safety of astronauts, CASIS and NASA should have a defined and transparent process for joint scientific and value-impact assessment.

Recommendation 3.2: CASIS use of funding and access to do research, even if it is designed to ultimately be marketable, is in conflict with every model of successful commercialization. Low TRL activity will not attract commercial sponsorship. De-conflicting the SLPSRA activity, the National Laboratory agenda, and the LEO commercialization agenda should be undertaken immediately, with consideration of the full R&D continuum – i.e. both R&D (SLPSRA), industrial development (ISSNL) and commercialization (Implementation Partners).

Recommendation 3.3: If NASA desires the ISSNL to operate as a National Laboratory in the traditional sense that advances NASA's primary missions of exploration, science and astronaut health, then NASA should commission a study to consider, at a minimum:

- Optimizing NASA management and oversight of both SLPSRA and the ISSNL to eliminate the current limitations of the authorizing language (i.e. for the ISSNL to do only non-NASA work);
- Vastly strengthening NASA oversight to assure that its primary mission is satisfied, with mechanisms that allow NASA to pivot responsibilities tasked to ISSNL based on NASA needs (reviewed annually, at a minimum)
- Potential duplication of services

Appendices

Appendix A: Acronym List

Advanced Regenerative Manufacturing Institute (ARMI)
Building Technologies Research and Integration Center (BTRIC)
Bureau of Ocean Energy Management (BOEM)
Center for the Advancement of Science in Space (CASIS)
Chief Executive Officer (CEO)
Cooperative Agreement (CA)
Cooperative Research and Development Agreement (CRADA)
Commercial Allocation Service (CAS)
Commercial Resupply Services (CRS)
Department of Defense (DoD)
Department of Energy (DOE)
Federally Funded Research and Development Center (FFRDC)
Fundamental Space Biology (FSB)
Good Manufacturing Practice (GMP)
Government Accountability Office (GAO)
Health and Medical Technical Authority (HMTA)
Human Exploration and Operations Mission Directorate (HEOMD)
Human Research Program (HRP)
Indefinite Delivery/Indefinite Quantity (IDIQ)
Independent Review Team (IRT)
Intellectual Property (IP)
International Space Station (ISS)
ISS National Laboratory (ISSNL)
ISS National Laboratory Advisory Committee (INLAC)
Just-In-Time (JIT)/Point-Of-Need (PON)
Low-Earth Orbit (LEO)
Manufacturing Innovation Institute (MII)
Management and Operations (M&O)
Marcus Langseth Science Oversight Committee (MLSOC)
Maximum Building Energy Efficiency Research Laboratory (MAXLAB),
Memorandum of Understanding (MOU)
National Aeronautics and Space Administration (NASA)
NASA Inspector General (NIG)
National Institutes of Health (NIH)
National Oceanic and Atmospheric Administration (NOAA)
National Science Foundation (NSF)
OIG (Office of the Inspector General)
Office of Naval Research (ONR)
Organ Procurement Organization (OPO)
Organ Procurement and Transplantation Network (OPTN)
ORNL (Oak Ridge National Laboratory)
Physical Sciences (PS)
Point-Of-Care (POC)
R&D (Research and Development)
Science Mission Directorate (SMD)
Space Life and Physical Sciences Research and Applications (SLPSRA)
Space Transportation System (STS)
Science, Technology, Engineering and Mathematics (STEM)

Technical Interchange Meeting (TIM)
Technology Readiness Level (TRL)
Tissue Engineering and Regenerative Medicine (TERM)
Translational Research Institute for Space Health (TRISH)
United States Coast Guard (USCG)
United States Geological Survey (USGS)
University-National Oceanographic Laboratory System (UNOLS)
Vision for Space Exploration (VSE)

Appendix B: Models for Successfully Leveraging Government Investment in Unique U.S. Capabilities

Model 1: The Research Vessel Langseth – part of the University-National Oceanographic Laboratory System (UNOLS) [13]

At its inception in 1971, UNOLS offered a coordinated response from 17 ship-operating laboratories to address a growing need to understand the impact of oceans on marine life, coastal regions, commerce, and the Earth. Nearly 50 years later, UNOLS has grown to an organization of 66 academic institutions and National Laboratories involved in oceanographic research. Support is traditionally provided by six federal agencies: National Science Foundation/Division of Ocean Sciences and Division of Polar Programs, Department of the Navy/Office of Naval Research (ONR), National Oceanic and Atmospheric Administration (NOAA), Department of the Interior/U.S. Geological Survey (USGS), Bureau of Ocean Energy Management (BOEM) and the U.S. Coast Guard (USCG). Awards for operation of individual ships is through cooperative agreements with their host academic institutions.

UNOLS operates independently from commercial activities and fulfills a mission dedicated to research and education. Its primary responsibility is to coordinate and schedule activities of its Academic Research Fleet with research and support vessels operated by NOAA and USCG. UNOLS also serves strategic roles, including planning for the future and identifying and meeting the scientific infrastructure requirements of the U.S. oceanographic research scientists, students and technicians. Through meetings, workshops, reports, studies, and daily communication, UNOLS provides a conduit for open dialog between federal agencies supporting oceanographic research and the scientific community being served. This enables the United States to make advances in science, education, and public awareness.

The Research Vessel Langseth is distinct among UNOLS ships in that it is a designated National Facility. Like the ISSNL, this status highlights the Langseth's key role in serving a broad community by providing a unique capability (in this circumstance, imaging beneath the oceans). Purchased by the NSF under a cooperative agreement with the intended operator of the vessel, Columbia University, Langseth's science operations are reviewed by the Marcus Langseth Science Oversight Committee (MLSOC) at the Lamont-Doherty Earth Observatory at Columbia. The MLSOC consists of scientists from the community and serves as a liaison between the science community, the facility operator, and the NSF. This unique operation highlights the importance of user committees with strong ties to the academic research community to maximize utilization of exclusive research vessels operating in special environments.

[13] We emphasize that UNOLS coordinates the activity of oceanographic assets that are owned and operated by dozens of academic institutions and National Laboratories. The scope of this system is considerably greater than the current ISSNL, thus the management activities of UNOLS are vastly more complex than CASIS. Although the ISS is not a multiplatform LEO research ecosystem, it could be an anchor tenant. As a laboratory research system develops in LEO on multiple independent platforms (a process that will take years or even decades), the relevance of UNOLS as a management model becomes more apparent.

Model 2: Building Technologies Research & Integration Center – a Department of Energy User Facility

The Building Technologies Research and Integration Center (BTRIC), established in 1993, is the Department of Energy's only designated user facility dedicated to performing early-stage research and development in building technologies. The BTRIC comprises a 38,000 sq. ft. research campus and includes the flagship Maximum Building Energy Efficiency Research Laboratory (MAXLAB), a multi-purpose laboratory to advance the energy efficiency and durability of building envelopes (e.g., large-scale wall assemblies), equipment, and appliances. Over its lifetime, the BTRIC has had 46 University partners and 157 Industry Partners**.** The BTRIC is run as a public-private partnership managed by the Oak Ridge National Laboratory (ORNL) to tackle basic research in conjunction with universities, while industry focuses on later stage research and development and implementation. BTRIC supports DOE programs, other federal agencies, state agencies, and the private sector through Cooperative Research and Development Agreements (CRADAs) or a variety of forms of User Agreements. More than 150 industry partners annually work with BTRIC to advance and commercialize building technologies. The industry partners can leverage ORNL's world-class buildings capabilities through user agreements and collaborations approved by DOE.

Model 3: Advanced Regenerative Manufacturing Institute (ARMI) – a Manufacturing USA Manufacturing Innovation Institute

The BioFabUSA Program is part of the Advanced Regenerative Manufacturing Institute (ARMI). The mission of ARMI is to make practical the large-scale manufacturing of engineered tissues and tissue-related technologies. ARMI is managed by DEKA Research and Development Corp, a Manchester NH technology firm founded in 1982 consisting of nearly 400 engineers, technicians, and support staff.

BioFabUSA is designed to attract and develop an ecosystem of both large and small industrial/commercial institutions. Given the nascent stage of the regenerative manufacturing industry, this includes Tissue-Engineering and Regenerative Medicine (TERM) startup companies as well as larger firms that see this as an attractive adjacent market opportunity. The technical scope for BioFabUSA work includes innovations across five thrust areas:

- Cell Selection, Culture and Scale-up
- Biomaterial Selection and Scale-up
- Tissue Process Automation and Monitoring
- Tissue Maturing Technologies
- Tissue Preservation and Transport

Funded in late 2016 as a Manufacturing Innovation Institute (MII), BioFabUSA seeks to make the large-scale manufacturing of engineered tissues and tissue-related technologies practical. With this goal in mind, BioFabUSA brings together engineering, life science, computer science, materials science, manufacturing and workforce development expertise from industry, academia, non-profit organizations, and local, state and federal government. Sixty corporate members in this multidisciplinary consortium had already committed $214 million when the DoD announced its 5-year, $80 million MII award in 2016.

MIIs are the core of the Manufacturing USA network. Manufacturing USA connects people, ideas, and technology to solve industry-relevant advanced manufacturing challenges, enhancing industrial competitiveness and economic growth and strengthening our national

security. Currently 14 institutes have been funded through nine federal agencies, with DoD and DoE as the most frequent sponsors. Each MII is a public-private partnership, jointly funded by the sponsoring agency and private industry, focused on a unique manufacturing technology and working toward a common goal that reduces a specific segment of research to practice. MIIs connect member organizations, work on cutting-edge research and develop collaboration projects to solve industry's toughest challenges and train people on advanced manufacturing skills. Across the Institutes, the Federal government has committed over $850 million, which has been matched by more than $1.8 billion in non-Federal investment.

New institutes are solicited by Requests for Application and funded through cooperative agreements. Applications must guarantee co-investment of private funding that at least equals the Government's investment and funding is typically in the range of $80-$100 million for five years.

Appendix C: Future Operations

Expectations, Deliverables and Accountabilities in Building the LEO Economy

The trajectories for innovation and successful commercialization are often unpredictable and final markets may differ from those originally envisaged. The trajectory for LEO will likely be no different than other markets (e.g. transportation, materials, telecommunications, computing and (bio)pharmaceuticals). Technology maturation and market evolution are typically preceded by a variety of challenges before the substantial financial investment and orderly development processes needed for final industrialization yield final products and services. The major difference facing the nascent LEO economy is that ISSNL is the only commercial testbed currently available. This contrasts with the much larger infrastructure, and of skilled personnel pool and for earth-based R&D, together with greater flexibility to expand manufacturing footprints and access to abundant investment capital from the public and private sectors and venture sources.

By definition, successful commercialization requires a market. Markets evolve either from incremental, typically linear, innovation to expand existing markets or by more dramatic, often non-linear, Schumpeterian disruptions that result in radical and rapid displacement and extinction of previous market(s). In either setting, the dynamics of market evolution are defined by the interplay between new technology (push) and perceived new market needs (pull). The history of NASA's strategic perspectives over the past three decades on the use of LEO (i.e. Space Transportation System and ISS), and the relatively slow commercial achievements of ISSNL activities to date suggest a need for increased focus on market assessment, in part to temper the belief that industry could immediately see the commercial value of LEO opportunities and commit the full capital, technology and intellectual resources required to relieve NASA and the US taxpayers of the cost of operating the Space Shuttle and ISS platforms over the coming decade.

Building a LEO Commercial Economy and the Role of the ISSNL

An inventory of the needs and opportunities for space commerce proposed by NASA, CASIS and the cadre of companies exploring research on the ISSNL reflect bold aspirations but the technical, regulatory and economic pathways to robust commercial revenues remain uncertain. The scalability challenge, infrastructure requirements and the time and cost to establish commercial viability will likely vary substantially between different industry sectors. In planning the future trajectory for LEO-based commerce, it appears there is a dichotomy between the timelines for successful industrialization of innovation in the physical sciences and engineering domains versus life sciences (biology)-based products

Many of the proposed ISSNL-based commercialization endeavors for non-biological products (e.g. advanced materials) focus on extending a single or small number of design elements from current terrestrial technologies to customize them for use in flight operations and facilitate building commercial prototypes. By contrast, few space-based life science applications (e.g. health, agriculture, ecology and human habitation in space) involve straightforward extrapolation from earth-based precedents, which will likely impose the need for extensive basic research before commercial potential can be assessed.

The timelines to validate commercial prototypes and scale to full industrialization remain largely ill-defined. NASA's stated objective to be 'one-of-many' customers for the ISSNL and future private sector LEO platforms to defray the cost of current launch and resupply activities is understandable, However the IRT believes that in the next 5-10 years, NASA will probably continue to be the preponderance of the funding source for launch and supply services. In the 10-20 year timeframe, the evolving landscape of more cost-effective private sector launch and supply capabilities, together with cost-reduction in experimental and prototyping costs of in-flight activities, may enable NASA to achieve the desired cost shifting.

CASIS and NASA Objectives for Use of the ISSNL to Promote the Commercial LEO Economy

It will be important for the operator of the ISSNL and NASA to develop cogent plans with current and future industry partners using the ISSNL to ensure that companies will be able to seamlessly transition their ongoing commercialization activities to the next-generation of private sector-based LEO platforms following retirement of the ISS in the 2024-2030 period without incurring costly redesign and/or reconfiguration of their production systems.

The use of the ISSNL in its remaining life as a unique LEO resource cannot be considered in isolation from NASA's other strategic objectives for the transition to alternative commercial LEO resources and support of activities that will contribute to later deep space missions.

The core tenets[14] are to:

- Implement an orderly transition of human space flights in LEO from current reliance on the ISSNL to new private sector LEO platforms
- Work with commercial partners to stimulate global demand and new markets for space-based products/services to sustain US competitiveness in the space frontier
- Develop a vibrant, financially self-sustaining commercial LEO market in which NASA is one of many customers in a LEO commercial ecosystem
- Advance the technology and systems required for long duration spaceflight systems, including systems for interplanetary travel and permanent space habitation

[14] Core tenets were derived from an analysis of:

- P. L. 115-10
- Forecasting Future NASA Demand in Low Earth Orbit, October 2018. https://www.nasa.gov/sites/default/files/atoms/files/forecasting_nasa_demand_in_leo_white_paper_final.pdf
- Strategy for Human Spaceflight in LEO and Economic Growth in Space joint submission to the National Space Council with the Departments of Commerce and State, November 2018. https://www.nasa.gov/sites/default/files/atoms/files/strategy_for_human_spaceflight_in_leo.pdf
- NASA Interim Directive (NID): Use of International Space Station (ISS) for Commercial and Marketing Activities, June 6, 2019. https://www.nasa.gov/sites/default/files/atoms/files/nid_8600_121_tagged.pdf
- Forecasting Future NASA Demand in Low Earth Orbit: Revision Two-Quantifying Demand, June 7, 2019. https://www.nasa.gov/sites/default/files/atoms/files/forecasting_future_nasa_demand_in_low-earth_orbit_revision_two_-_quantifying_demand.pdf
- NASA Plan for Commercial LEO Development. Summary and Near-Term Implementation Plans, June 7, 2019. https://www.nasa.gov/sites/default/files/atoms/files/commleodevt_plan_6-7-19_final1.pdf
- NASA's Plan to Foster the Low-Earth Orbit Economy. Presentation by D. Comstock at Wernher von Braun Memorial Symposium, Huntsville, Alabama, September 11, 2019. https://astronautical.org/dev/wp-content/uploads/2019/09/VBS_Wed_1230_Comstock_c.pdf

Industry Engagement and Investment in ISSNL-Based Commercialization Activities

At the present time, no commercial products of large U.S. or foreign companies are manufactured aboard ISS or any other space platform. The reason for this is multifold;

- The complexity and cost of a creating and operating in a space-manufacturing complex – something never before achieved
- Limited access and crew time constraints
- Production of marketable items in space involves resolution of many issues of safety, transportation and storage of raw materials, testing of products for quality and key properties, transportation of products to Earth, etc.

The lack of immediacy for commercial products in LEO facilities does not mean that U.S. commercial product development can't be stimulated using ISS resources. The IRT notes that prior to the formation of the ISSNL, commercial entities simply had no clear access point within NASA to propose let alone conduct research aboard the ISS. Therefore, as Fig. C.1 shows, the ISSNL may still be in the early stages of commercial product development. These stages start with scientific and technical knowledge know-how and the subsequent progression over reduces science to the practices needed to bring new products to the marketplace.

- **Science Development**
  - **Product Development**
    - **Business Definition**
      - **Production Development**
        - **Business Analysis**
          - **Market Testing**
            - **Product Manufacturing**
              - **Product Sales**

Figure C.1: Showing the progression of steps involved in commercialization of new products

Review of CASIS documents show that current commercial studies underway with the ISSNL now and over the next few years appear to fall under the categories of **Science Development** and **Product Development** in the above diagram. Even though these two initial activities have, from 2011-2019, generated approximately $180 million in economic activity associated with CASIS business development efforts, moving further down the ladder of business development is a will likely require more focus and a strategy for a faster pace..

Barriers to Proficient Commercial R&D and Industrialization in LEO

Notwithstanding the deficits in NASA-CASIS interactions and CASIS Board governance outlined in this report, the CASIS budget appears currently inadequate to fulfill the over-subscribed requests for ISSNL flights and crew usage. Collectively, the perhaps unexpected problems associated with over-subscription have contributed to bureaucratic, technical, operational and financial barriers to Implementation Partners in their pursuit of new markets that are scalable, standardized (by industry sector), sustainable and financially self-sufficient.

Intellectual Property and US Government Policies on Critical Technologies

The IRT believes that modification of the US Government's intellectual property (IP) position may be necessary to create LEO economy and sustainable demand. Development of novel

discoveries on the Government-owned ISS theoretically contaminates the IP rights of corporate partners and investors.

Although NASA has officially taken a position to indicate they will not exercise reach through rights into corporate IP, there is no evidence that NASA can speak for the entire Government and guarantee the security of a company's IP. As a result, companies may be reluctant to make major investments in research and manufacturing on the ISS. A change in legislation is the only way to ensure the security of corporate IP.

The Evolution of Space-Based Commerce: A Long-Term Journey

Opportunities for space-based commercialization in LEO and deep space missions fall into the following categories:

- products with unique properties conferred by reduced gravity either for exclusive manufacture in space (currently with likely limited scalability) or confirmation of proof-of-concept commercial prototypes that merit transfer of production to terrestrial manufacturing facilities
- space-based production platforms that are superior to terrestrial manufacturing of comparable products/services to terrestrial manufacturing in terms of speed, quality and/or cost
- production of physical/electronic materials and robotic platforms destined exclusively for use in the construction/repair of space vehicles in LEO or deep space
- in-flight just-in-time/point-of-need production of small batches of biopharmaceuticals and other countermeasures to mitigate in-flight risks to crew health and performance
- development of scalable supply chains for food, water and other renewable resources to support extended deep space missions

The potential utility of LEO environments for pharmaceutical manufacturing and new approaches to bioengineering of cells, tissues and organs has received particular emphasis in both NASA and CASIS research priorities and NASA external public relations. A detailed critique of the technical status and feasibility of these claims is provided in Appendix D, but several general comments on the challenge of bioprocess product development in LEO warrant commentary.

Unlike traditional pharmaceuticals based on a single chemical compounds, the use of biotechnology and synthetic biology to produce genetically engineered proteins, genetic therapies and genetically-modified living cells as therapeutic agents has required regulatory agencies to constantly adapt new policies to address the rapid pace of innovation for these new product classes and production methods. Any commercial LEO effort to produce proteins and living cells, tissues and organs, whether for down-transfer for use in terrestrial healthcare or exclusive use in space habitats to sustain astronaut health will be subject to similar comprehensive regulatory oversight. This requirement assumes even more relevance in the proposed use of LEO as a platform to produce tissue engineering and regenerative medicine (TERM) products which contain cellular components that are known to exhibit different patterns of gene expression than their homologous counterparts studied in terrestrial laboratories. Other challenges in space-based TERM efforts ongoing or proposed for the ISSNL are discussed in detail in Appendix D.

All of these questions are addressable. However, the timelines to identify solutions and satisfy regulatory requirements dictates that space-based biocommerce must be viewed as a 10-year exercise at a minimum.

The intrinsic variability and phenotypic plasticity of biological systems is recognized as a key factor in the so called 'reproducibility crisis' in life sciences research in which a disturbingly high fraction of published results cannot be replicated[15]. This problem, together with statistical standards for scientific validation, dictate that life sciences R&D has a 'large N' requirement to establish data consistency. The 'N' challenge is particularly problematic in the use of genomics and other molecular methods for the analysis of biological systems (multiOmics) in which hundreds of thousands or millions of DNA, RNA or protein sequences are measured simultaneously in a very small number (N) of specimens. This almost guarantees statistical overfitting and bias in data analysis and the risk of false correlations[16]. The genomic and multiOmics profiling technologies deployed to date on the ISS to study living organisms suffer this fate due to the very small number of biospecimens that can be studied due to space limitations in ISS racks and laboratory bays.

The intrinsic differences in the technical complexity, maturation and timeframes for space-based commerce for non-biological and biological applications suggests a bifurcation in how NASA, and the operator of the ISSNL, as well as commercial partners define priorities for the most productive use of the ISS in its remaining life.

a) For non-biological products/services the emphasis should be to continue advanced development activities in materials science to achieve compelling proof-of-concept for commercial prototyping and scalable LEO manufacturing together with proactive planning to ensure that the production platforms are compatible with production infrastructure on the next generation of private sector LEO platforms.
b) For biological products/services greater transparency about the barriers and timelines for feasible LEO manufacturing would be a welcome reform. In concert with commercialization plans, development of cogent, transparent plans and priorities by NASA's HRP and Health and Medical Technical Authority (HMTA) would logically guide this important area.

[15] Reproducibility and Replicability in Science (2019) National Academies Press
[16] L.M. Weber et. al. (2019) Genome Methods 20, 123 and I. Zappia et. al. (2018) PLOS Comp. Biol. 14e1006245

Appendix C Findings

Finding C.1: Stimulating industrial activities in LEO will require more options and reliable access over the long-term.

Finding C.2: ISS alone is not sufficient to stimulate the commercial market.
As a growing number of commercial space companies are providing low-cost and frequent access to suborbital and orbital space for humans and research payloads, it is important to fully utilize these capabilities to effectively stimulate the commercial market.

Finding C.3: Industrial R&D in microgravity is just one R&D tool for those companies - those multitude of tools compete for resources with each other inside companies. Proponents of using ISS need to be cognitive of the other R&D tools (i.g. Artificial Intelligence, etc) to see if they can successfully compete within the company for resources by creating superior products in a cost-effective manner.

Finding C.4: The market timeframe for viable market needs reliability of access and clear IP terms. Smaller companies may not have the resources to reach out to new customers in microgravity. Larger companies need to see NASA as a partner in the longer game.

Finding C.5: The high cost and high risk of space missions, the imperative for comprehensive assessment of health risks for crew members and any prospect of evolution of self-sustaining commercial activities will require a coherent systems-based, end-to-end approach involving diverse stakeholders that span the full spectrum from basic research discovery conducted by NASA, academia and industry to prototyping development of cost-effective commercial products and creation of new markets for space-based manufacturing.

Finding C.6: There is a lack of an integration mechanism (like IDIQ) to address strategic and operational barriers faced by companies and Implementation Partners to increase the reliability of access to space-based facilities.

Finding C.7: There is still significant need for low TRL R&D with a goal to reduce basic science findings to improved practice in the marketplace (manufacturing, clinical practice, etc.) Bifurcating the authority without clear joint planning, common NASA oversight and the development of a broad and integrated use community has had limited success. Conversely, SLPSRA has been stymied from similar issues, such as lack of funding, operational resources, and prioritization that has limited its capacity to execute.

Finding C.8: Restricting the ISSNL to non-NASA research may have reduced the Agency's ability to stimulate disruptive research that improves astronaut health and safety.

Finding C.9: The requirement for CASIS to design and implement a STEM education program using ISSNL resources, while laudable in intent, adds to the challenge of productive allocation of scarce ISSNL resources.

Finding C.10: The biopharmaceutical, diagnostic and biomedical device industries are among the most highly regulated segments of the advanced technology economy. These regulatory policies will likely also apply to these product classes manufactured in space.

Finding C.11: Any commercial LEO effort to produce proteins and living cells, tissues and organs, whether for down-transfer for use in terrestrial healthcare or exclusive use in space habitats to sustain astronaut health will likely be subject to similar regulatory oversight.

Appendix C Recommendations

Recommendation C.1: The ISSNL has the opportunity to maximize the utilization of the ISS as an "industrial incubator in LEO." However, even with regular, reliable up-and-down mass to the ISS, a lack of access to regular, reliable flight opportunities on a variety of platforms (i.e., free flyers, suborbital platforms, etc.) will stymie the progress of commercialization in LEO.

Recommendation C.2: Future considerations should be given to how the commercialization of LEO mandate expands beyond the concept of an industrial incubator to additional platforms. We acknowledge that such activities are beyond the current scope of ISSNL authorization language. NASA can and should stimulate broad discussion among all stakeholders to develop a model for cross-platform (i.e., free flyers and suborbital platforms, etc.) considerations spanning the entire panorama of basic research to applied research to product development.

Recommendation C.3: The Government can help stimulate the commercialization of LEO by conducting a study or workshop on what would be necessary to have robust trans-atmospheric and orbital supply chain processes that support LEO industrialization. This should look at the complete system of potential platforms, policies, procedures and practices to be used by any commercial entity whether they are operating platforms or production processes and could include ISSNL as an option.

Recommendation C.4: With respect to commercialization activities, NASA should consider a more active approach that allows development of a clear set of steps leading from early science work to full product production and distribution. This will necessitate definition of progressive levels of required privacy and proprietary ownership of IP for their product(s).

Recommendation C.5: If NASA repositions the ISSNL as an industrial incubator in LEO, it should evaluate how the ISSNL can be used to support translational research that furthers the Agency's exploration goals.

Appendix D: Brief Review of the Status and Feasibility of Proposed Initiatives in Space-Based Biocommerce

Unique Challenges for Space-Based Biocommerce and Medicine

Investment by NASA, CASIS and industry partners have focused primarily on potential applications in biopharmaceutical manufacturing and tissue engineering and regenerative medicine (TERM). The IRT recognized that maturation of viable LEO-based commercial markets across all industrial sectors will require some level of longer-term government funding and new incentives for private sector investment. The life sciences sector in particular faces a longer, and currently less clear, pathway to commercial success.

The biopharmaceutical, diagnostics and medical device industry are among the most highly regulated elements of the high technology economy. It is difficult to envisage any bioproduct produced in space being approved for routine terrestrial use without fulfillment of these comprehensive regulatory requirements. Demonstration of the efficacy and safety of drugs, biologicals, diagnostics and devices requires extensive clinical trials and compliance with the stringent QA/QC demands of Good Manufacturing Practice (GMP). GMP compliance will require sterile production bays to avoid product contamination risks from the high particulate debris density in the ISS and/or from microbial films that coat the internal surface of the spacecraft and biocontainment protocols to eliminate transfer of astronaut microbiomes to the surfaces of production bays.

Any product manufactured in space destined for use when deployed in routine clinical medicine on earth would also need to demonstrate full therapeutic potency plus formulation fidelity and stability in the terrestrial setting. Neither of these parameters are guaranteed. The demonstrated accelerated degradation of drugs and other molecules in microgravity is but one feature will need to be addressed[17] to ensure product quality and suitably lengthy therapeutic lifetimes.

Unlike traditional pharmaceuticals based on a single chemical compounds, the use of biotechnology and synthetic biology to produce genetically engineered proteins, genetic therapies and genetically-modified living cells as therapeutic agents has required regulatory agencies to constantly adapt new policies to address the rapid pace of innovation for these new product classes and production methods. These high levels of regulatory requirement assume even more relevance in the proposed use of LEO as a platform to produce tissue engineering and regenerative (TERM) products which contain cellular components that are known to exhibit different patterns of gene expression than their homologous counterparts studied in terrestrial laboratories. Other challenges in space-based TERM efforts ongoing or proposed for the ISSNL are discussed in detail in Appendix D.

Challenges for MultiOmics Approaches

The intrinsic variability and phenotypic plasticity of biological systems is recognized as a key factor in the so called ‘reproducibility crisis’ in life sciences research in which a disturbingly high fraction of published results cannot be replicated. This problem, together with statistical standards for scientific validation, dictate that life sciences R&D has a ‘large N’ requirement to

[17] See R.S. Blue et. al. (2019) npj Microgravity 5, 14 and R.S. Blue et. al. (2019) arXivi 1905.06377v1

establish data consistency. The 'N' challenge is particularly problematic in the use of genomics and other molecular methods for the analysis of biological systems (multiOmics) in which hundreds of thousands or millions of DNA, RNA or protein sequences are measured simultaneously in a very small number (N) of specimens. This almost guarantees statistical overfitting and bias in data analysis and the risk of false correlations[18]. The genomic and multiOmics profiling technologies deployed to date on the ISS to study living organisms suffer this fate due to the very small number of biospecimens that can be studied due to space limitations in ISS racks and laboratory bays.

These considerations dictate that contemplation of in-flight manufacture of drugs, biologics or diagnostics would probably be confined to two scenarios: 1) just-in-time (JIT)/point-of-need (PON) production of small batches of existing FDA-approved products to treat astronaut disease occurring during extended flight in situations of where these therapies are not available from the on-board pharmacy or cannot be resupplied from earth in the needed time frame; and 2) the need for an entirely novel category of diagnostic and therapeutic products tailored specifically to detect and treat any new categories of in-flight diseases whose causal molecular pathology is unique to exposure to low gravity environments (ie. space-associated syndromes/phenomes) and distinct from disease processes arising in the same organ/tissue/cell type(s) in populations on earth. SANS (spaceflight-associated neuro-ocular syndrome) is a pre-eminent example of an apparent new disease risk arising from extended space flight.

If this perspective is valid, space-based biocommerce is likely to remain the preserve of earth-based industries for large-scale production of diverse drugs, vaccines, diagnostics, devices and sensors for patient care. However, given that 'space-based industrial biomedicine' is now highlighted by NASA and CASIS as one of two thematic areas for prioritized use of the ISSNL to advance space biocommerce, a brief review of the status and feasibility of these proposed initiatives is merited.

Appendix D.1 Protein Crystallization in Space and Identification of New Drug Targets for Earth-and Space-Based Manufacturing of Biopharmaceuticals

This topic has been the most consistently publicized aspect cited by NASA and CASIS of the potential utility for LEO-based for commercial activity in the biopharmaceutical sector.

There is an extensive multi-decade literature on the use of X-Ray Crystallography (XRC) to define the three-dimensional (3D) structure of proteins at the Ångstrom level to guide drug design. Knowledge of 3D structure of a target protein allows rational design and synthesis of candidate drug molecules with the optimum structure and shape to 'dock' with the presumed 'active site' of the target protein to block (antagonists) or stimulate (agonists) its function.

Microgravity environments such as LEO have been advocated as a unique resource to generate high quality crystals of protein drug targets that cannot be easily crystalized on earth. Microgravity eliminates the convection and sedimentation effects that occur under 1g gravity that may retard and/or prevent crystallization, enabling higher quality crystals to be generated, including different crystal isomorphs with shapes, size and densities from earth-generated crystals. While a few interesting exceptions have been documented, the data on protein crystallization in microgravity environments show that in the majority of cases the form, quality

[18] See L.M. Weber et. al. (2019) Genome Methods 20, 123 and I. Zappia et. al. (2018) PLOS Comp. Biol. 14e1006245

and reproducibility of protein crystals are no different from terrestrial crystallizations.[19] The caveat for this conclusion is that far fewer proteins have been crystallized in LEO compared to the order of magnitude greater number of proteins crystallized on earth the academic and industrial communities over the same period.

Notwithstanding the continued investment by NASA and CASIS in 'one-off' protein crystallization studies using the ISSNL the pragmatic reality is that the biopharmaceutical industry places a low priority on crystallization as a routine platform for identification of new targets for drug discovery. The overwhelming fraction (>97%) of drugs approved by the FDA over the last three decades were developed against protein targets which were identified by high throughput phenotypic screening assays using cultured cells and more recently using cultured organoids. These highly automated screening systems, supplemented constant refinements offered by rapid advances in genomic, transcriptomic and proteomic profiling and the use of gene/protein knockout such as CRISPR-CAS and other gene editing tools, provide highly productive platforms to identify new target proteins for drug development or for direct use as biological therapeutics. These modalities allow large scale rapid screening of extensive chemical libraries (10^6 to 10^8 different molecules) against thousands/millions of putative drug targets.

The utility of crystallography in mapping the 3D structure of potential drug target proteins has also been eclipsed in the last decade by cryo-electron microscopy which now provide the majority of published papers on Ångstrom-level 3D resolution of protein structures from both academia and industry (ref).

For the five reported protein target molecules crystallized in LEO in Space Shuttle or ISSNL missions on behalf of industry review of the published R&D pipelines of the sponsor companies as of December 2019 indicated that no candidate drugs targeting these proteins have emerged (one target from Eli Lilly was not disclosed publicly). The results from several sponsor companies have yet to be published in the scientific literature several years after the LEO experiments were conducted.

The crystallization of Merck's immuno-oncology drug Keytruda (pembrolizumab) flown on SpaceX-CRS10 in 2017 is the only publication with any apparent novel commercial potential. The higher density and different shape of the pembrolizumab crystals in LEO may be valuable for new formulations of this asset for improved ease and frequency of dosing. These findings may also enable Merck to file additional IP on novel isomorphs as future protection against generic competition on Keytruda's patent expiration. However, there would be no rationale for Merck to switch at this time from the current Keytruda formulation and incur the cost and time to conduct new bioequivalence and accelerated stability testing on the new crystal formulations to replace the current formulation. This also assumes that the LEO-generated crystals have comparable bioequivalence and clinical efficacy and safety to the original formulation. Given the known complex adverse event (AE) profile of Keytruda and other PD-1 inhibitors[20] it is likely that FDA would require additional preclinical and clinical studies for reassurance that the AE profile of the isomorph(s) is comparable to the original product.

Any assessment of the comparative merits of biopharmaceutical production in space versus on earth must also recognize the growing use of artificial intelligence and deep-learning technologies by academia and industry for algorithmic mining of large libraries of diverse

[19] M. Braddock (2019) Current Drug Disc. Technol. 16, 1
[20] Y. Yang et. al. (2019) JAMA Oncology 5, 108

chemical structures[21] rule sets to better predict drug target structure-activity relationships (SAR). Early findings suggest that the interrogation of very large libraries of potential therapeutic molecules by these advanced data science methods can substantially accelerate selection of drug targets and drug-target molecule pairings.[22]

Collectively, these trends in industry practice dictate that high throughput screening and clinical trials of new drugs seem destined to remain an exclusively terrestrial endeavor. As already mentioned, the only corollary to this conclusion would be if expanded manned space flights reveal a catalog of in-flight disease(s) (or their manifestation on return to earth) that are caused by LEO and induce different molecular pathologies than terrestrial disease(s) affecting the same organ system(s). If this eventuality becomes a reality, new therapies would be needed to counter these unique pathophysiological states. As human habitation of space expands in the next half century the need for this category of unique countermeasures may increase. However, all the time the number of individuals affected by idiosyncratic space-associated syndromes remains small there is little incentive for commercial industry to engage to develop countermeasures. The responsibility to develop countermeasures against the unique space-flight associated syndromes would then fall to the government agencies and private sector companies deploying personnel to space. This scenario also assumes that any space-associated disease syndromes are non-communicable. If, however, altered host-pathogen interactions arising in space environments were to generate a novel, highly transmissible contagious agent capable of causing significant morbidity/mortality that might be carried back to earth by returning astronauts then an entirely different set of public health containment actions and incentives to develop countermeasures would apply.

Appendix D.2 Generation of Novel Microbial Metabolites in LEO as New Sources of Chemical Diversity for Industrial Applications

Microbes and their secondary metabolites are the predominant source of today's antibiotics. Genetically engineered microorganisms are a core manufacturing platform for many new classes of therapeutic proteins and other biologicals. New genome engineering and gene-editing tools are being used to modify a broad range of prokaryote and eukaryote cells for vaccine development, improve crop yields, engineer pest resistance in plants and production of synthetic biofuels and other high value chemicals.

The need for new classes of antibiotics to combat the alarming increase in drug-resistant infections has stimulated substantial government and private sector investment in this imperative[23]. To date, however, this quest has not resulted in any upsurge in biopharmaceutical corporate interest or venture investment to explore whether the altered metabolic pathways exhibited by microorganisms in LEO environments might be a source of novel candidate antibiotics.

The commercial challenge is identical to the hurdles described in the previous section on protein crystallography in LEO: what is the likelihood that LEO-based experiments will be superior to the high throughput automated screening systems being used by the biopharmaceutical and chemical manufacturing sectors to commercialize microbial metabolites as medicines or other

[21] See F. Lake (2019) Future Drug Disc. 1, 1 and H.C.S. Chan et al (2019) Trends Pharm. Sci. 40, 592
[22] A. Zhavoronkov et. al. (2019) Nature Biotechnol. 37, 1038
[23] See M. Renwick et. al. (2018) Expert. Opin. Drug Disc. doi.10.1080/17460441.2018.1515908 and P.H.D. Batista et. al. (2019) Int. Rev. Intell. Prop. Comp. Law 50, 30

high value products. The (N-of-one) "one-off" nature of many of the experiments conducted on the Space Shuttle and ISSNL carries the obvious shortcoming of reproducibility. Without robust evidence of reproducibility, the prospect of industry interest will remain low.

Appendix D.3 Tissue Engineering, Regenerative Medicine (TERM) and Mechanobiology

The dream of regeneration of damaged body parts following trauma, to offset the damaging ravages of disease and ameliorate the progressive frailties of aging has deep historical Promethean origins[24]. NASA, CASIS and a few startup companies have identified TERM as a strategic opportunity for space-based commercialization.

The use of genomics and molecular biology to map the molecular information networks that encode biological function is one of the major intellectual achievements of the past 50 years. The convergence of these powerful analytical platforms with advances in synthetic biology, biocompatible materials, miniaturization and automation engineering, microfluidics and computer-controlled 3D fabrication technologies for 'bioprinting' of living cells has established TERM as a vibrant new domain in the life sciences ecosystem with the goal to engineer synthetic 'biomimetic' systems that emulate the structure and function of diverse body tissues and organs in humans and other species.

These activities fall into three broad categories:

- cultivation of inducible pluripotent human stem cells (iPSCs) for scalable production of specialized cell types for clinical use in tissue replacement/repair (e.g. bone marrow, neurodegeneration) and as screening assays for more accurate drug discovery versus historical reliance on non-human animal cells as surrogates
- new techniques for laboratory cultivation of 3D assemblies of cell types as organoids or as so called 'tissue-or organ-on-a-chip' to profile the efficacy of candidate drug molecules and more effective preclinical evaluation of potential toxicity risk(s) to for early elimination of toxic compounds before incurring the high cost of their failure later in clinical trials. These tools are also being used to incorporate living cells and tissues into devices and sensors as 'sentinel systems' to monitor environmental exposures to toxins or other hazardous materials and detection the emergence of new microorganisms as threats to humans and important agricultural resources.
- the most ambitious bioengineering TERM aspirations reside in efforts to use 3D printing technologies to assemble complex structures comprising multiple cell types to reproduce the structure, function and complex architectures of human tissues, and ultimately, to construct whole organs for clinical transplantation. Success will require the need to duplicate the exact number and proportion of each cell type present in the natural counterparts and assemble them with the correct 3D relationships. While the goal to replicate 'higher-order' functional structures for clinical use is still distant, iterative improvements in biomimetic engineering will provide valuable insights into the biological mechanisms factors that control the assembly and organization of tissue architectures including potential identification of new drug targets and biomaterials to improve tissue repair and reversal of degenerative disease processes.

These intellectually fascinating vistas of technology 'push' and the perceived major market opportunities ('pull') are attracting substantial private sector investment with applications in healthcare, agriculture and ecosystem sustainability. DARPA has also established several

[24] J. Kozubek (2016) Modern Prometheus. Cambridge University Press

ambitious TERM programs to assess potential utility in warfighter combat care, human performance optimization and the design of diagnostics/sensors containing living cells as sentinel systems for a variety of defense and national security applications.

In assessing the feasibility and timeframe for commercialization of these opportunities, whether in terrestrial or LEO settings, a brief primer of current knowledge of the design principles for construction of synthetic biomimetic systems of escalating complexity is appropriate as context for the technical challenges and long term time horizons for success of TERM aspirations on earth and in space.

The structure, function and coordinated homeostatic integration of different cell types, tissues and organs in the human body is a marvel of biological design, honed over long evolutionary timescales. Each organ contains hundreds of different cell types arranged in rigorously controlled 3D spatial patterns. The different functional properties of each cell type, in turn, is determined by their selective responses to thousands of distinct chemical, optical, electrical and mechanical stimuli delivered by nerves, the blood, lymph and other body fluids. The resulting patterns of inter-cellular communication involve highly-ordered, cell-specific, molecular signaling networks (wiring diagrams) that process the molecular information flows that define normal functions (physiology) and when perturbed lead to disease (pathology).

Different body organs and tissues exhibit different patterns of cell turnover and replacement that depend on stem cells with apparently unlimited replication potential and the capacity to generate progeny that transit along discrete differentiation pathways to create end stage cells with highly specialized functions. Some tissues, most notably the brain and spinal cord, exhibit limited regenerative capacities. Pursuit of how to reactivate/reprogram a regeneration response in these vital tissues is a major topic of research enquiry.

When viewed against this holistic perspective of biological design operating across hierarchical scales from molecules to intact organisms and the multiple molecular networks that regulate the information flow to choreograph different biological functions it is not surprising that significant knowledge gaps exist and major technical gains will need to be made before synthetic biomimetic engineering can reliably reproduce these complex functions. These knowledge gaps and technical barriers are proportional to the degree of “hierarchical” biological order and complexity to be duplicated. Research on how pluripotent stem cells can be induced to produce a variety of specialized end-stage cells and demonstration of their safety is likely to be simpler (a relative term) than the grand challenge of building complete tissues/organs for clinical transplantation.

In the short term (5-10 years), the most pertinent and intriguing dimension for TERM bioengineering in lower gravity environments perhaps resides in opportunities to advance knowledge in the emerging field of mechanobiology. The effects of physical forces on cell shape and function and on the assembly and stability of 3D tissue architectures are largely unexplored. Understanding how cells sense and respond (mechanotransduction) to mechanical forces will be fundamental to making TERM products a reality in both normal and reduced gravity environments.

Proponents of the merits of 3D bioprinting to fabricate tissues and organs in space argue that construction will be facilitated by the weakened physical forces in LEO and allow more precise control of manipulation of cell shape and mobility in the biofabrication of complex multicellular assemblies. In contrast, other highlight that the changes in cell shape and behavior in reduced gravity more closely resemble the aberrant disruption of tissue architecture seen in disease

processes such as EMT (epithelial-to-mesenchymal) in cancer and metastatic progression citing this as a rationale for the potential value of using LEO-based cell and 3D organoids as assays for more accurate profiling of anti-cancer drugs. If this second scenario is the reality, then aspirations to undertake LEO-manufacturing of tissues/organs for clinical use on earth will be imperiled.

One fact is indisputable. Reduced gravity alters the pattern(s) of gene expression in every biological system studied to date. Adaptive phenotypic plasticity in the face of new environmental selection pressures is a fundamental tenet of biological evolution. The obvious corollary is that production of specific cell lineages from stem cell precursors or construction of synthetic quasi-tissues/organs in LEO for proposed use in healthcare on earth will face regulatory scrutiny to ensure that the 'space-phenotypes' in these materials do not pose any immediate safety risk and that any phenotypic reversion over time to an 'earth-phenotype' will not alter their efficacy or safety.

This brief overview of the bioengineering landscape should not be interpreted as a nihilistic perspective on unsurmountable barriers. The record of research ingenuity imparts confidence that solutions will evolve. The central question, once again, is the timing to achieve these feats of advanced bioengineering and whether LEO offers any tangible technical, clinical, logistical or economic advantages over production in a terrestrial setting and what is the probability that LEO-based platform can outpace progress anticipated from the substantial R&D investments in TERM being made by earth-based companies and academic institutions.

Appendix D.4 Human Health Risks from Extended Exposure to Reduced Gravity: New Horizons in Space Medicine and Under-Leveraged Opportunities for Commercial Development of Countermeasures?

Given the renewed political momentum and budget commitments to NASA to reinvigorate and expand manned space flights to the Moon and beyond, the importance of NASA and the ISSNL in preparing plans for more expeditious use of the ISS in its remaining life as the only manned flight resource to assess health risks from LEO and deeper space missions cannot be over-emphasized.

The study and manipulation of living systems, whether in space or on-earth, must accommodate the following multi-dimensional complexities. Many of the biological functions of relevance to biocommerce and assessment of health risks comprise multiple components and analysis across a broad spatio-temporal range from quantum effects in molecular interactions to pathophysiological processes in intact organisms. Living systems alter their properties (phenotypes) in response to new environments. This adaptive 'plasticity' is particularly relevant since multiple LEO studies on the ISSNL have demonstrated that microorganisms, plants, worms, insects, arachnids, fish, rodents and humans exhibit rapid and variously reversible changes in gene expression and epigenetic regulation. These insights into perturbation of biological pathways at the molecular level complement the long-recognized effects of LEO on anabolic/catabolic processes in bone and muscle seen in astronauts and animal models. These effects are now complemented by a growing list of pathophysiological changes in astronauts involving multiple organ systems, including changes in cardiovascular hemodynamics, metabolic and circadian cycles, reactivation of latent viruses and alterations in immune, vision, sensorimotor and cognitive functions.

Studies on a broad spectrum of species from microorganisms to mammals and profiling of astronaut pathophysiology on Space Shuttle and LSS missions of varied duration have revealed

rapid changes in gene and protein expression and altered epigenetic markers in LEO. These studies have also documented changes in microbial virulence and increased propensity to form biofilms plus dysbiosis in astronaut gut microbiomes with yet unknown implications for risks to astronaut health. The well recognized effects of microgravity in altering anabolic and catabolic processes in bone and muscle have received considerable attention to develop countermeasures to sustain astronaut fitness. Elucidation of molecular mechanisms underlying these processes are relevant to ongoing industry activities to develop improved therapies for osteoporosis, cachexia and other aspects of aging processes on earth. To date, however, LEO experiments have not identified any new targets or molecular pathways for therapeutic intervention not identified previously in studies of these pathophysiological events in clinical settings on earth.

Appendix D.5 In-Flight Production of Pharmaceuticals and Other Countermeasures for Space Flight-Associated Health Risks

Given the limited industry interest to date and the technical, logistical and economic barriers to the discovery and manufacturing of biopharmaceuticals in LEO as a superior alternative to terrestrial production the strategic focus for NASA, CASIS and private companies contemplating extended manned flight operations might logically shift to ensuring that a suitable inventory of diagnostic tests, drugs and other countermeasures are available to minimize in-flight health risks and effective treatment of any overt disease episodes. The latter need is illustrated by the recent publication of successful in-flight resolution of a serious blood clotting problem in an ISS astronaut[25].

These considerations raise the question of how far JIT/point-of-care (POC) in-flight production capabilities for important medical interventions will need to be developed versus reliance on onboard pharmacy supplies and/or (re)supply by up-transfer from earth. The balance between these different supply chain options will be influenced by mission duration, resupply frequency, the prevalence and predicted probability of different health risks, the complexity of the countermeasure production process and stowage constraints for any materials that require specialized transport and storage conditions (e.g. refrigeration, sterile reconstitution).

For known in-flight health threats which mirror comparable conditions on earth (e.g. nausea, diarrhea, migraine, headaches, hypertension, cardiac arrythmias) a relatively limited on-board pharmacy and resupply should suffice. For more complex clinical situations this may not be the case. For acute, life-threatening clinical episodes (including infection from on-board microbes that acquire new virulence features or drug resistance) the on-board pharmacopeia may be inadequate. Without the prospect of *immediate* up-transfer of needed countermeasures from earth, JIT/PON production may be the only option. This capability may become essential for missions beyond LEO to the Moon and deep space for which the transit time for up-transfer supply may be inadequate to counter acute clinical events that pose a risk of serious morbidity or mortality.

The biotechnology and synthetic biology industries are exploring JIT/PON miniaturized instruments for fully automated, multistep synthesis of complex molecules, including therapeutic proteins[26]. The recent development of 'digital-to-bioproduct convertor' production systems extends the horizon of automatic biosynthesis in a more dramatic way. These new platforms emulate the biological reactions that are the hallmark of every living organism in being able to translate genetic code into proteins in a single instrument of modest size heralds.

The most important dimension of the 'convertor' story is that it enables distributed, democratized manufacturing in local settings. Digital information on gene sequences can be transmitted via the internet to convertor instruments in any location for local production of the protein(s) of interest. These innovations have attracted government (DARPA, BARDA, DoE) and private sector investments to develop JIT/PON capabilities for the synthesis of diagnostic assays, drugs and vaccines. Envisaged applications include: production of medicines for combat care in forward-deployed military operations; manufacture of essential biomedical products in low income countries that lack large scale manufacturing infrastructure; and rapid ('stat') production of countermeasures for public health campaigns in geographically remote locations for faster

[25] S.M. Aunon-Chancellor et. al. (2019) New England J. Med. 382, 99
[26] C. Arnold (2019) Nature 515, 275

containment of infectious disease outbreaks with epidemic/pandemic potential (e.g. Ebola, Zika, Coronaviruses).

The small footprint of these production systems are well suited to in-flight bioproduction and merit strategic assessment by NASA and CASIS to engage new commercial partners for the ISS. It may be prudent for NASA and CASIS in concert with companies planning future LEO and extended duration space missions to design bays on the ISS in its remaining life to prototype JIT/PON production modules for treating in-flight medical emergencies in crew members during extended duration flights.

How regulatory agencies will assess the efficacy, safety and metabolism of any new class of medicines produced in space as countermeasures to treat in-flight crew health risks arising from space-induced abnormal pathophysiology and molecular network disruptions unique to the space environment remains unresolved.

Appendix E: ISS Cooperative Agreement IRT Review

1. Background

In 2005, Congress passed the National Aeronautics and Space Administration Authorization Act of 2005 (P.L. 109-155). Section 507 designated the U.S. segment of the ISS as a National Laboratory and directed the NASA Administrator to "seek to increase the utilization of the ISS by other Federal entities and the private sector through partnerships, cost-sharing agreements, and other arrangements that would supplement NASA funding of the ISS." Additional Congressional direction on the operations, management, and independent assessment of the ISS National Laboratory was provided in the National Aeronautics and Space Administration Authorization Act of 2008 (P.L. 110-422). In August 2011, NASA awarded a 10-year, $136 million cooperative agreement to the Center for the Advancement of Science in Space (CASIS) to manage non-NASA research activities on the National Laboratory portion of the ISS. In July 2017, NASA extended the CASIS cooperative agreement to September 2024, increasing its total cost to $196 million.[27]

The CASIS organization has gone through a number of changes and has evolved its operational model over time as it has learned. In light of the ongoing discussion of the lifetime of the International Space Station and the commercialization of low-Earth orbit, the ISS National Laboratory plays an important role as part of NASA's strategy to send astronauts to the Moon and to Mars. During the current time of leadership transition at CASIS, it is in NASA's interest to convene an independent group to provide an assessment of the NASA cooperative agreement with CASIS and the structure of the cooperation between NASA and CASIS, and to provide recommendations on how to best encourage and maximize ISS utilization in support of NASA's strategies, to include commercialization.

2. Terms of Reference

The IRT will provide an assessment on the status of the cooperative agreement with CASIS over the past year or so, and its ability to meet NASA's needs over the next five years, through September 2024. The IRT should focus its work in five areas:

1. Clarity of mission
    a. Does the cooperative agreement with CASIS meet the intent of the authorizing legislation?
    b. Is the purpose of the cooperative agreement with CASIS clear and shared among stakeholders?
2. Alignment to achieve mission
    a. Does the cooperative agreement foster utilization of the ISS that optimizes the balance between scientific research and commercialization?
    b. Does the cooperative agreement incentivize CASIS and its partners to achieve success?
3. Challenges to achieving mission
    a. Does the NASA relationship and partner organizational structure enable priority-setting and timely decision-making to achieve the goals of the authorizing language?
    b. Are there cultural or other operational mismatches between stakeholders that slow success?

[27] https://oig.nasa.gov/docs/IG-18-010.pdf

    c. Are enabling resources available?
4. Opportunities to increase and accelerate commercialization objectives to achieve NASA's strategies
    a. What have we learned from successes and successful partnerships thus far?
    b. What have we learned from failures thus far?
    c. How do we apply lessons learned from other National Laboratories and government-funded commercialization organizations?
5. Recommended path forward
    a. What changes are needed to enable NASA to most effectively achieve its mission?
    b. What changes are needed to the implementation of Section 602 of P.L. 110-422, the International Space Station National Laboratory Advisory Committee?

We anticipate engagement on a biweekly basis over a period of about 3 months in Fall 2019, including travel to Washington, DC and Cape Canaveral, FL.

3. Management

The convening authorities for the IRT are the Associate Administrators (AAs) for NASA's Human Exploration and Operations Mission Directorate (HEOMD) and Science Mission Directorate (SMD) to reflect both the importance of commercialization objectives in the context of the human exploration infrastructure and scientific research. As such, the IRT will report jointly to the HEOMD and SMD AAs, with anticipated report-outs to NASA leadership as well to government and external stakeholders. This IRT shall be comprised of members with considerable current experience in commercialization of research results, International Space Station utilization and operations, and the operation and commercialization of National Laboratories or similar entities.

The HEOMD and SMDs AA will assure the necessary financial support for the IRT and will jointly agree to the chair and composition of the committee. SMD will provide a Review Manager throughout the process. The IRT Chair and the Review Manager will run all activities of the IRT, and ensure the quality of review deliverables. The final report will be verbally presented to the HEOMD and SMD AAs and other NASA stakeholders, followed by the provision of a final written report.

4. Notional Schedule

The IRT will conduct the assessment over a 11-week period from initial meeting to completion of the final report. The final schedule will be determined following discussions between the IRT, HEOMD and SMD AAs, and other NASA stakeholders. Work should conclude in December 2019.

Week #1	Organizational Telecon; read background materials [scope the effort; develop plan for activities]
Week #2	Team Telecon
Week #3	Fact-finding trip #1 (NASA HQ/Washington DC) [2-3 days, including travel]
Week #4	Team Telecon
Week #5	Fact-finding trip #2 (Cape Canaveral, FL) [2-3 days, including travel]

Week #6	Team Telecon
Week #7	Develop and discuss draft findings for report; draft any final questions for further discussion (Location TBD) [2-3 days, including travel]
Week #8	NASA review of draft report
Week #9	Review NASA comments on draft report; close out remaining questions and revise draft report (Location TBD) [2-3 days, including travel]; NASA reviews revised draft report and submits final comments
Week #10	Complete draft report [a PowerPoint presentation or narrative report]
Week #11	Prepare final report and brief HEOMD and SMD AAs and other NASA stakeholders in Washington, DC

5. Deliverables

The IRT shall produce a non-consensus final report with observations, findings, concerns, and recommendations consistent with Section 2 above. The IRT shall present a summary of its review results to the HEOMD and SMD AAs and other NASA stakeholders.

6. Communications

IRT members shall not engage in public discourse about the work during the review period. Any media or other inquiries related to this assessment shall be referred to the Science Communications Lead in the Office of Communications. Following completion of the work, a public rollout strategy will be developed.

7. Personnel

The IRT membership includes:

Dr. Elizabeth (Betsy)	Cantwell	University of Arizona
Dr. Peter	Banks	Independent
Dr. James	Pawelczyk	Penn State University
Dr. George	Poste	Arizona State University
Dr. Al	Sacco	Texas Tech University
Mr. Tommy	Sanford	Commercial Spaceflight Federation
Mr. Christian	Zur	U.S. Chamber of Commerce

Ex Officio (Review Manager): Ms. Ellen Gertsen

Appendix F: ISS Cooperative Agreement IRT Meeting Agendas

October 7, 2019 - Washington, DC

Time	Track	Speakers
8:00a	Meeting Introduction	B. Cantwell/E. Gertsen
8:30a	NASA Perspectives	T. Zurbuchen/K. Bowersox
9:15a	ISS Program/CASIS Leadership Challenges	Marybeth Edeen/Robyn Gatens
10:00a	Break/Group Discussion	IRT Members
11:00a	SLPSRA	Craig Kundrot
11:30a	OIG Perspective	Ridge Bowman/Ray Tolomeo
12:00p	Working Lunch	IRT Members
1:00p	Congressional Perspective (Current)	Pam Whitney, Tom Hammond, Joel Graham, Alicia Brown
1:30p	Congressional Perspective (Historical)	Jeff Bingham
2:00p	Break/Group Discussion	IRT Members
2:30p	Commercialization Discussion	Alex MacDonald/Doug Comstock
3:00p	STPI	Bhavya Lal
3:30p	NSpC/OMB Perspectives	Scott Pace/Mike Beavin/Sam Black
4:00p	ASGSR	Gale Allen
4:30p	Group Discussion	IRT Members
5:00p	Adjourn	

October 21, 2019 – Washington, DC

Time	Track	Speakers
8:00a	Meeting with CASIS Leadership	Andrei Ruckenstein/Lewis Duncan Ken Shields
9:15a	Break/Group Discussion	IRT Members/Grey Hautaluoma
9:30a	CASIS Communications	Cindy Martin-Brennan/Christopher Ingraham
10:15a	Nanoracks	Jeffrey Manber
11:00a	Space Angels	Chad Anderson
11:30a	Historical Discussion	Bill Gerstenmaier
12:00a	Wrap-Up/Next Steps	IRT Members
12:30p	Adjourn	

October 24, 2019 – Virtual

Time	Track	Speakers
9:00a	CASIS Communications (Continued)	Cindy Martin-Brennan

October 25, 2019 – Virtual

Time	Track	Speakers
9:00a	NASA ISS Program Perspective	Sam Scimemi

October 29, 2019 – Merritt Island, FL

Time	Track	Speakers
8:30a	Meeting with Joe Vockley	Joe Vockley/ Rick Leach
10:00a	Welcome and Introductions	Ken Shields
10:15a	Business Development Approach	Christine Kretz & Mike Roberts
10:45a	Proposal Development and Submission Process	Dan Blaettler
11:15a	Proposal Review, Value Impact, and Selection Process	Brian Greene & Dan Blaettler
1:30p	Agreement Types Used for ISSNL Users	Melissa Montgomery
1:45p	Break	
2:00p	Research and Utilization Planning	Robbie Hampton
2:30p	Past Market Surveys Conducted	Mike Roberts
3:00p	Board Vision, Strategy, and Look Ahead	Andrei Ruckenstein
4:00p	Adjourn	

November 4, 2019 – Virtual

Time	Track	Speakers
9:00a	Made in Space	Andrew Rush

November 7, 2019 – Virtual

Time	Track	Speakers
9:00a	NASA Commercialization Discussion	Alex MacDonald

November 21, 2019 – Tucson, AZ + Virtual

Time (AZ)	Track	Speakers
8:00a	Eli Lilly	Jeremy Hinds
8:30a	Merck	Paul Reichert
9:15a	Space Tango	Twyman Clements
10:00a	Break/Group Discussion	
11:30a	Adjourn	

November 25, 2019 – Virtual

Time	Track	Speakers
9:00a	NIH Perspective	Lucie Low

December 5, 2019 – Virtual

Time	Track	Speakers
9:00a	GAO Perspective	Jose Ramos/Molly Traci/Cristina Chaplain/Shep Ryan/James Mittar