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National Aeronautics and Space Administration
Johnson Space Center
Human Exploration and Operations Mission Directorate
Human Research Program
Houston, TX 77058

Human Exploration Research Opportunities (HERO)

NNJ14ZSA001N-NSBRI
Appendix B

The National Space Biomedical Research Institute (NSBRI)

Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions

Step-1 Proposals Due: September 4, 2014, 5 PM Eastern Time
Notification of Proposal Status: October 1, 2014

Step-2 Proposals (By Invitation) Due: December 3, 2014, 5 PM Eastern Time

You must read and understand this solicitation in its entirety to prepare a competitive proposal. Key requirements are identified here:

- **The information and specific submission instructions in this NRA supersede that found in the NASA Guidebook for Proposers. Proposals that do not conform to the requirements in this NRA may be declared noncompliant and declined without review (sections D.4 and E.3.a).**
- For Step-1 and Step-2 proposals: You and your organization must be registered with NSPIRES. Your proposal must be submitted by an authorized representative of your organization. All team members listed on the proposal must be registered with NSPIRES.
- For Step-1 and invited Step-2 proposals: Your specific aims must address the research emphases in this solicitation, and must be clearly outlined in the project description of your proposal.
- For Step-2 proposals: Proposals must identify Integrated Research Plan (IRP) risks and gaps addressed by the research.
- For Step-2 proposals: The length of the project description of the proposal cannot exceed 20 pages using standard (12 point) type.
- For Step-2 proposals: Investigators submitting a proposal in response to this solicitation, and whose most recent submission that included similar specific aims to any NASA or NSBRI sponsored research announcement was not accepted, must address prior review comments (2 pages maximum).
- Investigators resubmitting a proposal in response to this solicitation may only submit a proposal with similar hypothesis(es) and aims a total of three times (original submission plus two resubmissions). Significant changes must be made to the proposal hypothesis(es) and specific aims for consideration after the third attempt or the proposal will be declined without further review.
- For Step-2 proposals: If you have received past NASA or NSBRI supported research within the last three years, you must provide specifics (2 pages maximum) to the productivity of your research in a section separate from the project description.
- For Step-2 proposals: If using vertebrate animals, your proposal must meet requirements of the Vertebrate Animal Scientific Review section of this solicitation.
- For Step-2 proposals: Your proposal must meet requirements of the Compliance Review section of this solicitation.
- For Step-2 proposals: If applicable, inclusion of the Flight Experiment Resource Worksheet or Analog Study Resource Worksheet.
- ~~NASA HRP has adopted the National Institutes of Health (NIH) policy concerning salary limitations on grants.~~
- NASA HRP has adopted the NIH policy concerning the sharing of software produced through grants.
- Step-1 and Step-2 selection decision information can be accessed after the selection announcement date listed in this solicitation. After logging in, the PI selects the "Proposals" link, the "Submitted Proposals/NOIs" link, and then clicks on the proposal submitted to the solicitation identified above. The document(s) provided by NASA will be displayed under the heading "PI Information Package" located at the bottom of the "View Proposal" page.

Appendix B

NSBRI Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions

A. Funding Opportunity Description

1. Introduction

The National Space Biomedical Research Institute (NSBRI) is a non-profit organization competitively-selected by NASA that uses an integrated team approach to advance biomedical research and countermeasure development. NSBRI works in partnership with NASA. Research, development, testing and evaluation are conducted with the goal of ensuring safe and productive long-term human exploration of space. Proposals that lead to the development of operationally relevant countermeasures in high priority areas are encouraged. Moreover, where appropriate, applications should take into consideration research resources, as listed in section G of the HERO Overview. The HERO Overview document is posted alongside this solicitation at http://nspires.nasaprs.com. The current NSBRI research program consists of approximately 50 science and technology projects organized into research teams.

This section of the NRA, Appendix B, solicits proposals for the opportunity to become a **member of an integrated Science and Technology team** of the NSBRI.

Research Emphases:
The NSBRI portion of this NRA solicits proposals addressing research emphases in one of the following Science and Technology discipline Teams:

1) Cardiovascular Alterations
2) Human Factors and Performance
3) Musculoskeletal Alterations
4) Neurobehavioral and Psychosocial Factors
5) Sensorimotor Adaptation
6) Smart Medical Systems and Technology

Proposals solicited through this NRA will use a two-step proposal process. Only proposers submitting Step-1 proposals determined to be relevant with respect to the Research Emphases outlined in Section A.2 of this appendix will be invited to submit full Step-2 proposals.

Proposals that impact more than one emphasis should be directed to one primary research area, although a secondary research area may be designated if the proposal has substantial overlap with that area. Studies using integrated methods are encouraged. Proposals that synergistically

bridge multiple disciplines for the purpose of modeling the effects of microgravity on the human body to aid in the development and testing of countermeasures, or proposals to develop technologies that enable research in one or more NSBRI research area(s), and which are potentially applicable for flight are strongly encouraged.

It is critical for investigators to read carefully all of the instructions in this NRA. All proposals will undergo peer review using the same processes and procedures. **All proposals must be submitted electronically, and all proposers are required to use NASA Solicitation and Proposal Integrated Review and Evaluation System (NSPIRES). Any proposals not submitted through the NSPIRES portal and sent directly to NSBRI by email, fax or other means will be returned without review.** Programmatic balance is maintained by the selecting official(s) for the program.

Information describing the research needs for human space exploration as defined by NASA's Human Research Program (HRP) can be found in Section B of the HERO Overview. Proposals to NSBRI must address the Research Emphases outlined by team in Section A.2 of this document.

Investigators are encouraged to review summaries of currently funded research by accessing NSBRI's website at http://www.nsbri.org and the NASA Advanced Capabilities Division Research and Technology Task Book at http://taskbook.nasaprs.com/peer_review/index.cfm.

NSBRI is governed by a consortium of twelve institutions: Baylor College of Medicine, Brookhaven National Laboratory, Harvard Medical School, The Johns Hopkins University, Massachusetts Institute of Technology, Morehouse School of Medicine, Mount Sinai School of Medicine, Rice University, Texas A&M University, the University of Arkansas for Medical Sciences, the University of Pennsylvania Health System, and the University of Washington. The Institute's Headquarters are located in Houston at Baylor College of Medicine.

Consortium membership is not a requirement for research program participation. NSBRI's External Advisory Council (EAC) is responsible for advising Institute management concerning program strategy, tactical implementation and effectiveness. NSBRI also includes a User Panel of former and current astronauts and flight surgeons, which is responsible for assuring that the research program is focused squarely on astronaut health, safety and performance. The User Panel advises senior management on the operational relevance and feasibility of science and technology projects. An Industry Forum of representatives from space and biomedical companies advises and assists NSBRI concerning Earth-based applications of Institute research. The Institute coordinates its research activities with NASA through several committees and working groups, including a joint NASA/NSBRI Steering Committee. In addition to its research program, NSBRI has developed a robust Career Development and Outreach Program that leverages the Institute's core research activities.

2. Research Teams and Emphases

Each of the NSBRI science and technology teams consists of a set of complementary projects focused in a particular discipline. Team Leaders oversee the value added among the projects, to ensure that the integrated team approach leads to more effective outcome-driven research than might be attainable by a single project alone. Proposers are encouraged to look at each of the seven Team Executive Summaries and the current composition of the teams in preparing their proposals. Proposers are also required to: (1) Define clear milestones for their project; and (2) If appropriate, describe a plan as to how they intend to collaborate with any NASA or NSBRI scientists, engineers, flight surgeons, and astronauts. An explanation should be provided as to how any collaboration will: (1) Increase the likelihood of success; (2) Improve the delivery of results or products; and (3) Positively impact the proposed research.

Proposers applying to NSBRI's integrated research program must identify the primary NSBRI discipline team and the secondary discipline NSBRI team (if applicable) responsible for the area their proposal is addressing below. Proposers must also identify the countermeasure readiness level (CRL) and/or technology readiness level (TRL) of their research proposal. Proposers should refer to Figures 1 and 2 in the Overview for detailed descriptions of the CRL and TRL scales. This information will be collected online as Cover Page elements during electronic proposal submission. Research emphases may relate to one or more type of proposal (ground-based, analog definition, flight definition), as described in section E of the HERO Overview.

Proposals must be responsive to the research emphases specifically described in the bullet points below in order to be reviewed as significant to the goals of this solicitation. The proposed research approach must adhere to all constraints and guidelines outlined in this solicitation.

a. Cardiovascular Alterations Team

The Cardiovascular Alterations Team is determining the effects of long-duration space flight on the heart and blood vessels and researching ways to reduce the risks and to improve pre-flight detection and management of cardiovascular diseases. The Team has a number of aims, which include quantifying the risk of coronary events associated with changes in coronary artery calcium scores and determining whether high levels of fitness or use of cholesterol-lowering medication can influence this risk. Researchers are especially concerned about whether space radiation affects the endothelial cells lining blood vessels (which might initiate or accelerate coronary heart disease) and examining the efficacy of countermeasures. The Team is also addressing a newly described space flight-associated medical condition called visual impairment and intracranial pressure (VIIP) by examining the effects of changes in hydrostatic gradients on arterial and venous pressures and flows and intracranial hemodynamics. Team information, including the Team Executive Summary, current projects, and research goals and priorities, is located at: http://www.nsbri.org/science-and-technology/cardiovascular-alterations

Proposals are sought that address the area described below:
Develop and Validate "Early" Biomarkers to Detect Asymptomatic Cardiovascular Disease.

Human Research Program Requirements Document (HRPRD) Risk:
Risk of Cardiac Rhythm Problems

Integrated Research Plan (IRP) Gap:

- **CV8**: Can manifestations of sub-clinical or environmentally induced cardiovascular diseases during spaceflight be predicted?

Background:
Coronary artery disease (CAD) is a major risk factor for middle-aged experienced astronauts, particularly those who are on long-duration space missions where a sudden acute cardiovascular event could incapacitate an individual astronaut and put all crewmembers and the mission at risk. NSBRI is motivated to develop sensitive and specific biomarker assays to detect very early but clinically relevant asymptomatic CAD. The goal of these biomarker studies is to detect and define the early inflammatory processes in both men and women that lead to asymptomatic cardiovascular disease (ASCVD) /CAD, as well as to detect and classify the stage of the atherosclerotic disease– from initial inflammatory response, to soft non-calcified lipid plaques, to mixed soft and calcified plaques and eventually obstructive ASCVD/CAD. Biomarkers may facilitate the quantification of risks based on atherosclerotic plaque burden analyses without the need for invasive testing. These biomarkers could allow early preventive measures, treatments and interventions to prevent the development of CAD risks - years or even decades before vulnerable plaques and obstructive lesions occur.

Research Questions:
Using integrated 21st Century omics approaches (i.e. concomitantly performing genomic, transcriptomic, proteomic, metabolomic, metagenomic and epigenomic analyses such as those employed by Chen *et al*; *Cell*. 2012 Mar 16; 148:1293-1307) to identify and validate "early" genomic, proteomic, and other omic biomarkers that can be employed to longitudinally detect and monitor sub-clinical ASCVD, particularly coronary artery disease, in middle-age (i.e. 35 – 55 years of age) apparently healthy men and women.

These "early" biomarkers should be readily detectable in biofluids such as blood, saliva, urine, or stool prior to any routinely observed physiological manifestations of cardiovascular disease in apparently healthy human subjects.

These "early" biomarkers may manifest as either the presence or absence of certain biomolecular motifs (e.g. post-translational protein modifications or epigenetic changes such as methylation) or may be observed as increased or decreased levels of certain biomolecules (relative to levels observed in healthy controls).

At least one fully validated "early" biomarker assay should be developed as a precursor to a screening test for detecting ASCVD in astronaut crew members over the course of their flying careers, i.e. before, during, and after space flight.

The validated biomarker assay may utilize a single biomarker, but it is more likely that a panel of validated biomarkers will be required to follow these processes over time and characterize different stages of early cardiovascular disease.

b. Human Factors and Performance Team

The Human Factors and Performance Team is studying ways to improve daily living and keep crewmembers and other personnel healthy, productive and safe during long duration space exploration missions. Overall Team aims are to reduce performance errors and mitigate habitability, environmental and behavioral factors that pose significant risks to mission success. The Team develops guidelines for human systems design and information tools to support crew performance. Team members are examining ways to improve sleep and scheduling of work shifts as well as how specific types of lighting in the spacecraft and habitat can improve alertness and performance. Other projects address improving the interactions between automated and manual control of a spacecraft and how factors in the environment, such as dust in microgravity, can impact crew health. Team information, including the Team Executive Summary and research goals and priorities, is located at: http://www.nsbri.org/science-and-technology/human-factors-and-performance

Proposals are sought that address the area described below:
Measure and Model the Level of Crew Member Trust of Automation During Autonomous Operations, and Develop Adaptive Technology Countermeasures To Mitigate Situational Stressors.

HRPRD Risk:
Risk of Inadequate Design of Human and Automation/Robotic Integration

IRP Gap:

- **SHFE-HARI-02**: We need to develop design guidelines for effective human-automation-robotic systems in operational environments that may include distributed, non-colocated adaptive mixed-agent teams with variable transmission latencies.

Background:
Situational stressors, such as fatigue, environmental factors (e.g. elevated O_2, CO_2, or radiation levels), high workload, and perceived danger, can significantly degrade task performance (including interacting with automated systems) by astronaut crew members. Research is needed to characterize performance changes resulting from such stressors (such as sleep deprivation) and identify technology adaptations that can mitigate these decrements on human performance when interacting with automated systems such as robotic arms or rovers.

Trust (or lack thereof) of astronaut crew members in automated systems may significantly amplify the deleterious effects of situational stressors when astronaut crew members interact with automated systems. An important aspect of situational awareness when employing automation in spaceflight operations is developing an accurate understanding of what actions automated systems will take, under what conditions actions will be taken, and what are the expected outcomes of automated actions. This detailed understanding should make it possible for

astronaut crew members to reliably predict what the automation can and cannot do in different operational scenarios. Without such understanding, the astronaut crew member may either override automation unnecessarily due to mistrust, or conversely over-rely on automation due to misplaced complacency. Either scenario could result in inefficient automated operations, or at worst conceivably lead to the development of unsafe situations that might result in the loss of equipment or even compromise the mission, and risk the lives of crew members.

The combined effects of a multiplicity of situational stressors and inappropriate levels of trust in automated systems will likely be amplified during autonomous or semi-autonomous operations such as those likely to be encountered during a deep space 3.5 year exploration mission to Mars.

Research Questions:
Develop mitigation strategies and/or technologies that re-optimize human-system integration in response to evidence of degraded human performance. Such technology mitigations may include: (1). Adaptive display technologies; (2) Adaptation of vehicle/system control modes; and (3) Alteration of visual perspectives and camera views. The selected technology mitigations should be tested with astronaut-like subjects, employing realistic operational scenarios, in analog environments.

Model and measure the level of trust that astronaut like subjects have in automated systems. Develop techniques to quantitatively measure these levels of trust, and detect when the user's level of trust is inappropriate - either overly distrustful or overly complacent and measure the resulting task performance outcomes

These technology mitigations against situational stressors and techniques to calibrate the level of trust in automated systems should be configured in such a way that they are useful in autonomous or semi-autonomous spaceflight operations, when crew members are working with robotic arms or rovers.

c. Musculoskeletal Alterations Team

The Musculoskeletal Alterations Team is studying the mechanisms involved in bone and muscle loss and whether reduced gravity increases the risk of bone breaks and impairs fracture healing. The Team is also researching radiation-induced bone loss. In addition to identifying ways to enhance the benefits of exercise during space flight for maintaining muscle and bone function, the Team is investigating methods to prevent or reduce the loss through nutritional and pharmaceutical interventions to complement exercise. Team information, including the Team Executive Summary and research goals and priorities, is located at:
http://www.nsbri.org/science-and-technology/musculoskeletal-alterations

Proposals are sought that address the area described below:
Characterize Genetic Mosaicism in Muscle and Bone Tissues of Rodents Exposed to Simulated Space Radiation and Microgravity.

HRPRD Risks:

1. Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance.
2. Risk Of Early Onset Osteoporosis Due To Spaceflight.
3. Risk of Cardiovascular Disease and Other Degenerative Tissue Effects From Radiation Exposure.
4. Risk of Radiation Carcinogenesis.

IRP Gaps:

- **M23**: Determine if factors other than unloading contribute to muscle atrophy during space flight.
- **Osteo 4**: We don't know the contribution of each risk factor on bone loss and recovery of bone strength, and which factors are the best targets for countermeasure application.
- **Degen – 2**: What are the mechanisms of degenerative tissue risk in the heart, circulatory, endocrine, digestive, lens and other tissue systems? What surrogate endpoints do they suggest?
- **Degen – 5**: What quantitative procedures or theoretical models are needed to extrapolate molecular, cellular, or animal results to predict degenerative tissue risks in astronauts? How can human epidemiology data best support these procedures or models?
- **Cancer 05**: How can models of cancer risk be applied to reduce the uncertainties in individual radiation sensitivity including genetic and epigenetic factors for SPE and GCR?

Background:

Mosaicism is a condition in which cells within a single, discrete organism - exhibit different genetic variants. This condition can likely affect any type of cell, including muscle and bone cells. Somatic mutations, as precursors to mosaicism within a given organism, are prevalent in the beginning and end stages of life, [De, Subhajyoti, "Somatic mosaicism in healthy human tissues." *Trends in Genetics*. June 2011. **27** (6): 217–223]. DNA copy errors and damage due to environmental insults (e.g. radiation, environmental, chemical or psychological stress, and trauma) accumulate over a lifetime and lead to greater occurrences of mosaic tissues in aging humans. A similar burden of somatic mutations also presumably accumulates in model organisms as they age and reach the limits of their natural lifespans. Cancer research has shown that somatic mutations become increasingly manifest throughout a lifetime and are responsible for most leukemia, lymphomas, and solid tumors, [Jacobs, Kevin B. *et al*. Detectable Clonal Mosaicism and Its Relationship to Aging and Cancer." *Nature Genetics.* 2012. **44** (6): 651–U668].

Considerable interest exists in detecting and describing the presence of mosaicism in astronaut crew members as well as in model organisms, such as rodents, that have or will fly in space. These studies will have the specific goal of observing the effect of the space environment (ionizing radiation, microgravity, close confinement, stress, danger, elevated CO_2 levels) at the most fundamental biomolecular level on the DNA of individual humans and animals as a result of their unique spaceflight experiences. As a fore-runner to these flight experiments there is therefore the need to carefully observe and characterize the frequencies and genetic coordinates of somatic mutations by undertaking ground based experiments. As a first step, the effects of

simulated space radiation and simulated microgravity in inducing somatic mutations within the underlying DNA of mice or rats should be studied. The overarching, strategic purpose of this work is to identify putative drug targets (e.g. proteins, non-coding RNA's, promoter regions) within specific biological pathways, which may in due course guide countermeasure development.

Research Questions:
NSBRI wishes to fund a Team of researchers that will perform "deep sequencing" and / or employ other advanced genetic analysis techniques to detect and confirm the presence of somatic mutations (mosaicism) in the musculoskeletal tissues of rodents, i.e. rats and / or mice.

There is specific interest in detecting somatic mutations in both muscle and bone tissues that have been exposed to simulated space radiation (i.e. heavy ions such as ^{56}Fe, plus protons) and / or simulated microgravity, (i.e. hind-limb unloading). Interest also exists in interrogating the adjacent cartilage and tendon tissues for the presence of somatic mutations, however performing genetic analysis to detect mosaicism in cartilage and tendons is desired and not required, in order to be responsive to this research emphasis.

Wherever possible – use should be made of existing repositories of rodent musculoskeletal tissues. Muscle and bone biomedical space researchers are also strongly encouraged to collaborate with omics researchers to elucidate the extent of mosaicism in the musculoskeletal tissues of rodents that have been exposed to ionizing radiation and / or that have been "unloaded."

d. Neurobehavioral and Psychosocial Factors Team

The Neurobehavioral and Psychosocial Factors Team is concerned with methods crews use to deal with stress, isolation, confinement, and the challenges of long-duration space exploration missions. In addition to identifying neurobehavioral and psychosocial risks to crew health, safety, and productivity, Team objectives include developing methods to monitor cognitive function and behavior and countermeasures to enhance performance, motivation, and quality of life. The Team's efforts also include projects conducted during the Mars 500 study in Russia and other analog environments. Team information, including the Team Executive Summary and research goals and priorities, is located at: http://www.nsbri.org/science-and-technology/neurobehavioral-and-psychosocial-factors.

Proposals are sought that address either of the **two (2)** areas described below:

1. Test Countermeasures for Space-Radiation Induced Neurobehavioral Deficits.

HRPRD Risks:
1. Risk of Acute and Late Central Nervous System Effects from Radiation Exposure
2. Risk of Adverse Behavioral Conditions and Psychiatric Disorders

IRP Gaps:

- **CNS - 4**: What are the most effective biomedical or dietary countermeasures to mitigate CNS risks? By what mechanisms are the countermeasures likely to work?
- **BMed6**: We need to identify and validate effective treatments for adverse behavioral conditions and psychiatric disorders during exploration class missions.

Background:

NSBRI and NASA seek to advance countermeasure development to mitigate the potentially deleterious effects of space radiation on the neurocognitive functions of astronauts. Rats exposed to low doses of proton radiation exhibit performance decrements in attention, inhibitory control ("impulsivity") and psychomotor speed, in a rodent version of the human psychomotor vigilance test (Davis *et al., Radiat Res*. 2014 Mar; 181(3): 258-71). Using this assay, NSBRI-funded researchers demonstrated that different strains of rats are not uniformly susceptible to the deleterious effects of radiation exposure. In fact, resistance and susceptibility appear to be correlated with protein levels of the dopamine transporter and, to a lesser extent, the dopamine D2 receptor in whole brain lysates. It is unclear the extent to which the dopamine pathway is involved in conferring different levels of radiation susceptibility to the organism, or whether other neurotransmitter pathways are affected by ionizing radiation that can indirectly modulate components of the dopamine pathway.

Research Questions:

Test whether FDA-approved pharmaceutical agents that modulate the dopamine pathway (directly or indirectly) can protect against the deleterious effects of simulated space radiation (i.e. heavy ions plus protons) on mammalian neurocognitive function and behavior.

Certain experimental conditions should be met:

- Medications should exhibit safety profiles commensurate with use as long-term prophylaxis treatments.
- Space-relevant radiation exposures should be used (dose, dose-rates, ion species). For more information regarding radiation exposures considered mission relevant by NSBRI and NASA, see text of recent solicitations: NSBRI-RFA-13-02 at http://www.nsbri.org/FUNDING-OPPORTUNITIES/Current-Announcements/NSBRI-RFA-13-02/; and NNJ13ZSA002N-Radiation at http://bit.ly/1zknLnZ
- Appropriately-aged animal models resembling middle aged (i.e. 45 – 55 human years) astronauts should be exposed.
- The time-frame for the radiation-effects studied should be equivalent to the length of a Mars exploration mission (1-3 years for humans); i.e., aging studies are not of interest.
- Neurobehavioral paradigms should test vigilance, learning and memory, and adaptive social behaviors.

2. Detect and Optimize Stress in Astronauts or Astronaut-like Subjects Prior to Mission.

HRPRD Risks:

1. Risk of Adverse Behavioral Conditions and Psychiatric Disorders
2. Risk of Performance Errors Due to Fatigue Resulting From Sleep Loss, Circadian Desynchronization, Extended Wakefulness and Work Overload

IRP Gaps:

- **BMed1**: We need to identify and validate countermeasures that promote individual behavioral health and performance during exploration class missions.
- **BMed2**: We need to identify and validate measures to monitor behavioral health and performance during exploration class missions to determine acceptable thresholds for these measures.
- **Sleep Gap 9:** We need to identify an integrated, individualized suite of countermeasures and protocols for implementing these countermeasures to prevent and/or treat chronic partial sleep loss, work overload, and/or circadian shifting, in spaceflight.

Background:

First hand reports from several astronauts (e.g. Thomas, Don, "Orbit of Discovery", Akron Press, 2014, p. 15) have indicated that some crew members report experiencing significantly higher stress levels and greater tiredness in the months and weeks immediately prior to launch than during actual spaceflight missions or post-flight, with some individuals being affected more than others, (e.g. Dinges *et al*. "Effects of Time In Mission: ISS Astronauts Ratings Of Stress"; 2014 NASA Human Research Program Investigators' Workshop; http://www.hou.usra.edu/meetings/hrp2014/pdf/3256.pdf).

This preloading with stress and tiredness may potentiate neurobehavioral vulnerability to stressors in spaceflight and pose a risk to behavioral health and performance. Alternatively, exposure to stress prior to the mission may have a hermetic effect, providing protection against in-flight or post-flight stress, such as has been seen in stress inoculation training (e.g. Saunders, T. *et al*, "The effect of stress inoculation training on anxiety and performance." *J. Occup Health Psychol*. 1996. 1(2); 170-86).

Accordingly there is a need to optimize both the levels of pre-flight stress and the types of pre-flight stressors, in astronauts. Identifying ways to do so while still having crew members accomplish the multitude of tasking and training that must be performed pre-mission will bring a clear behavioral health benefit and reduce the risk of behavioral health problems and performance deficits manifesting when in space.

Research Questions:

Determine the most effective and sensitive methodologies for the measurement and monitoring of behavioral stress experienced by astronaut crew members during the months prior to a mission.

Propose and explore the use of techniques and methods to personalize the levels and types of behavioral stress experienced by astronaut crew members during the months prior to launch.

Validate these customizable techniques and methods via testing astronaut like subjects in an appropriate analog environment.

e. Sensorimotor Adaptation Team

The Sensorimotor Adaptation Team is studying adaptation in the sensory and motor systems of crewmembers following gravitational transitions, as well as during extended periods of micro- and fractional gravity. Disorientation, vestibular-autonomic responses, and changes in vision (e.g. specifically visual impairment associated with the VIIP condition), proprioception, cognition, balance and motor control may lead to impaired performance and compromised mission success. In addition to identifying individual risk factors, the Team examines sensory systems, their interactions, and integration with the brain and motor behavior relevant for long-duration space exploration missions. Research to understand fundamental physiological and biomolecular processes is complemented by development of personalized countermeasures, with particular emphasis on high priority gaps and operational needs. Team information, including the Team Executive Summary, current projects, and research goals and priorities, is located at: http://www.nsbri.org/science-and-technology/sensorimotor-adaptation-team.

Proposals are sought that address the area described below:

Commission a Task Force of World Experts to Characterize Sensorimotor and Neurocognitive Effects Associated with the Spaceflight-Induced Intracranial Hypertension/Vision Alterations (VIIP) Syndrome; and based on these Findings, Propose Alternative Hypotheses To Illuminate the Cause(s) of VIIP.

HRPRD Risk:
Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations

IRP Gap:

- **VIIP1**: We do not know the etiological mechanisms and contributing risk factors for ocular structural and functional changes seen in-flight and post-flight.

Background:
Astronauts on long duration ISS missions have experienced increased intracranial pressure (as measured post-flight), ophthalmic anatomical changes, and visual performance decrements of varying degrees. This syndrome, spaceflight-induced intracranial hypertension/vision alterations (VIIP), is of unknown etiology, although increased intracranial pressure [ICP] is the leading hypothesis. A host of space environmental factors as well as individual variability and possibly even sex (female/male) related factors may play a role in the development of the syndrome. For more information see: http://humanresearchroadmap.nasa.gov/evidence/reports/VIIP.pdf; and http://humanresearchroadmap.nasa.gov/Risks/?i=105.

It is unknown to what extent the alterations associated with the VIIP syndrome in astronauts could impact crew performance. In patients on Earth experiencing sustained elevations in intracranial pressure, concomitant neurocognitive and sensorimotor functions may be affected. Therefore, VIIP associated neurological sequelae may also be concern for astronauts during long-duration spaceflight missions. It is also possible that the observed visual changes are

indicative of underlying processes that might cause neural or other damage to the brain and surrounding tissues, as yet unnoticed.

Research Questions:

Stand up a Task Force of outstanding clinicians, scientists, and engineers who will:

(1). Observe and characterize any *concomitant sensorimotor and neurocognitive effects* of the spaceflight-induced intracranial hypertension/vision alterations (VIIP) syndrome – that may impact crew performance;

(2). Based on these findings, propose and test *alternative hypotheses* to explain the etiology and causes of spaceflight induced visual impairment.

(3). *Recommend appropriate countermeasures* that focus on mitigating any sensorimotor and neurological effects of VIIP.

This Task Force must work in close partnership with NASA and help "solve" the VIIP problem. This ambitious goal will be pursued by studying sensorimotor and neurological manifestations associated with the syndrome, considering fresh hypotheses and commissioning new work to prove or disprove these alternative hypotheses, and recommending appropriate sensorimotor or neurological countermeasures.

Proposers must provide a research plan including the following information:

(1).Which sensorimotor and neurological sequelae will be studied; how measurements will be made and analyzed, or (existing data mined), and a description of the study subjects.

(2). Which alternative hypotheses will be considered and tested.

(3). Details of proposed pilot studies to measure sensorimotor and neurological sequelae and test alternative hypotheses to potentially explain the etiology of the VIIP syndromes.

(4). Details of recommended novel countermeasures to mitigate the sensorimotor and neurological effects of VIIP.

As a precursor to commissioning new experimental work, the Task Force must organize a multi-day symposium, attended by subject matter experts - not all of whom will be Task Force members. This symposium will review what is already known, as well as what remains to be characterized, in regards to concomitant sensorimotor and neurological effects of VIIP. Another important outcome of this workshop will be to list and prioritize alternative hypotheses to explain spaceflight induced visual impairment. In this way the initial concepts proposed by members of the Task Force, including which neurological sequalae should be studied and which alternative hypotheses should be considered, will receive expert feedback and validation, prior to any experimental work being initiated.

The Task Force will use the preponderance of its funding to commission and implement small to medium scale pilot research studies to study the neurological sequelae of VIIP, test alternative hypotheses, and demonstrate efficacy of potential countermeasures. Experimentation, data analysis and other significant activities associated with these research studies should be conducted in the laboratories of Task Force members.

The Task Force must be led by a senior investigator with compelling scientific credentials (i.e. established via publishing in the peer reviewed scientific literature – or equivalent contributions) in the VIIP area, who has a primary appointment at an academic institution in the United States. Investigators drawn from a minimum of three (3) academic institutions must be teamed together to comprise the Task Force. International collaborations are strongly encouraged.

A minor portion of the funding may be used to cover administrative costs including establishing a leadership structure and gathering expert input from the scientific community to develop an agreed-upon comprehensive research plan that broadly leverages the capabilities of the research community. Infrastructure should be established to simplify and facilitate the sharing of data, ideas, and resources. This Task Force should establish a transparent and collaborative environment among the members in order to manage potential conflicts of interest, authorship on publications, and intellectual property.

To ensure maximum efficiency and avoid duplication of effort, the Task Force must take full account of NASA's many existing (and future) efforts and research activities in the area of VIIP research. Specifically the Task Force must establish regular operating mechanisms to interface with NASA Managers and the VIIP Research Clinical Advisory Panel (RCAP). Task Force members should work collaboratively with NASA funded scientists and clinicians that are performing VIIP related research.

f. Smart Medical Systems and Technology Team

The Smart Medical Systems and Technology Team is developing intelligent, integrated medical systems to assist in delivering quality health care during space flight and exploration. These systems must be small, low-power, minimally invasive, versatile, and highly automated. Possible technologies needed include ultrasound diagnostics and therapeutics, lab-on-a-chip systems, patient and health physiologic monitors, and automated systems and devices to aid in medical decision making, training and diagnosis. New technologies developed by this Team will have immediate benefits to medical care on Earth. Team information, including the Team Executive Summary and research goals and priorities, is located at:
http://www.nsbri.org/science-andtechnology/smart-medical-systems-and-technology

Proposals are sought that address the area described below:
Define and Validate Mechanical Countermeasures for Microgravity-Associated Cephalad Fluid Shifts.

HRPRD Risk:
Risk of Spaceflight-Induced Intracranial Hypertension/Vision Alterations

IRP Gap:

- **VIIP13**: We need to identify preventative and treatment countermeasures (CMs) to mitigate changes in ocular structure and function and intracranial pressure during spaceflight.

Background:
Astronauts on long duration International Space Station (ISS) missions have experienced increased intracranial pressure (as measured post-flight), ophthalmic anatomical changes and visual performance decrements of varying degrees. This syndrome, spaceflight-induced intracranial hypertension/vision alterations (VIIP) is of unknown etiology. For more information see: http://humanresearchroadmap.nasa.gov/evidence/reports/VIIP.pdf;
and http://humanresearchroadmap.nasa.gov/Risks/?i=105

Current options to mitigate VIIP-related changes are limited to preflight screening, corrective lenses (in-flight and post-flight), and return to Earth. Potential countermeasures include pharmaceutical and mechanical [i.e. lower body negative pressure (LBNP) devices, artificial gravity, and Braslet thigh cuffs] interventions. Ongoing funded ground-based and flight studies aimed at understanding the etiology and risk factors implicated in VIIP will inform appropriate countermeasures. However, it is generally accepted that the unrelenting and long-duration cephalad fluid shifts that occur in microgravity are a contributing factor.

Mechanical interventions such as LBNP and Braslet devices have been used as a fluid shifting countermeasure by the Russian space program for many years, with good success in temporarily counteracting cephalad fluid shifts.

Russian crewmembers use Braslets intermittently during the first few days of flight (donning during the day, and doffing at night), in order to sequester venous blood in the lower extremities (in the vascular and interstitial spaces). Braslet-use thereby potentially reduces the blood volume available to shift head-ward, thus decreasing edema of the head and face and easing the discomfort crewmembers report early in flight. Anecdotally, some crewmembers have worn the Braslet thigh cuffs intermittently throughout the flight.

LBNP is typically used by Russian crewmembers towards the end of a long-duration flight, for the purpose of increasing tolerance to post-flight orthostasis, by simulating gravity's effect on the cardiovascular system.

Neither of these devices, which are available onboard the ISS for immediate use, have been used (or tested for use) as a VIIP countermeasure. Due to operational constraints (bulk, non-mobile nature of the device, availability, and potential medical side effects) use of the LBNP device as a routine, broadly adopted countermeasure for all crewmembers may not be feasible. Thigh cuffs may be of use as a VIIP countermeasure, however, their effect on VIIP related parameters is unknown. Additionally, it is unknown whether thigh cuffs can sequester fluids sufficiently to counteract the microgravity effects on VIIP related parameters. Further, it is unclear whether wearing these devices for long periods of time would result in a rebound effect or any other adverse effects after discontinuation.

The purpose of this solicitation is therefore to define a mechanical countermeasure and validate a recommended prescription for its use, as a precursor to a flight study that would validate effectiveness during spaceflight.

Research Questions:
How does use of the mechanical countermeasure device affect VIIP-relevant parameters, and in particular: intracranial pressure (ICP), cerebral blood flow, intraocular pressure, structural eye parameters, and various vascular parameters? Proposals that include direct invasive measurements of ICP would be preferred over those that only use noninvasive surrogates to direct ICP.

What is the optimal prescription for use of the mechanical countermeasure device? (i.e., specify recommended length of use in number of hours per day, quantitative level of compression or vacuum, etc.)

Is there a rebound effect or any other adverse occurrences when use of the mechanical countermeasure device is discontinued?

Is gradual discontinuation of device use safer than abrupt discontinuation of use?

Are there pharmacologic or non-pharmacologic approaches (such as diuretics, nitrates, etc.) that might mitigate the risk of a rebound effect, if any?

Are there any adverse health effects from long term use?

3. Career Development and Public Outreach

NSBRI has a Career Development and Outreach Program that operates in collaboration with other NASA programs to enhance and broaden public knowledge, understanding, and appreciation of biological and biomedical research, and the value of this research in the space environment. NSBRI's Career Development and Outreach Program is integrated with the NSBRI Science and Technology Program, as well as with collaborative research projects between NSBRI and NASA. Further information about NSBRI's Career Development and Outreach Program is available at: http://www.nsbri.org/EDUCATION-and-TRAINING/.

4. Vertebrate Animal Scientific Review

NASA has adopted the National Institute of Health (NIH) policy for all research proposals that require vertebrate animals, and requires that any and all research proposals that request funding for vertebrate animal research shall be reviewed as described in the Vertebrate Animal Scientific Review (VASR) as posted on the NSPIRES solicitation download site alongside this NRA. Each response to this solicitation that requires vertebrate animals must address the five points outlined in the VASR. The VASR requirements are in addition to Institutional Animal Care and Use Committee (IACUC) requirements as outlined under section B.2.b of the HERO Overview, Special Matters. All vertebrate animal research conducted under NSBRI auspices shall conform to the VASR requirement.

5. NASA Civil-Servant Investigators or Collaborators

Invited Step-2 research proposals entered in the NASA Solicitation and Proposal Integrated Review and Evaluation System (NSPIRES) system that include NASA civil servants will be required to provide complete information concerning percent effort and total dollar amount requested for each NASA employee listed in the proposal. NSBRI funding will be withheld if the following items are not included in the proposal a) SECTION VIII - OTHER PROJECT INFORMATION should capture the total full-time equivalents (FTE) for all NASA civil servants combined per year. For an FTE fraction, please use the format "0.xx"; b) SECTION X (Budget) – under F- OTHER DIRECT COSTS - for each budget period, list the name of each NASA civil servant on a separate line and specify total support (salary, materials, travel and equipment) for each individual; and c) in the BUDGET JUSTIFICATION section of the written proposal, itemize each fractional FTE and include the total dollar amount for salary, materials, travel and equipment per year per civil servant. Please contact the NSPIRES Help Desk at 202-479-9376 if you encounter any difficulties entering civil servant information.

6. NASA Safety Policy

Safety is NASA's highest priority. Safety is the freedom from those conditions that can cause death, injury, occupational illness, damage to or loss of equipment or property, or damage to the environment. NASA's safety priority is to protect: (1) the public; (2) astronauts and pilots; (3) the NASA workforce (including employees working under NASA instruments); and (4) high-value equipment and property. All research conducted under NSBRI auspices shall conform to this policy.

7. Availability of Funds for Award

NSBRI's obligation to make awards is contingent upon the availability of the appropriated funds from which payment can be made and the receipt of proposals that are deemed acceptable for award under this solicitation.

B. Award Information

All proposals will be evaluated for overall merit by independent peer-review panels and also will be assessed by NSBRI for relevance and proposed cost. Proposals to continue or supplement existing grants, if selected, will result in a new grant.

NSBRI will accept proposals with a maximum budget of $400,000 per year for a maximum of two years. NSBRI reserves the right to return proposals that exceed $400,000 per year or two years in duration. NSBRI does not provide separate funding for direct and indirect costs; thus, the amount of the award requested is the total of all costs submitted in the proposed budget.

NSBRI will make funding allocations in one-year increments based on the submitted budget, available funds and project review. All NSBRI award recipients will be reimbursed on expenses incurred in the performance period. NSBRI may withhold payment of any expenditure

that appears questionable, or for which additional information or support is required. Annual renewals are contingent on meeting all NSBRI Investigator Requirements including NASA-NSBRI customer-supplier agreements where appropriate.

NSBRI may, in certain cases, elect to fund only a portion of a proposed effort. In this case, the applicant will be given the opportunity to accept or decline such partial funding. The initial selection will be announced no earlier than April 2015. Once an award is made, NSBRI may elect to fund collaborating institutions participating in a given project directly. Budgets will then be required from each participating institution.

It is anticipated that NSBRI grants issued in response to this NRA will begin no earlier than May 2015. It is also expected that these grants will end by 30 May 2017. No extensions for these grants will be provided.

C. Eligibility Information

1. Eligibility of Applicants

All categories of United States (U.S.) institutions are eligible to submit proposals in response to this NRA. Principal Investigators may collaborate with universities, Federal Government laboratories, the private sector, and state and local government laboratories. In all such arrangements, the applying entity is expected to be responsible for administering the project according to the management approach presented in the proposal.

The applying entity must have in place a documented base of ongoing high quality research in science and technology, or in those areas of science and engineering clearly relevant to the specific programmatic objectives and research emphases indicated in this NRA. Present or prior NSBRI or NASA support of research or training in any institution or for any investigator is not a prerequisite to submission of a proposal.

2. Guidelines for International Participation

a. Guidelines for International Proposals

NASA's policy is to conduct research with non-U.S. organizations on a cooperative, no exchange-of-funds basis. Although Co-Investigators or collaborators employed by non-U.S. organizations may be identified as part of a proposal submitted by a U.S. organization, NSBRI funding through this NRA may not be used to support research efforts by non-U.S. organizations at any level; however, the direct purchase of supplies and/or services that do not constitute research from non-U.S. sources by U.S. award recipients is permitted. See NASA FAR Supplement Part 1835.016-70 for additional information on international participation, which can be referenced at http://www.hq.nasa.gov/office/procurement/regs/1835.htm#35_016-70.

Also see NASA Policy Directive 1360.2B Initiation and Development of International Cooperation in Space and Aeronautics Programs, which is located at http://nodis3.gsfc.nasa.gov/displayDir.cfm?Internal_ID=N_PD_1360_002B_&page_name=main

b. Assurance of Compliance – China Funding Restriction

All proposals submitted to this NRA must comply with the following: Assurance of Compliance with The Department of Defense and Full-Year Appropriation Act, Public Law 112-10 Section 1340(a); The Consolidated and Further Continuing Appropriation Act of 2012, Public Law 112-55, Section 539; and future-year appropriations herein after referred to as "the Acts", whereas:

a) NSBRI and NASA are restricted from using funds appropriated in the Acts to enter into or fund any grant or cooperative agreement of any kind to participate, collaborate, or coordinate bilaterally with China or any Chinese-owned company, at the prime recipient level and at all subrecipient levels, whether the bilateral involvement is funded or performed under a no-exchange of funds arrangement.
b) Definition: "China or Chinese-owned Company" means the People's Republic of China, any company owned by the People's Republic of China, or any company incorporated under the laws of the People's Republic of China.
c) The restrictions in the Acts do not apply to commercial items of supply needed to perform a grant or cooperative agreement.
d) By submission of its proposal, the proposer represents that the proposer is not China or a Chinese-owned company, and that the proposer will not participate, collaborate, or coordinate bilaterally with China or any Chinese-owned company, at the prime recipient level or at any subrecipient level, whether the bilateral involvement is funded or performed under a no-exchange of funds arrangement.

For a practical interpretation and application of these "China Funding Restrictions", proposers should carefully review the PRC FAQ for ROSES:
http://science.nasa.gov/researchers/sara/faqs/prc-faq-roses/

c. Export Control Guidelines Applicable to Proposals Including Foreign Participation

Proposals including foreign participation must include a section discussing compliance with U.S. export laws and regulations, e.g., 22 CFR Parts 120-130 and 15 CFR Parts 730-774, as applicable to the circumstances surrounding the particular foreign participation. The discussion must describe in detail the proposed foreign participation and is to include, but not be limited to, whether or not the foreign participation may require the prospective investigator to obtain the prior approval of the Department of State or the Department of Commerce via a technical assistance agreement or an export license, or whether a license exemption/exception may apply. If prior approvals via licenses are necessary, discuss whether the license has been applied for or, if not, the projected timing of the application and any implications for the schedule. Information regarding U.S. export regulations is available at http://www.bis.doc.gov/.

3. Cost Sharing or Matching

NSBRI awards require a cost-sharing arrangement with all non-government entities consisting of an augmentation of at least 10% of the total annual NSBRI award. This contribution should not be identified in the submitted project budget but will be requested at the time the institutional award is made.

4. Data Accessibility

All research data resulting from NSBRI funded studies must be submitted to NSBRI Headquarters. These data will subsequently be archived in the NASA Life Sciences Data Archive (LSDA) (http://lsda.jsc.nasa.gov/) for the benefit of the greater research and operational spaceflight community. Archival data products may include but are not limited to low-level (raw) data, high-level (processed) data, meta-data, and data products such as calibration data, documentation, related software, and other tools or parameters that are necessary to interpret the data. Once a grant is awarded, the PI, NSBRI Science Office staff, and the supporting NASA HRP Element Scientist shall work with LSDA to outline specific archiving requirements in an LSDA Data Submission Agreement. These requirements shall include which data are to be included, the format of the data, and the timeframe in which the data is expected to be submitted for archiving.

5. Software Sharing Policy

NSBRI has adopted the National Institute of Health's (NIH) policy concerning the sharing of software produced through NSBRI grants. A software dissemination plan, with appropriate timelines, is expected in the application only if software development is a part of the application. There is no prescribed single use license for software produced through grants responding to this announcement. In accordance with federal law, NSBRI will protect the privacy and ownership rights of software developers. However, NSBRI does have goals for software dissemination, and reviewers will be instructed to evaluate the dissemination plan relative to these goals:

1. The software should be freely available to biomedical researchers and educators in the non-profit sector, such as institutions of education, research institutions, and government laboratories.
2. The terms of software availability should permit the dissemination and commercialization of enhanced or customized versions of the software, or incorporation of the software or pieces of it into other software packages.
3. To preserve utility to the community, the software should be transferable such that another individual or team can continue development in the event that the original investigators are unwilling or unable to do so.
4. The terms of software availability should include the ability of researchers to modify the source code and to share modifications with other colleagues. An applicant should take responsibility for creating the original and subsequent "official" versions of a piece of software.
5. To further enhance the potential impact of their software, applicants are expected to propose a plan to manage and disseminate the improvements or customizations of their

tools and resources by others. This proposal may include a plan to incorporate the enhancements into the "official" core software, may involve the creation of an infrastructure for plug-ins, or may describe some other solution.

The plan for software sharing will be evaluated during peer review together with any other resource sharing plans.

The adequacy of the software sharing plans will be considered by NSBRI when making recommendations about funding applications as appropriate. In making such considerations, prior to funding, NSBRI may negotiate modifications of software sharing plans with the Principal Investigator. Any software dissemination plans represent a commitment by the institution (and its subcontractors as applicable) to support and abide by the plan.

D. Proposal and Submission Information

1. Source of Application Materials

All information needed to submit an electronic proposal in response to this announcement is contained in this NRA and in the companion document entitled "Guidebook for Proposers Responding to a NASA Research Announcement (NRA)" (hereafter referred to as the *Guidebook for Proposers*) that is located at:
http://www.hq.nasa.gov/office/procurement/nraguidebook/.

Additionally, applicants shall prepare proposals in accordance with the "Instructions for Responding to NASA Research Announcements," NASA Federal Acquisition Regulations (FAR) Supplement (NFS), Part 1852.235-72 (November 2004), hereafter referred to as the *NASA FAR Supplement*, that is located at:
http://www.hq.nasa.gov/office/procurement/regs/5228-41.htm#52_235-72.

The information in this NRA **supersedes** and provides additional direction to that found in the *Guidebook for Proposers* and provides additional direction consistent with the *NASA FAR Supplement*. Proposals that do not conform to the standards outlined in this solicitation will be declared noncompliant and will be handled in accordance with the *NASA FAR Supplement*.

Proposal submission questions received will be answered and published in a Frequently Asked Questions (FAQ) document. This FAQ will be posted on the NSPIRES solicitation download site alongside this NRA, and will be updated periodically between submission release and the Step-2 proposal due date. Any supplemental information will also be posted alongside this NRA.

2. Content and Form of Proposal Submission

a. Registration in NASA Proposal Data System

This NRA requires that the proposer register key data concerning their intended submission with the NASA Solicitation and Proposal Integrated Review and Evaluation System (NSPIRES)

located at http://nspires.nasaprs.com. **Potential applicants are urged to access this site well in advance of the proposal due date(s) of interest to familiarize themselves with its structure and enter the requested identifier information. It is especially important to note that every individual named on the proposal's *Cover Page* (see further below) must be registered in NSPIRES and that such individuals must perform this registration themselves. Team members will be asked to confirm their organization affiliation when added to a proposal.** No one may register a second party, even the Principal Investigator (PI) of a proposal in which that person is committed to participate. This data site is secure and all information entered is strictly for NASA's use only.

Every organization that intends to submit a proposal to NSBRI in response to this NRA, including educational institutions, industry, nonprofit institutions, NASA Centers, the Jet Propulsion Laboratory, and other U.S. Government agencies, **must be registered in NSPIRES**, regardless of the electronic system used to submit proposals. Such registration must be performed by an organization's electronic business point-of-contact (EBPOC) in the Central Contractor Registry (CCR).

b. Electronic Submission

Proposals must be submitted electronically. Step-1 and Step-2 proposals must be submitted electronically by one of the officials at the PI's organization who is authorized to make such a submission. All team members must be registered in NSPIRES and confirm their organizational affiliation when added to a proposal before the PI organization official can submit. It is strongly recommended that the PI work closely with his/her team members and organization official to ensure the proposal is submitted by the due date and time listed in this solicitation. **Proposals submitted after the listed due dates and times will be will be declared noncompliant and will be handled in accordance with the NASA FAR Supplement.**

NSBRI Step-1 proposers must use NSPIRES for proposal submission. All proposers, team members, and agency officials must be registered before proposal submission with NSPIRES regardless of the electronic system used to submit proposals. NSPIRES remains the only system through which a Step-1 proposal can be continued as a Step-2 proposal. Proposers submitting a Step-1 proposal who receive an invitation to submit a Step-2 proposal will have the option of building on a stored Step-1 proposal within the NSPIRES database. All invited proposers must use NSPIRES for Step-2 proposal submission.

NSPIRES accepts fully electronic proposals through a combination of data-based information (e.g., the electronic *Cover Page* and its associated forms) and uploaded PDF file(s) that contain the body of the proposal. The website will provide a list of all elements that make up an electronic proposal, and the system will conduct an element check to identify any item(s) that is(are) apparently missing or incomplete. Proposers are particularly encouraged to begin their submission process early.

Requests for assistance in accessing and/or using this Website may be directed by E-mail to nspires-help@nasaprs.com or by telephone at 202-479-9376 Monday through Friday, 8:00 AM – 5:00 PM Eastern Time. Frequently Asked Questions (FAQs) may be accessed through the

Proposal Online Help site at http://nspires.nasaprs.com/external/help.do. Tutorials of NSPIRES are available at http://nspires.nasaprs.com/tutorials/index.html.

3. Intent to Propose and Step-1 Proposals

Proposals solicited through this NRA will use a 2-Step proposal process for which the Notices of Intent (NOI) take the form of a required Step-1 proposal.

The NSPIRES system will guide proposers through submission of all required proposal information. **Please note that the Proposal Summary, Business Data, Program Specific Data, and Proposal Team are required Cover Page Elements for a Step-1 proposal.** The proposal summary should be between 100-300 words (4000 characters maximum) and understandable by the layman reader. Budgets should not be included with the Step-1 proposal. The project team is not considered binding for Step-1 and can be adjusted in an invited Step-2 proposal. **Failure to include any of the key components may result in return of your Step-1 proposal without review**.

To initiate a Step-1 proposal:

- Log in using your NSPIRES user name and password.
- Click on Proposals under the NSPIRES Options.
- Click on the Create Proposal button in the upper right hand corner of the screen.
- Select "Solicitation" to prepare a new proposal.
- Click the button for "The National Space Biomedical Research Institute (NSBRI) Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions" (NNJ14ZSA002N-NSBRI).
- Follow the step-by-step instructions provided in NSPIRES to complete your Step-1 proposal.

Step-1 proposals submitted to NSBRI will include a synopsis of the intended research, with the total length of the proposal not to exceed five 8 ½ by 11 inch pages using a standard 12-point font and one inch margins. This synopsis will be provided as a PDF proposal document upload, and must not be password protected or locked in any way. **Required elements** of the five-page, Step-1 application include:

(1) a proposed NSBRI team assignment
(2) a clear indication of the relevance to one or more of the research emphases (Section A.2.a-f)
(3) a plan outline for countermeasure(s) and/or technology development (including approach and key personnel)
(4) the project impact
(5) the rationale for the significance of the proposed research in mitigating risks associated with human exploration of space
(6) the Earth-based applications, and if applicable, commercialization potential.

No additional documents should be uploaded with the Step-1 proposal. Budget and detailed program data should not be included with the Step-1 proposal. Project personnel are not considered binding for Step-1 and can be adjusted in an invited Step-2 proposal. References are not required for the Step-1 proposal, and if included, count towards the 5-page limit.

If your proposal is a resubmission, you should identify it as such in your Step-1 submission; you are not, however, required to address prior reviews unless invited to submit a full proposal. Please be aware that submission of a Step-1 proposal to re-introduce a proposal invited during a previous review cycle to submit as a Step-2 proposal, but not funded (i.e. a re-submission from a previous round of review), does not guarantee that this newly submitted Step-1 proposal will necessarily be judged as responsive to the areas of focus in the current NRA and therefore invited to submit as a Step-2 proposal.

Step-1 proposals are prepared by the PI or a designated representative of the PI. **Step-1 proposals are submitted by an official of the PI's organization after the PI has released the prepared proposal to the institution official.** It is strongly recommended that the PI work closely with his/her organization official to ensure the proposal is submitted by the due date and time listed in this solicitation. Proposals will not be accepted after the listed due dates except for as provided in the *NASA FAR Supplement 1852.235-72(g).*

Step-1 proposals shall be electronically submitted by the due date and time listed in Section G. Electronic submission of Step-1 proposals will be open during the period listed in Section G.

All submitters of Step-1 proposals must log in to NSPIRES on or after the Step-1 notification date listed in Section G to receive their Step-2 full proposal invitation status. A courtesy email will be generated by NSPIRES as a reminder to check full proposal invitation status; however, it is the responsibility of the submitter to log in to NSPIRES to receive their full proposal invitation status.

Decision information can be accessed in two ways:

1) After logging in, the PI selects the "Proposals" link, the "Submitted Proposals/NOIs" link, and then clicks on the proposal submitted to the solicitation identified above. The document(s) provided by NASA will be displayed under the heading "PI Information Package" located at the bottom of the "View Proposal" page.

2) After logging in, the Authorized Organization Representative selects "Organization Mgmt" link and, from within the submitting organization, selects the "Organization Proposals" link, the "Submitted Proposals" link and then clicks on the proposal submitted to the solicitation identified above. The document(s) provided by NASA will be displayed under the heading "PI Information Package" located at the bottom of the "View Proposal" page.

4. Instructions for Preparation of Invited Step-2 Proposals

Step-2 proposals are due by the due date and time listed in Section G. **Step-2 proposals will be accepted from invited proposers only.** Invited Step-2 proposals must be submitted through the NSPIRES system.

The NSPIRES system will guide proposers through submission of all required proposal information. Select **prior-phase proposal** when creating an invited Step-2 proposal. Please note that the Proposal Summary, Business Data, Budget, and Proposal Team and Program Specific Questions are required Cover Page Elements for all Step-2 proposals. The proposal summary should be between 100-300 words (4000 characters maximum) and understandable by the layman reader. In addition to the Cover Page online budget forms, proposers are encouraged to provide expanded budgets as needed (i.e. subcontracts) as part of their budget justification (see number 11 below and the Guidebook for proposers). **For proposals with NASA civil servant team members only:** Proposers are required to enter the NASA civil servant team member name and fraction of full-time equivalent (FTE) involvement in the same field under the Item column in section F "Other Direct Costs" of the online budget. The funds requested should be entered as the Total Requested Funds for the NASA civil servant, including salary, fringe, materials, travel, etc. (see the FAQ posted alongside this document for additional budget instruction). This budget entry should be made for each year of NASA civil servant involvement, and is in addition to the agency identification under the team member section and the NASA civil servant FTE designation under the business data section.

To ensure proper Step-2 proposal transmission, please provide only **one** PDF attachment upload ordered as below. **For proposal sections 2 through 9 and section 17, specific instruction are given in this NRA (see section D.4.a though D.4.g). These specific instructions supersede those found in the NASA Guidebook for Proposers. Proposals that do not conform to these requirements may be declared noncompliant and declined without review.** For sections 11-16, proposers are encouraged to reference the NASA Guidebook for Proposers; however, there are no specific submission compliance requirements for these sections (format, structure, page counts, etc).

1. *Table of Contents*
2. *If applicable, inclusion of the Flight Experiment Resource Worksheet, or Analog Study Resource Worksheet.*
3. *Software Sharing Plan, if applicable.*
4. *Map to HRP Integrated Research Plan (IRP) (see D.4.a below).*
5. *Animal Care or Human Subjects certifications, if applicable (see D.4.b below).*
6. *Response to prior review, if applicable (see D.4.c below).*
7. *Productivity of currently funded research, if applicable (see D.4.d below).*
8. *Vertebrate Animal Scientific Review, if applicable (see D.4.e below and VASR posted on NSPIRES solicitation site).*
9. *Scientific or Technical Project Description (see section D.4.f below).*
10. *References and Citations.*
11. *Management Approach (see Guidebook for Proposers and NASA FAR Supplement).*
12. *Personnel Curriculum Vitae (CV's) (see Guidebook for Proposers and NASA FAR*

Supplement).

13. *Current and Pending Support (see Guidebook for Proposers and NASA FAR Supplement).*
14. *Facilities and Equipment (see Guidebook for Proposers and NASA FAR Supplement).*
15. *Budget Justification of Proposed Costs (see Guidebook for Proposers and NASA FAR Supplement).*
16. *Letters of Collaboration or Support.*
17. *Appendices or Reprints (See D.4.g below).*

While the NSPIRES system allows for the upload of supporting documents as separate uploads, please provide the information above in only one PDF proposal document upload. It is essential that all PDF files generated and submitted meet NASA requirements. At a minimum, it is the responsibility of the proposer to:

1) ensure that all PDF files are unlocked and that edit permission is enabled – this is necessary to allow NSPIRES to concatenate submitted files into a single PDF document; and
2) ensure that all fonts are embedded in the PDF file and that only Type 1 or TrueType fonts are used. In addition, any proposer who creates files using TeX or LaTeX is required to first create a DVI file and then convert the DVI file to Postscript and then to PDF.

See http://nspires.nasaprs.com/tutorials/PDF_Guidelines.pdf for more information on creating PDF documents that are compliant with NSPIRES.

There is a recommended 10 MB size limit for proposals (Section 2.3(c) of the NASA Guidebook for Proposers). Large file sizes can impact the performance of the NSPIRES system. Most electronically submitted proposals will be less than 2 MB in size.

NSPIRES accepts electronic proposals through a combination of data-based information (e.g., the electronic Cover Page) and the uploaded PDF file that contains the proposal as outlined above. The NSPIRES proposal submission process ensures that a minimum set of required proposal cover page fields are completed. Provision of the proposal summary and business data elements of the cover page will be necessary in order for the Authorized Organizational Representative (AOR) to submit the proposal to NASA. If either of these two proposal elements is incomplete, the "View Proposal/ Check Elements" function of NSPIRES will display red "error" flags and messages to alert the user to the information that is required but missing, and the "Submit Proposal" button will not be available. Although the PI will be able to release the proposal to the AOR, the proposal cannot be submitted by the AOR to NASA until these required fields are complete. Any additional information that is missing will be identified by yellow "warning" flags. Proposers are reminded to check the solicitation instructions to ensure compliance with all instructions, as adherence to these two element validation checks alone is insufficient to guarantee a compliant proposal. Additionally, in those cases where instruction in the NRA contradicts an NSPIRES warning, the NSPIRES yellow “warning” may be ignored. Proposers should follow the NRA instructions closely to help ensure submission of a compliant proposal.

The NSPIRES system is limited in the character sets that can be used in filling out on-line forms. Please refer to the on-line tutorials when using special characters. Alternatively, spell out special characters where possible (such as micro rather than the Greek symbol). Applicants are encouraged to preview their proposal prior to releasing the proposal to their designated Organization by clicking the "Generate" button at the bottom of the View Proposal Screen in NSPIRES. The "Generate" feature allows applicants to preview their entire proposal in a single PDF file prior to submittal, but it is not a required step in the submission process. Please contact the NSPIRES Help Desk for assistance with this feature (e-mail nspires-help@nasaprs.comor by Telephone at 202-479-9376).

a) Human Research Program Human Research Roadmap

The investigator must examine and understand the research emphases outlined in this NRA and the risks identified in the HRP Human Research Roadmap (HRR) (http://humanresearchroadmap.nasa.gov). Proposers must include a description as part of their proposal of how their research aims map to the identified IRP risks, gaps and deliverables. This description is limited to two pages and does not count towards the 20-page limit of the project description.

b) Special Matters

For proposals employing human subjects and/or animals, assurance of compliance with human subjects and/or animal care and use provisions is required.

Policies for the protection of human subjects in NASA sponsored research projects are described in NASA the NASA Policy Directive (NPD) 7100.8E "Protection of Human Research Subjects" (http://nodis3.gsfc.nasa.gov/displayDir.cfm?t=NPD&c=7100&s=8E)

Animal use and care requirements are described in the NASA Code of Federal Regulations (CFR) 1232 (http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title14/14cfr1232_main_02.tpl).

NASA utilizes a just-in-time practice for approval of the use of human subjects or animals. If the IRB/IACUC certification is already approved at proposal submission, attach a copy of the certification as part of the proposal.

After award, a statement must be provided from the Applicant institution which identifies the selected proposal by name and which certifies that the proposed work will meet all Federal and local requirements for human subjects and/or animal care and use. This includes relevant documentation of Institutional Review Board (IRB) approval and/or approval by the Institutional Animal Care and Use Committee (IACUC). NASA will require current IRB and IACUC certification prior to each year's award.

For delivery of any certifications received after the proposal due date, please contact Kevin Willison, Senior Scientist, NASA Research and Education Support Services, at kwillison@nasaprs.com.

c) Revised Proposals

Investigators submitting a proposal in response to this solicitation, and whose most recent submission that included similar specific aims to any NASA or NSBRI sponsored research announcement was not accepted, are required to submit an explanation of how the current proposal addresses criticisms from previous review cycles. This explanation shall be presented preceding the research description as part of the main proposal upload and is limited to two pages. This explanation should include changes to the current proposal as a result of review comments and, or explanation as to why prior review comments are not applicable to the current proposal.

Investigators resubmitting a proposal in response to this solicitation may only submit a proposal with similar hypothesis(es) and aims a total of three times (original submission plus two resubmissions). Significant changes must be made to the proposal hypothesis(es) and specific aims for consideration after the third attempt or the proposal will be declined without further review.

These two pages are not considered part of the 20-page project description. Proposal reviewers will be provided with the evaluations of prior submissions. Proposers must respond to prior criticisms relevant to any portion of the new proposal under consideration. Proposers who have questions concerning their response to a prior review are encouraged to contact Kevin Willison, Senior Scientist, NASA Research and Education Support Services, at kwillison@nasaprs.com.

d) Productivity of NASA- or NSBRI-Funded Research

Proposers currently funded by or who have received funding within the last three (3) years from NASA or NSBRI must provide specifics to the productivity of the supported research including progress in experiments, completion of milestones and deliverables, research publications, and new findings. This explanation should be presented preceding the research description as part of the main proposal upload and is limited to two pages. These two pages are not considered part of the 20-page project description. Related impacts, if any, to the proposed research plan should be highlighted in the body of the project description. **Proposers that request continued support that do not include this productivity section will be returned to the submitter without panel review and will not be considered for funding.**

e) Vertebrate Animal Scientific Review (if applicable)

Each response to this solicitation that requires vertebrate animals must address the five points outlined in the Vertebrate Animal Scientific Review (VASR) instructional document posted alongside this NRA. This response should be presented as part of the main proposal upload and is limited to two pages. These two pages are not considered part of the 20-page project description. A sample VASR is provided in the VASR instructional document.

f) Scientific/Technical/Management Section (Project Description)

The length of the project description of the proposal shall not exceed 20 pages using standard (12 point) type. Text shall have one-inch margins. Referenced figures and tables must be included in the 20 pages of the project description; however, figure captions can use a 10-point font. The proposal shall contain sufficient detail to enable reviewers to make informed judgments about the overall merit of the proposed research and about the probability that the investigators will be able to accomplish their stated objectives with current resources and the resources requested. The hypotheses (if appropriate) and specific aims of the proposed research shall be clearly stated. If applicable, a statistical section with proper justification should be included in the project description. **Proposals that exceed the 20-page limit for the project description (inclusive of ALL figures and tables) will be declared noncompliant and will be handled in accordance with Appendix A. Cited literature and all other proposal sections are not considered part of the 20-page project description.** Reviewers are not required to consider information presented as appendices or to view and/or consider Web links in their evaluation of the proposal.

g) Reprints and Appendices

Reprints and Appendices, if any, do not count toward the project description page limit, and are to be included following all other sections of the proposal (**reviewers are not required to consider information presented in proposal appendices**).

E. Proposal Evaluation Process

1. Step-1 Proposal Relevancy Review

Each Step-1 proposal will be reviewed by members of the Institute's Executive Science and Medicine Council (ESMC). The ESMC will incorporate advice from NASA, and determinations of relevancy will be made, from which a final composite recommendation of "relevant" or "not relevant" will be made based upon research emphases outlined in Section A.2.. Only those Step-1 proposals having a final evaluation of “relevant” will be invited to submit a full Step-2 proposal.

2. Step-2 Proposal Intrinsic Scientific and Technical Merit

To be responsive to this research solicitation, proposed studies should produce research product(s) that address the research emphases stated in this solicitation, and lead to new knowledge within accepted scientific and technology standards.

All of the following criteria will be used in determining the merit score.

Significance:
Does this study address a research emphasis stated in this solicitation? Does the study test a significant hypothesis or produce data that would enable a significant hypothesis to be

generated? If the study is non-hypothesis driven, are the data produced needed to understand or reduce the risk addressed by the research emphasis? If the task will produce a software model or tool, how will it serve to better quantify or mitigate a risk? If the aims of the application are achieved, how well will the product(s) address the research emphases? If the aims of the application are achieved, how will scientific knowledge or technology advance?

Approach:
Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Is the proposed approach likely to yield the desired results? Does the applicant acknowledge potential problem areas and consider alternative tactics?

Statistical Plan:
Does the study provide adequate justification for sample size? For example, is the choice of primary outcome relevant for the stated Aims? Are assumed effect magnitudes reasonable? Are assumed variability estimates reasonable? Are they estimated properly? Are they relevant for the proposed experimental design and data analysis methodology? What Type I and Type II errors are assumed? Is there room for a tradeoff here to accommodate sample size constraints and still provide useful information from the study? Do the investigators provide a reasonable data analysis plan? For example, is it appropriate for the proposed experimental design (e.g. repeated measures)? Does it address research hypotheses or aims? Is it robust to the sampling and other constraints associated with the research venue?

Risk Mitigation:
For a study quantifying risks to crew health or performance; does the study adequately improve the understanding of the adverse consequences, the probability of its occurrence, or the timeframe in which the risk must be addressed? For a study developing countermeasures, will the proposed countermeasure reduce a risk to crew health or performance, reduce the impact of the risk or reduce the resources required to mitigate it? For a study developing technology, will the research product reduce the risk to crew health or performance, reduce its impact or better define it and is the technology feasible within the confines of the operational environment?

Investigators:
Are the investigators appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and any co-investigators? Is the evidence of the investigators' productivity satisfactory?

Environment:
Does the scientific environment in which the work will be performed contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

3. Step-2 Proposal Review and Selection Processes

a. Compliance Matrix

All proposals must comply with the general requirements of the NRA as described in this solicitation, the *Guidebook for Proposers*, and the *NASA FAR Supplement*. Upon receipt, proposals will be reviewed for compliance with these requirements including:

1) Proposals will not be accepted after the due dates and times listed in this announcement except for as provided in the *NASA FAR Supplement*.
2) The proposal project description must be no more than 20 pages in length, (including all tables and figures).
3) Submission of appropriate IRB or IACUC certification for all proposals using human or animal test Subjects in accordance with the Special Matters requirements listed in section D.4.b.
4) Submission of an appropriate and justified budget for a funding period not exceeding that described in the NRA.
5) Investigators who are submitting a proposal in response to this solicitation, and whose most recent submission that included similar specific aims to any NASA or NSBRI sponsored research announcement was not accepted, are required to submit an explanation of how the current proposal addresses criticisms from previous review cycles. This explanation should be presented in a separate form of no more than two pages. Related changes to the research plan should be highlighted in the body of the project description as described in section D.4.c.
6) A description of how the research aims map to the identified IRP risks and gaps as described in section D.4.a.
7) A description that provides specifics to the productivity of the previously supported research including progress in experiments and research publications and new findings as described in section D.4.d.
8) Proposals that require vertebrate animals must include a Vertebrate Animal Scientific Review component as outlined in the VASR, not to exceed two pages.
9) For flight proposals, submission of the Flight Experiment Resource Worksheet.
10) Submission of any required analog definition forms.
11) If applicable, inclusion of the Analog Study Resource Worksheet.
12) Submission of all other appropriate information as required by this NRA.

Note: At NSBRI's discretion, non-compliant proposals may be withdrawn from the review process and declined without further review. Compliant proposals submitted in response to this NRA will undergo an intrinsic scientific or technical merit review. Only those proposals most highly rated in the merit review process will undergo additional reviews for program balance and cost.

b. Scientific and Programmatic Reviews

The overall evaluation process for proposals submitted in response to this NRA will include a First Tier Merit Review and a Second Tier Program Alignment Review. The **First Tier Review** will be a merit peer review by a panel of scientific or technical subject matter experts. The number and diversity of experts required will be determined by the response to this NRA and by the variety of disciplines represented in the proposals relevant to the research emphases described in this NRA. The merit review panel will assign ***a score from 0-100, or assign a Not Recommended for Further Consideration (NRFC)*** based upon the intrinsic scientific or technical merit of the proposal. The final score or NRFC designation will reflect the consensus of the peer review panel. After the merit review is complete the panel will be asked to include in their critique of each proposal any comments they may have concerning the proposal's budget. Proposals that are highly rated in the merit review process will undergo a **Second Tier Review** for program alignment.

For research requiring vertebrate animals, the first tier review will also include a VASR as outlined in the VASR posted on the NSPIRES solicitation download site alongside this NRA.

In addition, analog definition proposals and flight definition proposals will undergo reviews for feasibility as described below.

For NSBRI, a separate evaluation for program balance and proposed project cost will be performed. Evaluation of the cost of a proposed effort includes consideration of the reasonableness of the proposed cost. Programmatic balance will include an evaluation of how the proposed work may help achieve an appropriate balance of team, scientific and technical tasks in alignment with the IRP and the NSBRI missions. In accordance with the NIH policy that NSBRI has adopted, all applications will also be reviewed with respect to:

- Adequacy of plans to include males and females, members of minority groups, and their subgroups, as appropriate for the scientific goals of the research;
- Plans for the recruitment and retention of subjects;
- Reasonableness of the proposed budget and duration in relation to the proposed research;
- Adequacy of the proposed protection for humans, animals or the environment to the extent they may be adversely affected by the project proposed in the application.
- For proposals requiring vertebrate animals, coding of the VASR rated as Acceptable. NSBRI staff will work with the applicant to resolve concerns prior to award. **Coding of the VASR as Acceptable is required prior to award**.

The NSBRI User Panel (UP) will review those Step-2 proposals in the fundable range for operational relevance and feasibility. A set of selection recommendations will be developed by the NSBRI External Advisory Council (EAC) based on the merit review scores, programmatic balance, recommendations from the UP, and costs. These recommendations will be reviewed with NASA prior to selection by the NSBRI Director.

c. Analog Definition Proposals

Only those analog definition proposals that are most highly rated in the merit review process will undergo additional reviews for analog feasibility. A panel of technical experts from NASA will evaluate the feasibility of carrying out the analog experiment and the potential for establishing teams of investigators to optimize utilization of human subjects, samples, data, and analog resources. This review will be conducted by technical experts familiar with the development and conduct of analog studies.

d. Flight Definition Proposals

Only those flight definition proposals most highly rated in the merit review process will undergo additional reviews for flight feasibility. A panel of technical experts from NASA will evaluate the feasibility of carrying out the flight experiment and the potential for establishing teams of investigators to optimize utilization of human subjects, samples, data, and flight resources. This review will be conducted by technical experts familiar with the development of spaceflight experiment hardware, ground and flight operations, crew training, and vehicle resources (e.g., power, volume, mass, etc.).

e. Selection

The information resulting from these two levels of review, as described above, will be used to prepare selection recommendations developed by the NSBRI EAC. Selection for funding will be made by the respective selecting official identified in the Submission section of this NRA.

In order to optimize resources, NASA and NSBRI pursue the intentional formation of investigator partnerships between individual investigators whose experiments will leverage resources by addressing different facets of the same questions. NASA anticipates that such intentional teaming arrangements will result in better utilization of available resources to resolve specific critical questions. NASA and NSBRI strongly encourage investigators submitting applications in response to this NRA to consider identifying collaborations between individual investigators as part of the development of their individual proposals and to identify this pre-coordination in their management plan. Additional information can be referenced in the NASA FAR Supplement. Finally, NASA and NSBRI may integrate proposals if, in their judgments, the goals, objectives or products of the proposals are similar.

For some NASA and NSBRI research topics, NASA is considering utilizing individual research proposals to form a Virtual NASA Specialized Center of Research (VNSCOR) where NASA aligns a set of individual awards into an NSCOR-like team project. Individual proposals may be selected to become Elements of a VNSCOR. Elements of the VNSCOR will also join a working group organized by NASA on the specific research topic. VNSCORs will be composed of four to six individual research elements, each with its own specific aims.

Where appropriate for analog definition or flight definition studies, NSBRI and NASA reserve the right to form teams of investigators whose experiments have compatible requirements for human subjects, specimens, operations, data, and treatment and sharing of biological samples. A

selected investigator who becomes a member of a research team will be required to work with other team members to develop an integrated set of objectives that can be met within fiscal and analog or flight resource constraints. Development of this integrated approach may result in modification, transfer, addition or deletion of some objectives put forth in an individual proposal. Specifics associated with the definition period will be addressed with the investigator at the time of selection.

Additionally, proposals submitted in response to this solicitation found to have strong programmatic relevance and scientific merit that cannot be funded due to limited resources may be forwarded to partner programs or agencies for consideration. NASA reserves the right to select proposals submitted to NSBRI that NSBRI does not select; such a selection will result in the award of a NASA grant. Similarly, NSBRI reserves the right to select proposals submitted to NASA that NASA does not select; such a selection will result in the award of a NSBRI grant. In these instances, the PI will be given the opportunity to accept or decline the offer.

f. Ombudsman

Resolution of concerns during the pre-award and post-award phases of this solicitation is under the auspices of the NSBRI Chief Scientist, Dr. Graham Scott (ph. 713-798-7227; fax 713-798-7413; email: Graham.Scott@bcm.edu).

F. Award Administration Information

1. Award Notices

At the end of the selection process, each Step-2 proposing organization will be notified of its selection or non-selection status. NSBRI will provide debriefings to those investigators who request one. Selection notification will be made by a letter signed by the designated NSBRI selecting official. The selection letters are not an authorization to begin performance. The selected organization’s business office will be contacted by a representative of the NSBRI to negotiate an award. Any costs incurred by the investigator in anticipation of an award are at their own risk until contacted by NSBRI. NSBRI will determine the type of award instrument, request further business data, and negotiate the resultant action. NSBRI awards will be issued and funded by NSBRI. NSBRI reserves the right to offer selection of only a portion of a proposal. In these instances, the investigator will be given the opportunity to accept or decline the offer.

2. Administrative and National Policy Requirements

All grant awards are subject to the NASA Grant and Cooperative Agreement Handbook. This handbook consists of four sections that prescribe the policies and procedures relating to the award and administration of NASA grants. Section A provides the text of provisions and special conditions and addresses NASA's authority, definitions, applicability, amendments, publications, deviations, pre-award requirements and post-award requirements currently covered by 14 CFR Part 1260. Section B relates to grants with institutions of higher education, hospitals, and other

nonprofit organizations. Sections A and B, with the special considerations in subpart 1260.4(b), apply to awards with commercial firms that do not involve cost sharing. Section C adopts the administrative requirements of OMB Circular No. A-102 and relates to administrative requirements for grants to state and local governments. Section D relates to awards with commercial firms. The Handbook is located at http://prod.nais.nasa.gov/pub/pub_library/grcover.htm.

3. Individual Researcher Reporting

a. Annual Reporting

The PI shall provide an annual written report to NSBRI. This report is due 30 days prior to the commencement of the next year of potential support. Receipt of the annual report is a prerequisite for continued funding installments. This information will be used to assess the degree of progress of the project. A component of this annual report will be used for the NASA Space Life & Physical Sciences Research & Applications Division Task Book (https://taskbook.nasaprs.com/Publication/welcome.cfm). The Task Book includes descriptions of all peer-reviewed activities funded by the Human Exploration and Operations Mission Directorate (HEOMD). The Task Book is an invaluable source of information for NSBRI and NASA biological and biomedical researchers as well as the external scientific and technical communities. This information will consist primarily of:

- an abstract;
- a bibliographic list of publications;
- invention disclosures;
- a statement of progress, including a comparison with the originally proposed work schedule;
- results of periodic data reviews

Additional reporting requirements may be added to ensure timely integration of the research or technology development into NSBRI.

b. Intellectual Property Reporting

Institutions awarded NSBRI funding must report each invention disclosure or patent application resulting from their NSBRI research grant to **both** NSBRI and NASA within 60 days of investigator disclosure to the home institution.

For NASA: Submit either a hard copy of Form 1679 (see https://invention.nasa.gov/assets/downloads/nf1679.doc) to NASA Innovative Partnerships Office, Mail Code AF2, 2101 NASA Parkway, Houston, TX 77058 OR submit online at https://ntr.ndc.nasa.gov . In the field designating contract number, please cite NCC 9-58.

For NSBRI: In addition to reporting on intellectual property on the annual project report, please also send copies of the institutional invention disclosure AND NASA Form 1679 or the summary from the online disclosure at https://ntr.ndc.nasa.gov via email to info@nsbri.org.

c. Final Report

A final report must be provided to the NSBRI at the end of the award funding period, including a detailed listing of all peer-reviewed publications. The final report is a requirement for eligibility for future NASA/NSBRI solicitations. The information in this report will consist primarily of:

- statement of the specific objectives;
- significance of the work;
- background;
- overall progress during the performance period;
- narrative discussion of technical approaches including problems encountered;
- accomplishments related to approach; and
- an appendix with bibliography, copies of all publications and reports, and intellectual property disclosures. Any publications or other public materials containing data are particularly important to include in this section.

d. Publications

For NSBRI-funded research, please clearly identify support received from the National Space Biomedical Research Institute in all publications, invention disclosures, copyrights and patents, using the following phrase: "This work is supported by the National Space Biomedical Research Institute through NCC 9-58."

For all funded projects, HRP requests but does not require that scientific manuscripts prepared under HRP or NSBRI support be sent to the office of the HRP Chief Scientist before submission for publication. This is to determine if there may be inadvertent release of identifiable crew information, to identify synergies between projects, and to track program status. It will not be used to otherwise control the content of such manuscripts.

4. Other Considerations

Required Travel
The proposal must include travel costs for the following:

Annual Investigators' Workshop. All NASA and NSBRI Principal Investigators are required to attend the Annual Investigators' Workshop usually scheduled for February of each year in the vicinity of Houston, Texas.

In addition, NSBRI Principal Investigators will be expected to travel to Houston annually to NSBRI Headquarters and demonstration laboratories to exhibit their research.

Optional Travel
Visits to NASA Lyndon B. Johnson Space Center
Presentation at a professional society meeting (highly desirable)

G. Submission Dates

Solicitation Announcement Identifier: NRA NNJ14ZSA001N-NSBRI
Step-1 Response Period: July 30, 2014 – September 4, 2014
Step-1 Proposals Due: September 4, 2014, 5 PM Eastern Time
Step-1 Notification of Proposal Invitation Status: October 1, 2014
Step-2 Response Period: October 1, 2014 – December 3, 2014
Step-2 Proposals Due: December 3, 2014, 5 PM Eastern Time
Estimated Step-2 Selection Announcement: April 2015

H. NSBRI Contacts

Additional NSBRI Team and Research Emphases information is available from:

Graham B.I. Scott, Ph.D.
Vice President, Chief Scientist, & Institute Associate Director
National Space Biomedical Research Institute
Bioscience Research Collaborative
6500 Main St., Suite 910
Houston, TX 77030
Telephone: 713-798-7227
Fax: 713-798-7413
Email: Graham.Scott@bcm.edu

Additional information on the proposal submission process is available from:

NSPIRES
Telephone: 202-479-9376, Monday through Friday, 8 a.m. to 6 p.m. Eastern Time.
Email: nspires-help@nasaprs.com
Frequently Asked Questions: Available through the Proposal Online Help site at http://nspires.nasaprs.com/external/help.do.
Tutorials of NSPIRES: Available at http://nspires.nasaprs.com/tutorials/index.html

I. Summary of Key Information

Selection announcements are expected no earlier than April 2015, and selected awards will begin no earlier than May 2015.

Number of new awards pending adequate proposals of merit	6-8
Maximum duration of awards	2 years
First day for submission of Step-1 proposals	July 31, 2014
Last day for submission of Step-1 proposals	September 4, 2014
First day for submission of Step-2 proposals	October 1, 2014
Last day for submission of Step-2 proposals	December 3, 2014
Page limit for the central Science-Technical section of Step-1 proposal	5 pages
Page limit for the central Science-Technical section of Step-2 proposal	20 pages
General information and overview of this solicitation	See Human Exploration Research Opportunities (HERO) Overview posted http://nspires.nasaprs.com
Detailed instructions for the preparation and submission of proposals	See NASA Guidebook for Proposers at http://www.hq.nasa.gov/office/procurement/nraguidebook/
Submission medium	Electronic proposal submission is required; no hardcopy is required. See also HERO Overview and Chapter 3 of the *NASA Guidebook for Proposers*.
Web site for submission of proposal via NSPIRES	http://nspires.nasaprs.com/ (help desk available at nspires-help@nasaprs.com or (202) 479-9376)
NSBRI point of contact concerning this program	Graham B.I. Scott, Ph.D.