

**February 6, 2015
NSBRI-RFA-15-01**

**National Space Biomedical Research Institute
BioScience Research Collaborative
6500 Main Street, Suite 910
Houston, TX 77030-1402**

**NSBRI Announcement
Soliciting First Award Fellowship
Applications**



**A Request for Applications to the
National Space Biomedical Research Institute**

Applications Due: June 5, 2015

Executive Summary of Opportunity

NOTE: It is critical for First Award Fellowship Program applicants to carefully read all of the instructions in this NSBRI-RFA. Each Section includes guidelines, requirements, and instructions for preparing and submitting proposals and defines the administrative policies governing the particular components described in this NSBRI-RFA.

This National Space Biomedical Research Institute (NSBRI) Request for Applications (NSBRI-RFA) is soliciting applications for the First Award Fellowship Program. First Award Fellowships will be competitively awarded for one year in any laboratory in the U.S. conducting biomedical/biotechnological research aligned with NSBRI's goals (Section A). Applications will initially be scientifically and technically peer-reviewed by the NSBRI First Award Fellowship Committee, consisting of a number of eminent scientists that are familiar with space biomedical/biotechnological research. Non-NSBRI as well as NSBRI-supported researchers qualify as Mentors for this competitive funding. **The program is open to U.S. citizens, permanent residents, or persons with pre-existing visas obtained through their sponsoring institutions that permit postdoctoral training for the project's duration. To be eligible for this program, First Award Fellows may not have more than five years (cumulative) previous postdoctoral training as of the deadline for this proposal submission. The month and year of any previous postdoctoral experience(s) must be included in the curriculum vitae and any gaps detailed. Additionally, those earning a terminal degree more than seven years ago (i.e., terminal degree conferred on or before June 5, 2008) are ineligible for this opportunity. Applicants that anticipate earning a terminal degree (Ph.D., M.D., M.D./Ph.D., D.Sc., Sc.D., D.V.M., D.O., or equivalent) by the end of the 2015 calendar year are eligible to participate in this opportunity.**

All selected First Award Fellows will become members of an NSBRI Science and Technology Team as described in Section A. The First Award Fellowship will be funded as a stipend of \$43,340, plus an additional \$7,500 per annum allowance for health insurance and travel will be provided. Fellows will be expected to travel to a mandatory annual NSBRI/NASA Investigators' Workshop, a research team meeting to be determined and attend a 4-5 day NSBRI Summer Bioastronautics Institute at the NSBRI Consolidated Research Facility (CRF) in Houston, Texas.

An additional opportunity for applicants will be offered through this announcement. First Award Fellows with an interest in visiting a laboratory and conducting some of their research at the Institute of Biomedical Problems (IBMP) of the Russian Academy of Sciences in Moscow must specify their interest to be considered. While Russian language proficiency is not mandatory, it is highly desirable if First Award Fellows wish to spend time at IBMP.

First Award Fellows are encouraged to consider, in addition to U.S. academic and government laboratories, conducting research at other commercial entities focused on the advancement of human spaceflight endeavors. These entities can include government contractors and for-profit corporations aligned with the missions of both NSBRI and NASA. Fellows are responsible for identifying an appropriately qualified and experienced mentor.

A budget is not necessary for completion of an application. Funding is not provided for administrative costs, research supplies, reagents, equipment and instrumentation, or animals. The

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Mentor is responsible for supervision of the NSBRI First Award Fellow and for providing all resources required for the completion of the research proposed by the Fellow. After First Award Fellowships have been awarded, NSBRI will work with the funded institutions to execute the awards, which will include development of a budget for funding. **Indirect costs will not be awarded to the funded institution.** Additionally, NSBRI's traditional cost sharing of 10% of the funded award is welcomed, but not required, from institutions who receive awards for the training of First Award Fellows.

First Award Fellowship Program applicants must prepare proposals with the support of a Mentor and institution (university, national lab, commercial entity, etc.), and all proposals will be objectively and rigorously, scientifically and technically evaluated by the NSBRI First Award Fellowship Committee. Proposals should be written in their entirety by the Fellow, with the exception of the Mentor Statement. However, Mentors are encouraged to provide feedback and guidance, particularly in regards to developing and refining the specific aims and hypotheses of the proposed research. **In order to facilitate electronic submission from the institution at which the First Award Fellow will conduct the research, please note that the NSPIRES proposal submission system requires that the Mentor be identified as the Principal Investigator (PI) and the trainee be identified as the First Award Fellow.**

Mentors should have previous experience in training postdoctoral fellows (and/or graduate students), and in their letter of support should indicate their ability and commitment to financially and intellectually support the research activities of the trainee. **It is the responsibility of the First Award Fellowship Program applicant to arrange for a Mentor.**

Please contact Amanda Smith Hackler, Ed.D. (hackler@bcm.edu), Head of Career Development and Outreach at NSBRI, for information on available NASA mentors.

Selected research projects will become part of an NSBRI Science and Technology Team focused on advancing the research toward an applied intervention to ensure the health of humans living and working in space. Each First Award Fellowship Program applicant must identify the Countermeasure Readiness Level (CRL) and/or Technology Readiness Level (TRL) the research proposal addresses. Applicants should refer to Figure 1 and Table 1 in Section A, of this RFA for detailed descriptions of CRLs and TRLs.

In this NSBRI-RFA,

Section A provides an introduction and overview of the goals, objectives, and research implementation strategies of NSBRI.

Section B contains descriptions of the opportunity and eligibility, and instructions for proposal submission.

Section C contains the standard instructions for responding to NSBRI Requests for Applications.

Section D contains information on additional requirements for proposals utilizing vertebrate animals.

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NSBRI's scientific and career development goals are to fund research and development that will result in the delivery of countermeasures to ensure the health of astronauts in response to the space environment, and to apply research findings supported by the Institute to benefit human health on Earth. NSBRI is committed to maintaining a strong, openly competitive, peer-reviewed research program. The Institute also aims to inspire the next generation of space life scientists. Proposals submitted in response to this NSBRI-RFA must address one or more of the research emphases described in this document (see Section A, Part I for more details). Those that do not will be returned without review.

Proposals that synergistically bridge multiple disciplines for the purpose of modeling the effects of microgravity on the human body, aid in the development and testing of countermeasures, or develop technologies that enable research in one or more NSBRI research areas are strongly encouraged.

All proposals will be evaluated for overall scientific and technical merit by the NSBRI First Award Fellowship Committee. The First Award Fellowship Committee has been established by NSBRI. All committee members are eminent scientists familiar with space biomedical/biotechnological research that are selected by NSBRI. Relevance to NSBRI's programmatic needs and goals will also be evaluated by NSBRI management. NSBRI's obligation to make award(s) is contingent upon the availability of appropriated funds from which payment can be made and the receipt of proposals that NSBRI determines are acceptable for award under this NSBRI-RFA. Participation in this NSBRI-RFA is open to all categories of organizations, industry (including for-profit entities), educational institutions, other non-profit organizations, NASA laboratories, and other agencies of the U.S. Government.

Inclusion of Women and Minorities in Research Involving Human Subjects – NASA and NSBRI have adopted the policy of the NIH regarding this matter. Women and members of minority groups and their sub-populations must be included in NSBRI-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale is provided that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.

Proposals must be submitted electronically by June 5, 2015, 5:00 p.m. Eastern Time. (See Section B, Part IV of this NSBRI-RFA for specific instructions regarding electronic submission of proposals).

The following items apply only to this NSBRI-RFA:

Solicitation NSBRI-RFA Identifier: NSBRI-RFA-15-01

Required: Electronic application using NASA's NSPIRES System (See Section B, Part IV for details)

Proposals Due: June 5, 2015, 5:00 p.m. ET

Selection Announcement: Fall 2015

Funding Begins: Approximately 30-90 days following notification of selection

Selection Official: Director, National Space Biomedical Research Institute

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Information about NSBRI's research programs and the First Award Fellowship Program is available from:

Amanda Smith Hackler, Ed.D.
Head of Career Development and Outreach
National Space Biomedical Research Institute
BioScience Research Collaborative
6500 Main Street, Suite 910
Houston, TX 77030-1402
Telephone: (713) 798-3013
Email: firstaward@nsbri.org

All prospective applicants to this NSBRI-RFA are advised that the highest priority in all of NASA's programs is given to safety and mission assurance, occupational health, environmental protection, information technology, export control, and security. NASA's safety priorities are to protect (i) the public, (ii) astronauts and pilots, (iii) the NASA workforce (including employees working under NASA instruments); and (iv) high-value equipment and property. All proposals submitted in response to this solicitation are expected to comply with this policy.

NSBRI points of contact will be identified in selection letters to begin the funding process. Potential First Award Fellowship Program applicants should carefully review the program descriptions that are of interest and focus their proposals on the specific research emphases defined in this NSBRI-RFA. Your interest and cooperation in participating in this effort is appreciated.

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SECTION A

Introduction and Overview: Goals, Objectives and Research Implementation Strategies of NSBRI

I. Introduction to NSBRI

NSBRI is a NASA-funded, non-profit research consortium charged with developing biomedical countermeasures and technologies for potential health problems that could occur in astronauts either during long-duration spaceflight, on exploration missions, or upon return to Earth. NSBRI's current program, aligned with NASA's exploration objectives, consists of approximately 60 science and technology projects organized into seven teams.

NSBRI invites ground-based research applications for First Award Fellowships. Proposals should address topics of interest to one of the seven existing NSBRI Science and Technology Teams, which has importance to both NSBRI and the NASA Human Research Program (HRP). The seven NSBRI Science and Technology Teams are as follows:

1. *Cardiovascular Alterations* – Determining the effect of long-duration spaceflight on the heart and blood vessels and researching ways to reduce the risks and to improve pre-flight detection and management of cardiovascular diseases. Team information, including research goals and priorities, is located at: <http://www.nsbri.org/SCIENCE-and-TECHNOLOGY/Cardiovascular-Alterations/>.
2. *Human Factors and Performance* – Reducing performance errors and mitigating habitability, environmental and behavioral factors that pose significant risks to mission success. Team information, including research goals and priorities, is located at: <http://www.nsbri.org/SCIENCE-and-TECHNOLOGY/Human-Factors-and-Performance/>.
3. *Musculoskeletal Alterations* – Understanding and mitigating bone and muscle loss during spaceflight. Team information, including research goals and priorities, is located at: <http://www.nsbri.org/SCIENCE-and-TECHNOLOGY/Musculoskeletal-Alterations/>.
4. *Neurobehavioral and Psychosocial Factors* – Investigating methods and tools to predict, prevent, detect, and mitigate neurocognitive and psychosocial decrements in the space environment. Team information, including research goals and priorities, is located at: <http://www.nsbri.org/SCIENCE-and-TECHNOLOGY/Neurobehavioral-and-Psychosocial-Factors/>.
5. *Radiation Effects* - Determining the risks of space radiation with an emphasis on acute and degenerative effects, particularly as these long-term effects of space radiation impact the cardiovascular and circulatory systems. Team information, including research goals and priorities, is located at: <http://www.nsbri.org/SCIENCE-and-TECHNOLOGY/Radiation-Effects/>.
6. *Sensorimotor Adaptation* – Examining sensory systems, their interactions and integration with the brain and motor behavior relevant for long-duration space missions. Team information, including research goals and priorities, is located at: <http://www.nsbri.org/SCIENCE-and-TECHNOLOGY/Sensorimotor-Adaptation-Team/>.

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7. *Smart Medical Systems and Technology* – Developing new methods of noninvasive medical monitoring, diagnosis, and therapy using small, low-power instrumentation for use on space missions. Of particular interest to the team presently are approaches and technologies that can non-invasively assess elevated intracranial pressure that may be associated with spaceflight induced visual impairment. Team information, including research goals and priorities, is located at: <http://www.nsbri.org/SCIENCE-and-TECHNOLOGY/Smart-Medical-Systems-and-Technology/>.

Each of the seven Science and Technology Teams manages a portfolio of complementary projects focused on a common theme. Team management and coordination is the responsibility of the Team Leader. A Team Leader, assisted by an Associate Team Leader, heads each research team. Team Leaders play a pivotal role in guiding the Institute’s Science and Technology Program and in the ultimate success of the Institute. Their expertise and “hands-on” approach to research management adds value across both projects and teams. The seven Team Leaders are guided by NASA’s Integrated Research Plan (see Section A, Part III), which is the cornerstone for developing each team’s integrated strategic research plan, which collectively constitute the keys to accomplishing the Institute’s mission.

Please contact Amanda Smith Hackler, Ed.D. (hackler@bcm.edu), Head of Career Development and Outreach at NSBRI, for information on available NASA mentors.

Currently, NSBRI supports science and technology projects at approximately 60 institutions. The Institute is governed by a Board of Directors with representation from 12 consortium institutions. **This is an open solicitation. Consortium membership is not a requirement for First Award Fellowship Program participation and non-NSBRI researchers are encouraged to apply as mentors.**

II. NSBRI Mission, Vision and Strategic Goals

Mission

The Institute leads a national effort to conduct the integrated, critical path, biomedical research necessary to support long-term human presence, development and exploration of space and enhances life on Earth by applying the resulting advances in human knowledge and technology.

Vision for NSBRI

NSBRI will continue to be a world leader in translational space biomedical research, and is committed to achieving its mission using innovative science, technology, career development, and management strategies having high impact for all stakeholders. The Institute will remain focused on developing safe and effective countermeasures and technologies that substantially reduce significant biomedical risks associated with human space travel. These discoveries not only ensure crew health, but they also improve life on Earth.

By engaging a diverse, open community of outstanding scientists, engineers, clinicians, and educators to work on peer-reviewed projects within integrated teams, and by using the resources available through leading institutions, NSBRI can achieve its mission while inspiring the next generation of space life scientists. The Institute strives to be the focal point of, and a major resource

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for NASA-sponsored space biomedical research and education in the United States. Through international cooperation and collaboration, NSBRI also aims to serve as a leading space biomedical institute among space-faring nations.

Strategic Goals

NSBRI has a published strategic plan that sets forth goals for NSBRI over the next three years. Inevitably, there will be new opportunities and challenges as the U.S. moves forward with its next generation of vehicles, as other nations increase their prominence in human space exploration, and as new advances are made in science, technology, and medicine. NSBRI has a strong track record of adapting to change and in leading new initiatives in high-priority areas.

Strategic goals are to:

- Lead a national biomedical research effort to support human space exploration.
- Enhance life on Earth through advances made in space biomedical science and technology.
- Provide a comprehensive Career Development Program in space biomedical science and technology.
- Expand partnerships in space biomedical science, technology, and career development.
- Broaden capabilities as a national science and career development resource.

For more information on NSBRI's strategic plan, please visit:

http://www.nsbri.org/default/About/NSBRI_strategic_plan.pdf

III. The Integrated Research Plan (IRP)

The Integrated Research Plan describes NASA's research activities that are intended to address the needs of human space exploration and serve Human Research Program (HRP) customers, such as flight surgeons and astronauts. The Human Research Roadmap (HRR) is the web-based tool for communicating IRP content to identify the approach and research activities planned to address risk reduction strategies for human space exploration (<http://humanresearchroadmap.nasa.gov/>).

First Award Fellowship Program applicants should carefully review these documents and should identify in their proposals the risk(s) and specific gaps, as listed in the HRP IRP, addressed by the proposed research. Applicants must also describe how their proposed line of investigation will shed light on better defining or mitigating the risk(s) and closing or partially closing specific gaps. Proposals that do not comply with this requirement will be returned without review.

IV. Explanation of Countermeasure Readiness Levels (CRLs) and Technology Readiness Levels (TRLs)

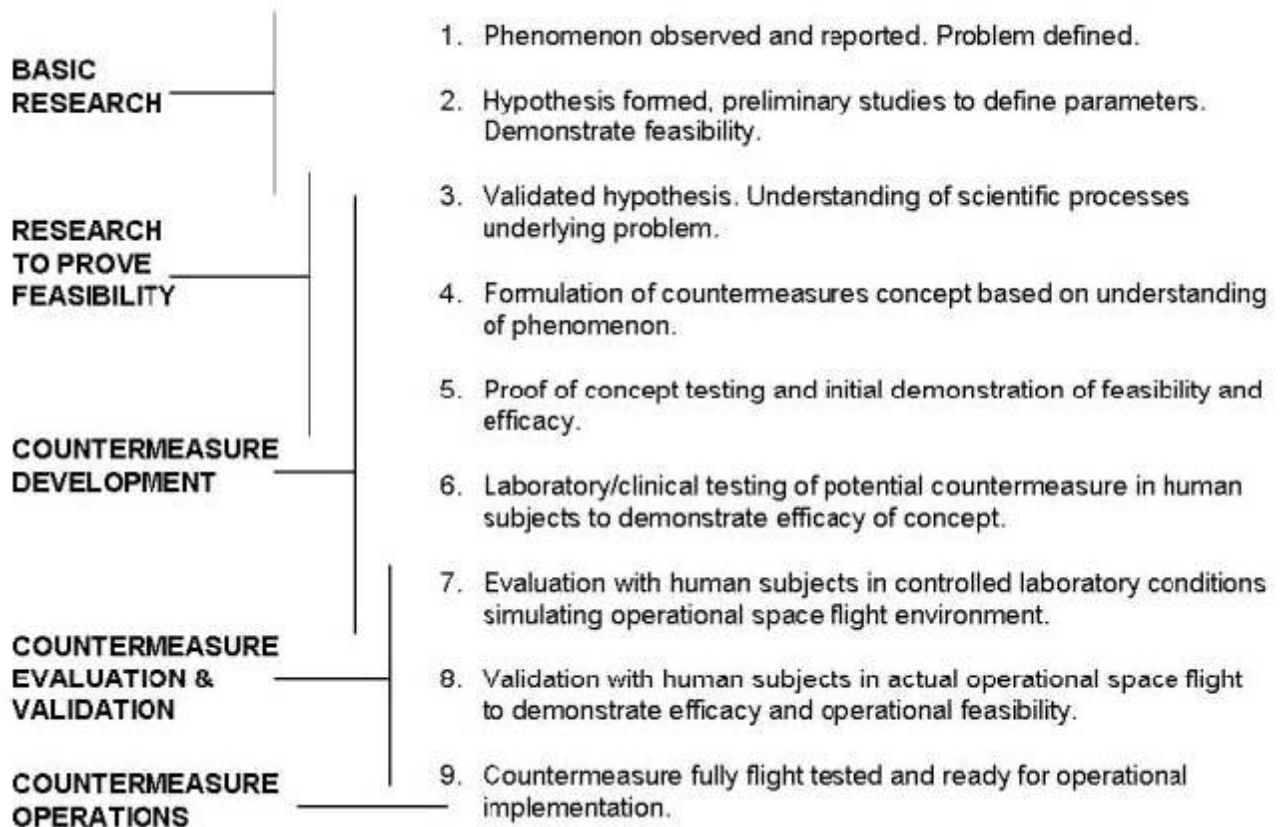
Countermeasure Readiness Level (CRL)

The use of the CRL scale allows NSBRI to:

- 1) Define, assess, and quantify the level of “countermeasure readiness;”
- 2) Determine and describe how each funded research project fits into the countermeasure development “flow;” and
- 3) Monitor progress in countermeasure development. This section describes this scale and how it is used. **The CRL of the proposed research must be identified in the application.**

Figure 1 illustrates the CRL scale. It describes an incremental research program ranging from fundamental studies that suggest potential countermeasures to applied studies that allow the systematic evaluation and validation of countermeasures ready for operational implementation. Countermeasure development usually progresses through systematic research. Research flows through various levels of countermeasure readiness.

Figure 1. Countermeasure Readiness Level Scale



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Technology Readiness Level (TRL)

The Technology Readiness Level scale is a systematic measurement system that supports assessments of the maturity of a particular technology and the consistent comparison of maturity between different types of technologies. In short, a TRL is a technology milestone (see Table 1 below). **Technology projects must identify the TRL of the proposed research.**

Table 1. Technology Readiness Level Scale

Level	Definition
TRL1	Basic principles observed
TRL2	Technology concept or application formulated
TRL3	Concept or application proven through analysis and experimentation
TRL4	Basic prototype validated in laboratory environment
TRL5	Basic prototype validated in relevant environment
TRL6	System or subsystem model or prototype demonstrated in a relevant environment
TRL7	System prototype demonstrated in a relevant environment
TRL8	Actual system completed and qualified for flight through test and demonstration
TRL9	Actual system proven through successful operation

V. Digital Resources and Bibliography

1. **National Space Biomedical Research Institute Website** (<http://www.nsbri.org/>). Contains information on the Institute's science, technology, and career development programs, including detailed team activities and project summaries for all current and completed projects.
2. **NASA Human Research Program Integrated Research Plan (HRP-IRP)**. The IRP describes the portfolio of HRP research and technology tasks. The IRP is the HRP strategic and tactical plan for research necessary to meet HRP requirements. See the Human Research Roadmap (HRR) website: <http://humanresearchroadmap.nasa.gov/>
3. **NASA Human Research Program Evidence Books**
<http://humanresearchroadmap.nasa.gov/Evidence/>
4. **Space Life Sciences Directorate Website**
<http://www.nasa.gov/centers/johnson/slsd/>
5. **Space Life Sciences Data Archive (LSDA)**. An online database containing descriptions and results of completed NASA-sponsored flight experiments. Descriptions include experiments, missions, procedures, hardware, bio-specimens collected, personnel, and documents. Bio-specimens and biofluids that are available for research purposes are described in detail. A limited number of experiments contain final reports and spreadsheet data suitable for downloading. Data from human subjects are unavailable online for reasons of privacy. Please visit: <http://lsda.jsc.nasa.gov/>

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6. **Small Clinical Trials: Issues and Challenges.** Institute of Medicine, National Academy Press, Washington, DC. <http://www.nap.edu/books/0309073332/html/>
7. **Sex and Gender: Exploring the Biological Contributions to Human Health.** NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research, 59 Fed. Reg. 14508 (2001). http://grants1.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm
8. **The Impact of Sex and Gender on Adaptation to Space: Executive Summary.** *Journal of Women's Health, Volume 23*, 941-947. DOI: 10.1089/jwh.2014.4914. <http://online.liebertpub.com/toc/jwh/23/11>
9. **The Impact of Sex and Gender on Adaptation to Space: Commentary.** *Journal of Women's Health, Volume 23*, 948-949. DOI: 10.1089/jwh.2014.1515. <http://online.liebertpub.com/toc/jwh/23/11>.
10. **Safe Passage, Astronaut Care for Exploration.** Institute of Medicine, National Academy Press, Washington, DC (2001). <http://www.nap.edu/openbook.php?isbn=0309075858>

SECTION B

Specific Details Related to the Request for Applications

NOTE: This program is open to U.S. citizens, permanent residents, or persons with pre-existing visas obtained through their sponsoring institutions that permit postdoctoral training for the project's duration. Please note that restrictions at NASA installations may impede full participation in some learning experiences by persons who have certain visa classifications. To be eligible for this program, First Award Fellows may not have more than five years (cumulative) of previous postdoctoral training as of the deadline for this proposal submission. The month and year of any previous postdoctoral experience(s) must be included in the curriculum vitae and any gaps detailed, also including the month and year. Additionally, those earning a terminal degree more than seven years ago (i.e., terminal degree conferred on or before June 5, 2008) are ineligible for this opportunity.

I. Research Opportunity – General Information

To carry out NSBRI's primary mission of identifying, designing, and developing effective countermeasures to address the biological and environmental impediments to human spaceflight, NSBRI focuses its research program on the primary needs of long-duration missions [e.g., several months on the International Space Station (ISS) or exploration-class missions outside of low Earth orbit (LEO)]. These missions pose the greatest challenge to present and future space travelers, and meeting these challenges with appropriate countermeasures lies at the core of NSBRI's responsibility.

Potential physiological changes that may occur during prolonged spaceflight include, among others, significant loss of muscle and bone mass, decreased dietary intake of nutrients, metabolic and endocrine alterations, important changes in cardiovascular function and deleterious effects on sensorimotor performance. By addressing long-term missions, increased crew safety, health, and performance will be realized for shorter-duration spaceflights.

NSBRI research is conducted in partnership with NASA using an integrated team approach. The teams focus on high-priority biomedical research problems, and investigators work together, within and between teams, to address complex risks that often require interdisciplinary expertise and resources. The value added in the integrated team approach leads to more effective outcome-driven research than what is obtainable by a single project alone.

NSBRI has an essential enabling role for NASA: providing research capabilities for the development of countermeasures. The Institute engages scientists, engineers, and clinicians and uses institutional resources to form a biomedical research community. Countermeasures research conducted by NSBRI's research community is integrated with the engineering and operational expertise of NASA to effectively manage health risks for long-duration human spaceflight.

The CRL and/or TRL that will result from the funding and conduct of the proposed research must be identified in the proposal. For further information, refer to Section A, Part IV.

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II. Award Information

Selected proposals are expected to be funded for one year. First Award Fellows are required to allocate 100% of their efforts towards fulfilling all requirements associated with this opportunity. The assumed start date will be October 1, 2015. The fellowship will conclude on September 30, 2016. This date is somewhat flexible, however, and will be negotiated with each selected First Award Fellow. The First Award Fellowship will be funded as a stipend of \$43,340 for the first year. An additional allowance for health insurance will be included. Additional funding will be provided for travel to a mandatory annual NSBRI/NASA Investigators' Workshop, a research team meeting, and a scientific meeting of the First Award Fellow's choice.

First Award Fellows will also be required to attend a 4-5 day NSBRI Summer Bioastronautics Institute at the Consolidated Research Facility (CRF) in Houston, Texas organized by the NSBRI Career Development and Outreach Team.

The mechanism of support will be an NSBRI cooperative sub-agreement with funds provided by NASA to NSBRI through a cooperative agreement (Cooperative Agreement NCC 9-58) with NASA Johnson Space Center.

III. Eligibility

A. Eligibility of Applicants

Scientists or physician-scientists who hold any of the following degrees are eligible: Ph.D., M.D., M.D./Ph.D., D.Sc., Sc.D., D.V.M., D.O., or equivalent. Applicants must have completed the clinical portion of the training program, if applicable to their field, by the time of award activation. **Applicants that anticipate earning a terminal degree (Ph.D., M.D., M.D./Ph.D., D.Sc., Sc.D., D.V.M., D.O., or equivalent) by the end of the 2015 calendar year are eligible to participate in this opportunity.**

Research proposals will be accepted from all categories of organizations, public and private, as well as from for-profit and non-profit entities, such as universities, colleges, hospitals, laboratories, companies, units of state, and local governments and eligible agencies of the federal government. In most cases, only approved applications from U.S. institutions will be selected for funding. First Award Fellowship Program applicants 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 Request for Applications. **Present or prior support by NASA or NSBRI of research or training in any institution or for any investigator is neither a pre-requisite to submission of an application nor a factor in the selection process. Non-NSBRI researchers are encouraged to apply as Mentors.**

B. Additional Guidelines Applicable to Foreign Applicants

The program is open to U.S. citizens, permanent residents, or persons with pre-existing visas

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obtained through their sponsoring institutions that permit postdoctoral training for the project's duration. Please note that restrictions at NASA installations may impede full participation in some learning experiences by persons who have certain visa classifications. All proposals must be in English and comply with all other submission requirements stated in the NSBRI-RFA.

IV. Application Procedures for the NSBRI First Award Fellowship Program

A. Source of Application Materials

All information needed to submit an electronic proposal in response to this solicitation is contained in this RFA and in a companion document entitled "2013 NRA and CAN Proposers' Guidebook" that is located at: <http://www.hq.nasa.gov/office/procurement/nraguidebook/>

In cases where the Guidebook for Proposers and this RFA conflict, the RFA language shall take precedence.

Proposal submission questions will be answered and published in a Frequently Asked Questions (FAQs) document. This FAQ will be posted on the NSPIRES solicitation download site alongside this RFA, and will be updated periodically between submission release and the proposal due date.

B. Content and Form of Proposal Submission

1. NSPIRES Proposal Data System

a) NSPIRES Registration

This RFA 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) 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 below) must be registered in NSPIRES and that such individuals must perform this registration themselves; that is, no one may register a second party, even the Mentor of a proposal in which that person is committed to participate. This data site is secure, and all information entered is strictly for NSBRI use only. In NSPIRES, the Mentor is identified as the Principal Investigator (PI) and the Trainee is identified as the First Award Fellow.

Every organization that intends to submit a proposal in response to this RFA, including educational institutions, industry, non-profit institutions, NASA Centers, and other U.S. Government agencies, **must be registered in NSPIRES prior to submitting a proposal.** Such registration must be performed by an organization's electronic business point-of-contact (EBPOC) identified in the Federal Government's System for Award Management (SAM) [www.sam.gov].

b) Electronic Submission

All proposers are required to use NSPIRES. Any proposal not submitted through the NSPIRES portal and sent directly to NSBRI by email, fax, or other means will be returned without review. NSBRI First Award Fellowship Program proposals must be submitted electronically

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by one of the officials at the Mentor's (PI) organization who is authorized to make such a submission. It is strongly recommended that the First Award Fellow work closely with his/her Mentor 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 date and time.

NSPIRES accepts fully electronic proposals through a combination of data-based information (e.g., the electronic *Cover Page* and its associated forms) and an uploaded PDF file that contains the body of the proposal. The NSPIRES system 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. Note that a failed element check will not preclude submission, but rather it will serve as a warning that a proposal may be incomplete. Proposers are particularly encouraged to begin their submission process early.

Requests for assistance in accessing and/or using NSPIRES may be directed by email to nspires-help@nasaprs.com or by telephone to (202) 479-9376, Monday through Friday, 8 a.m. to 6 p.m., 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>.

Before beginning an online application, the First Award Fellow must ensure that:

- 1) The organization to which the First Award Fellow is applying is registered with NSPIRES.
- 2) The Mentor (PI) is registered with NSPIRES and is affiliated with the organization to which the First Award Fellow is applying.
- 3) The Mentor (PI) knows the name of the Authorized Organizational Representative (AOR) of the organization, and the AOR is registered with NSPIRES.
- 4) The First Award Fellow is registered with NSPIRES.

2. Instructions for Preparation of Proposals

The NSPIRES system will guide proposers through submission of all required proposal information. Please refer to the online NSPIRES tutorials at <http://nspires.nasaprs.com/tutorials/index.html> for help.

Proposals must be prepared by the First Award Fellow in conjunction with their Mentor. Proposals will be submitted by the Mentor (PI) and an official from the Mentor's organization after the Mentor (PI) has released the prepared proposal to the Authorized Organizational Representative (AOR). It is strongly recommended that the First Award Fellow work closely with the Mentor to ensure the proposal is submitted by the due date and time listed in this solicitation. Proposals should be written in their entirety by the Fellow, with the exception of the Mentor Statement. However, Mentors are encouraged to provide feedback and guidance particularly in regards to crafting and refining the specific aims and hypotheses of the proposed scientific research. **Proposals will not be accepted after the listed deadline. Only the Mentor can initiate the creation of a new proposal and assign the First Award Fellow as a team member with editing privileges.** The First Award Fellow will then be able to access and create the proposal application.

Please note that the Proposal Summary, Business Data, Program Specific Data, and Proposal Team are required Cover Page Elements for a proposal. A budget is not required for this

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solicitation, and the budget forms do not need to be completed. The proposal summary should be between 100-300 words and written for the lay reader.

To ensure proper proposal transmission, please provide only one PDF attachment upload ordered as follows:

1. *Mentor Statement (See Section B, IV.B.2.a)*
2. *Three Letters of Recommendation (See Section B, IV.B.2.b)*
3. *Biographical Sketches for the Mentor and First Award Fellow (See Section B, IV.B.2.c)*
4. *Facilities and Equipment (See Section C, c.6)*
5. *Research Plan (See Section B, IV.B.2.e; no longer than 12 pages)*
6. *Current Support (See Section C, c.8)*
7. *Special Matters - Animal Care or Human Subjects Certifications, if applicable (see Section B, IV.B.2.g)*
8. *Vertebrate Animal Scientific Review (VASR), if applicable (see Section B, IV.B.2.h)*
9. *References and Citations (See Section B, IV.B.2.i)*
10. *Appendices and Reprints (See Section B, IV.B.2.j)*

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 AOR to submit the proposal. 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 until these required fields are completed. 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 RFA contradicts an NSPIRES warning, the NSPIRES yellow “warning” may be ignored. Proposers should follow the RFA instructions closely to help ensure submission of a compliant proposal.

It is essential that the PDF file generated and submitted meets NASA requirements. At a minimum, it is the responsibility of the proposer to:

1. Ensure that the PDF file is unlocked and that edit permission is enabled – this is necessary to allow NSPIRES to concatenate submitted files into a single PDF document; and 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.

The NSPIRES system is limited in the character sets that can be used for filling out online forms. Please refer to the online 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.

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You are encouraged to use a stand-alone PDF converter, such as Adobe Writer, to convert your proposal document to PDF for transmission. 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.

a) Mentor Statement

The Mentor must provide a “Mentor Statement” indicating that the First Award Fellow will be fully supported by his/her laboratory if the Fellowship is granted. The statement should indicate that a structured mentoring program will be in place and will address 1) the Mentor’s ability to cover the cost of all research to be performed by the First Award Fellow including animals, reagents and any unique support and/or required expertise beyond that of the Mentor’s laboratory (i.e., facilities, other scientific or technical expertise); 2) a plan for development of the Fellow’s career (to include research ethics, human subjects, animal use, grant preparation, effective curriculum vitae preparation, career interview skills, effective scientific writing and communication skills, networking, and mentoring skills for the future); 3) previous successful experiences in guiding the research efforts and career development of students and postdoctoral fellows; and 4) a discussion of the potential Fellow’s strengths as a researcher that will enable she/he to enjoy a successful career in space life sciences research. Although not required, the Mentor should consider providing the fellow with educational and outreach opportunities that will target K-12 teachers and non-science audiences in the community. Partnering with established outreach programs is particularly encouraged.

The Mentor Statement should be written considering the scientific and career development goals of NSBRI, especially the goal of the First Award Fellowship Program to train outstanding independent, productive investigators in space-related biomedical/biotechnological research.

With the exception of the Mentor Statement, the proposal must be written in its entirety by the First Award Fellow.

The entire Mentor Statement should not exceed four pages of single-spaced text using 12-point font with 1-inch margins.

b) Letters of Recommendation

The applicant should obtain three letters of reference from faculty members or professionals with detailed knowledge of the trainee’s abilities. Letters should be on institutional letterhead and must be signed.

The applicant’s proposed Mentor may not provide one of the three letters of reference since an opportunity was presented to address the applicant’s strengths in the Mentor Statement.

Applications without the three required letters will be considered incomplete, and may be returned without review.

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c) Biographical Sketches and Information

The First Award Fellowship applicant should provide a comprehensive curriculum vitae in a format of his/her choice; this document will not count toward the application page limitation, and should include the month and year of the award of the professional degree. The inclusive months and years of any previous postdoctoral experience(s) must be included in the CV and any gaps in professional training must also be detailed. If not included elsewhere, please list the previous and current teaching responsibilities and educational outreach activities of the candidate. The candidate's curriculum vitae should include professional activities during all months after the award of the terminal degree. A biographical sketch must be provided for the Mentor, and this document should not exceed four pages. NIH-style Biographical Sketch format is acceptable. See Section C, c.5 for more information.

d) Facilities and Equipment

See Section C, c.6 for more information.

e) Research Plan

The length of the Research Plan cannot exceed 12 pages. Please note that the Proposal Summary on the Cover Page is not considered part of the 12-page Research Plan. The Research Plan must be single-spaced, typewritten, English-language text, using an easily read font having no more than ~10 characters per inch (typically a 12-point font). In addition, there shall be no more than 5.5 lines per inch of text. Proposers should not use a smaller font or squeeze lines of text in order to gain more text per page as it makes the evaluation process difficult. Pages should have at least 1-inch (2.5 cm) margins on all sides. Fonts must be embedded.

Referenced figures must be included in the 12 pages of the project description; however, figure captions can use a 10-point font. The figures and legends should be of a size that is easily discernible to the reviewer. The proposal should contain sufficient detail to enable reviewers to make informed judgments about the overall scientific merit of the proposed research and about the probability that the First Award Fellow will be able to accomplish the stated objectives with the resources available and within the one year timeframe of the fellowship. The proposed research should directly benefit the career path of the potential First Award Fellow and allow the potential fellow to develop an independent research path. The hypotheses and specific aims of the proposed research must be clearly stated. **Research Plans that exceed the 12-page limit will be declined without review.** Literature cited and other proposal sections are not considered part of the 12-page limit. Please note that reviewers are not required to consider information presented as appendices or to view and/or consider web links in their evaluation of the proposal.

If this is a resubmission of a previously proposed project, the proposal must include a separate section listing specific responses to the critiques of any prior review and explain how each point has been addressed. This section should not exceed a two-page maximum and will not count against the 12-page Research Plan limit.

f) Current Support

See Section C, c.8 for more information.

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g) Special Matters (specific information on required animal or human subjects protocol approval, if applicable)

For proposals employing human subjects and/or animals, assurance of compliance with human subjects and/or animal care and use provisions is required. In addition, the application must include a statement from the applicant institution certifying that the proposed work will meet all Federal and local human subject requirements and animal care and use requirements.

NSBRI utilizes just-in-time practices for approval of the use of human subjects or animals. For proposals employing human subjects and/or animals, assurance of compliance with human subjects and/or animal care and use provisions is required within 90 days of notice of award. Please select “pending” or “approved” for the IRB/IACUC question on the Proposal Cover Page. If the IRB/IACUC certification is already approved at proposal submission, attach a copy of the certification as part of the proposal upload and select “approved.” Otherwise, select “pending.”

After award, a statement must be provided to NSBRI from the applicant institution that identifies the selected proposal by name and 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).

NSBRI will require current IRB or IACUC certification prior to each year’s award, including commencement of the first year of funding.

Policies for the protection of human subjects in NASA-sponsored research are described in the NASA Policy Directive (NPD) 7100.8E “Protection of Human Research Subjects (Revalidated with admin. Changes 12/18/2012)”

<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 (Care and Use of Animals in the Conduct of NASA Activities)*:
<http://law.justia.com/cfr/title14/14-5.0.1.1.22.html>

Additional Requirements for Research Employing Human Subjects and/or Animals

h) Vertebrate Animal Scientific Review (VASR), if applicable

Responses to this solicitation proposing experiments that require vertebrate animals must address the five points outlined in Section D. 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 12-page Research Plan. A sample VASR is provided in Section D.

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i) References, Citations, and Web Links

References cited are not considered part of the 12-page Research Plan. Reviewers are not, however, required to consider web links in their evaluation of the proposal.

j) Appendices and Reprints

If included, reprints and appendices do not count toward the Research Plan page limit and are to be included following all other sections of the proposal. **However, reviewers are not required to consider information presented in reprints or as appendices.**

C. Submission Dates

Solicitation NSBRI-RFA Identifier: NSBRI-RFA-15-01

Required: Electronic application using NASA's NSPIRES System (See Section B, Part IV for details)

Proposals Due: June 5, 2015, 5:00 p.m. ET

Selection Announcement: Fall 2015

Funding Begins: Approximately 30-90 days following notification of selection

Selecting Individual: Director, National Space Biomedical Research Institute

V. Review and Selection Process

Upon receipt, applications will be reviewed for compliance with the requirements of this Request for Applications. This includes the following:

1. Submission of complete applications as specified in this RFA.
2. Submission of all other appropriate forms, letters, and institutional and Mentor electronic signatures as required by this NSBRI-RFA and NSPIRES.

Note: Non-compliant applications will be withdrawn from the review process and returned without further review.

Compliant applications submitted in response to this NSBRI-RFA will undergo an intrinsic scientific and technical merit review by an objective, external peer-review committee, namely the First Award Fellowship Committee, which has been established by NSBRI. All committee members are eminent scientists, familiar with space biomedical/biotechnological research, that have been selected by NSBRI.

Criteria for Evaluation of Applications

Applications will be evaluated by the NSBRI First Award Fellowship Committee, on the basis of three criteria: (i) scientific merit and programmatic relevance of the proposal and the probability that the stated research objectives will be accomplished with the resources available (40%); (ii) training environment and mentoring plan (40%); and (iii) research, teaching, and educational outreach background and qualifications of the candidate (20%). Final selections for funding of proposals will be made by the NSBRI Director. Applicants are encouraged to review detailed project summaries for current and completed NSBRI research projects at <http://www.nsbri.org>. The technical summaries appear in the "Science and Technology Research Areas" section.

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Development of a Selection Recommendation

A selection recommendation will be developed based on the criteria as described above. **Deficiencies in any of these three criteria may prevent selection of an application.** The development of selection recommendations is the responsibility of the NSBRI First Award Fellowship Committee. Final selections for funding of proposals will be made by the NSBRI Director. Only grants will be awarded as a result of this NSBRI-RFA.

VI. Travel and Reporting Requirements

Travel Requirements

Annually, First Award Fellows selected in response to the NSBRI-RFA will be expected to attend the following meetings: a mandatory meeting of First Award Fellows at the annual NSBRI/NASA Human Research Program Investigators' Workshop in the Houston/Galveston area, the appropriate NSBRI research team meeting, and a scientific meeting of the First Award Fellow's choice. In the summer of 2016, the First Award Fellow will also be required to attend a 4-5 day NSBRI Summer Bioastronautics Institute at the Consolidated Research Facility in Houston, Texas organized by the NSBRI Career Development and Outreach Team. Funding, as available, will be provided to cover the costs associated with these meetings.

Peer-Reviewed Publications, Poster Presentations and Abstracts

It is expected that results from funded research will be published in peer-reviewed journals as the work is completed. **Published papers, as well as posters and abstracts, must acknowledge NSBRI support** by inclusion of the statement, "This work is supported by the National Space Biomedical Research Institute through NCC 9-58."

Final Report

A final report is required which will address the entire scope of the project and link the research to IRP risks. The report will also include peer-reviewed publications and intellectual property disclosures resulting from the NSBRI-supported work. This report must be submitted to NSBRI within 60 days after the end of the fellowship. First Award Fellows will also be requested and required to deliver a final project presentation to NSBRI scientific leadership (including Team Leadership), as well as NASA stakeholders within 90 days following submission of their final Annual Progress Reports.

Career Tracking

To assess the impact of First Award Fellowships on the career advancement of young scientists and to provide an active network of investigators in space biomedical research, NSBRI will request brief, periodic updates on the career status and accomplishments of NSBRI First Award Fellows throughout their careers. Requests for updates will be facilitated mainly by the NSBRI Head of Career Development and Outreach and will include, but not be limited to, interviews or a requested current curriculum vitae from participants.

Formative Assessment

NSBRI will be actively engaged in the on-going assessment of the First Award Fellowship Program to assure that the program has been implemented as planned and to make program enhancements. Formative assessments during the funding period will include, but not be limited to, institutional site visits to assess research facilities and accomplishments, and to interview the First Award Fellows and

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Mentors. This formative assessment will be facilitated mainly by the NSBRI Head of Career Development and Outreach. It is expected that both the First Award Fellow and the Mentor cooperate with these assessments.

SECTION C

**INSTRUCTIONS FOR RESPONDING TO NSBRI
REQUESTS FOR APPLICATIONS**

(a) General.

- 1) Proposals received in response to an NSBRI Request for Applications (NSBRI-RFA) will be used only for evaluation purposes. NSBRI does not allow a proposal, the contents of which are not available without restriction from another source, or any unique ideas submitted in response to an NSBRI-RFA to be used as the basis of a solicitation nor in negotiation with other organizations, nor is a pre-award synopsis published for individual proposals.
- 2) A solicited proposal that results in an NSBRI award becomes part of the record of that transaction and may be available to the public on specific request; however, information or material that NSBRI and the awardee mutually agree to be of a privileged nature will be held in confidence to the extent permitted by law, including the Freedom of Information Act.
- 3) NSBRI-RFAs contain programmatic information and certain requirements which apply only to proposals prepared in response to that particular announcement. These instructions contain the general proposal preparation information which applies to responses to all NSBRI-RFAs.
- 4) A cooperative sub-agreement will be used to accomplish an effort funded in response to an NSBRI-RFA. NSBRI will coordinate the implementation of the award instrument. Contracts resulting from NSBRI-RFAs are subject to the Federal Acquisition Regulation (FAR) and the NASA FAR Supplement. Any resultant grants or cooperative agreements will be awarded and administered in accordance with the NASA Grant and Cooperative Agreement Handbook (NPG 5800.1).
- 5) NSBRI has a mandatory format for responses to NSBRI-RFAs. All applications must be submitted utilizing the NSPIRES System. For further information, please see Section B, Part IV.B.
- 6) To be considered for award, a submission must, at a minimum, present a specific project within the research areas delineated by the NSBRI-RFA; contain sufficient technical information to permit a meaningful evaluation; be signed by an official authorized to legally bind the submitting organization; not merely offer to perform standard services or to just provide computer facilities or services; and not significantly duplicate a more specific current or pending NASA or NSBRI solicitation.

(b) NSBRI-RFA-Specific Items. Several proposal submission items appear in the NSBRI-RFA itself: the unique NSBRI-RFA identifier; dates for proposal deadlines; instructions for submission of proposals; electronic submission format; and sources for more information. Items included in these instructions may be supplemented by the NSBRI-RFA.

(c) The following information is needed to permit consideration in an objective manner. NSBRI RFAs will generally specify topics for which additional information or greater detail is desirable.

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(1) Proposal Cover Page

- i. The legal name of the organization and specific division or campus identification if part of a larger organization;
- ii. A brief, scientifically valid project title intelligible to a scientifically literate reader and suitable for use in the public press;
- iii. Type of organization: e.g., profit, non-profit, small business, woman-owned, socially and economically disadvantaged, etc.;
- iv. Name and telephone number of the Mentor (PI) and business personnel who may be contacted during evaluation or negotiation;
- v. Identification of the NSBRI-RFA, by number and title, to which the proposer is responding;
- vi. Desired starting date, and duration of project;
- vii. Date of submission;
- viii. Signature of a responsible official or authorized representative of the organization, or any other person authorized to legally bind the organization (unless the signature appears on the proposal itself); and
- ix. Signature of a Mentor for First Award Fellowship Program applications.

- (2) Restriction on Use and Disclosure of Proposal Information.** Information contained in proposals is used for evaluation purposes only. Offerors or quoters should, in order to maximize protection of trade secrets or other information that is confidential or privileged, place the following notice at the beginning of the Research Plan (which is in addition to the specified page limits) and specify the information subject to the notice by inserting an appropriate identification in the notice. In any event, information contained in proposals will be protected to the extent permitted by law, but NSBRI assumes no liability for use and disclosure of information not made subject to the notice.

Notice

Restriction on Use and Disclosure of Proposal Information

The information (data) contained in this proposal constitutes a trade secret and/or information that is commercial or financial and confidential or privileged (“Information”). It is furnished to NSBRI in confidence with the understanding that it will not, without permission of the Offeror, be used or disclosed other than for evaluation purposes; provided, however, that in the event a contract (or other agreement) is awarded on the basis of this proposal the Government shall have the right to use and disclose this Information to the extent provided in the contract (or other agreement). This restriction does not limit the Government’s right to use or disclose this Information if obtained from another source without restriction. The obligations in this Section shall not apply with respect to any Information which:

- (a) is disclosed in a printed publication available to the public, is described in a patent anywhere in the world, is otherwise in the public domain at the time of disclosure, or becomes publicly known through no wrongful act on the part of NSBRI;
- (b) is known to NSBRI or becomes known to NSBRI through disclosure by sources other than the Offeror having the right to disclose such Information;
- (c) is disclosed pursuant to the requirement of a governmental agency or any law requiring disclosure thereof;
- (d) is generally disclosed to third parties by the Offeror without similar restriction on such

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third parties; or

(e) is approved for release by written authorization of the Offeror.

- (3) **Proposal Summary.** Include a concise 100-300 word abstract describing the objectives and the methods of approach and written for the lay reader.
- (4) **Project Description (Research Plan).** The main body of the proposal shall be a detailed statement of the work to be undertaken and should include objectives and expected significance; relation to the present state of knowledge; and relation to previous work performed on the project and to related work in progress elsewhere. The project description (Research Plan) cannot exceed 12, 8½- by 11-inch pages using a standard 12-point font and 1-inch margins. The statement should outline the plan of work, including the broad design of experiments to be undertaken, and a description of experimental methods and procedures. Mentors should not contribute to the narrative of the project description, other than to review this section and provide editorial comments. The project description should also address the evaluation factors in these instructions and any specific factors in the NSBRI-RFA. Any substantial collaboration with individuals other than the Mentor, or use of consultants, should be described. Subcontracting significant portions of a research project is discouraged.
- (5) **Personnel.** The Mentor is responsible for supervision of the work. Short biographical sketches for both the First Award Fellow and the Mentor, a list of principal publications and any exceptional qualifications should be included. Omit social security numbers and other personal items which do not merit consideration in evaluation of the proposal.
- (6) **Facilities and Equipment.** Describe available facilities and major items of equipment relevant to the proposed project, and any additional major equipment that will be required. Identify any Government-owned facilities, industrial plant equipment, or special tools that are proposed for use. Include evidence of the availability of facilities and equipment, and the cognizant Government points of contact.
- (7) **Security.** Proposals should not contain security-classified material. If the research requires access to, or may generate, security-classified information, the submitter will be required to comply with Government security regulations.
- (8) **Current Support.** For other current projects being conducted by the First Award Fellow and Mentor, provide title of project, sponsoring agency, percent effort, and project starting and ending dates. Please include a brief description of any potential overlap with the work described in this NSBRI First Award Fellowship Program application.
- (9) **Special Matters.** Include any required statements of environmental impact of the research, human subject or animal care provisions, conflicts of interest, or such other topics as may be required by the nature of the effort and current statutes, executive orders, or other current Government-wide guidelines.
- (10) **Length.** Unless otherwise specified in the NSBRI-RFA, effort should be made to keep proposals as brief as possible, concentrating on substantive material. Necessary detailed information, such as reprints, should be included as attachments.

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(11) Withdrawal. Applications may be withdrawn at any time before award. Applicants are requested to notify NSBRI if the proposal is funded by another organization or of other changed circumstances which dictate termination of evaluation.

(12) Selection for Award.

(12.1) When an application is not selected for award, the applicant will be notified. NSBRI will explain generally why the application was not selected. Applicants desiring additional information may contact the selection official who will arrange a debriefing.

(12.2) When an application is selected for award, negotiation and award will be handled by NSBRI in the funding installation. The application is used as the basis for negotiation. The contracting officer may request certain business data and may forward a model award instrument and other information pertinent to negotiation.

(13) Cancellation of NSBRI-RFA. NSBRI reserves the right to make no awards under this NSBRI-RFA and to cancel this NSBRI-RFA. NSBRI assumes no liability for canceling the NSBRI-RFA or for anyone's failure to receive actual notice of cancellation.

SECTION D
Vertebrate Animal Scientific Review (VASR)

A. Vertebrate Animal Scientific Review (VASR)

If vertebrate animals are to be used, the following five points must be addressed completely by applicants in the VASR worksheet of their proposal:

- 1) Detailed description of the proposed use of animals, including species, strains, ages, sex, and number to be used.
- 2) Justification of the use of animals, choice of species and numbers to be used (it is strongly suggested that power calculations be included to justify numbers of animals), and proposer's assessment of potential benefits and knowledge to be gained.
- 3) Information on the veterinary care of the animals.
- 4) Description of procedures for ensuring discomfort, distress, pain, and injury are minimized.
- 5) Method of euthanasia and the reasons for its selection.

Each of the five points must be addressed, for all performance sites, in the VASR worksheet. The VASR worksheet will be reviewed by the First Award Fellowship Committee and the proposal coded as either "No Vertebrate Animals," "No Concerns/Acceptable," or "Concerns/Unacceptable." If coded as "Concerns/Unacceptable," NSBRI staff will work with the applicant to resolve concerns prior to award. Coding of the proposal as "No Concerns/Acceptable" or "No Vertebrate Animals" is required prior to award.

In order to be coded as "No Vertebrate Animals," the vertebrate tissue used in the study must be obtained from other sources (e.g., tissue repository, animals euthanized for an unrelated purpose). The source of the tissue should be included in the VASR to validate the coding as "No Vertebrate Animals" used. If vertebrate tissues are obtained through euthanasia for tissue harvest, the proposed research is coded as "Use of Live Vertebrate Animals." The generation of custom antibodies is coded as "Use of Live Vertebrate Animals."

A "performance site(s)" is defined as the institutions where procedures with animals will be performed. If the applicant institution is not the site where animal work will be performed, the performance site must be identified. If there is more than one performance site, the description of animal care and use at each site must be included and must address the five points.

Applicants should be aware that NSBRI may release information contained in specific funded proposals pursuant to Freedom of Information Act requests.

B. Detailed Instructions for Preparation of the VASR

These instructions are to assist applicants in preparing their VASR information.

Preparation of the VASR Worksheet:

Typically, all of the required elements for the VASR can be addressed within 1-2 pages.

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Point 1 - Description of animals and how they will be used

A concise, complete description of the proposed procedures must be included in the VASR. While additional details may be included in the Research Strategy, a coherent, albeit brief, description of the proposed use of the animals must be provided within the VASR. The description must include sufficient detail to allow evaluation of the procedures. Examples of the types of procedures that should be described include blood collection, surgical procedures, administration of substances, tumor induction, and post-irradiation procedures. In describing the animals, investigators must provide the following information for each species and/or strain to be used:

- Species
- Strain
- Ages
- Sex
- Number of animals to be used (power calculations are suggested)

Point 2 - Justifications for use of animals

Investigators must justify the use of animals in the proposed research. The justification must indicate why alternatives to animals (e.g., computer models, cell culture) cannot be used and should indicate the potential benefits and knowledge to be gained. In addressing this point, researchers are encouraged to consider means to replace, reduce, and refine the use of animals. Rationale for the choice of species must be provided. The rationale should indicate the advantages of the species chosen and why alternative species are not appropriate. If less highly evolved or simpler animal models are available, justification must be provided for using more advanced species. For example, the use of non-human primates (NHP), dogs or cats, should be thoroughly justified. If NHP species are to be used, a comparison to other NHP species may be appropriate. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and power calculations for the number of animals used.

Estimates for the number of animals to be used should be as accurate as possible. Justification for the number of animals to be used should include considerations of animal availability, experimental success rate, inclusion of control groups, and requirements for statistical significance; cite power calculations where appropriate.

Point 3 - Veterinary care

Descriptions of veterinary care should indicate the availability of veterinarians or veterinary technicians. For example, the VASR might indicate the number of veterinarians and veterinary technicians associated with the applicant institution, and their proximity to the performance site(s).

The frequency with which veterinary staff observe or monitor animals should be stated. If survival surgeries are proposed, veterinary involvement or post-surgical monitoring should be described. For example, if animal use involves invasive approaches that might result in discomfort, distress, or pain, the investigator should indicate if or when veterinary care is necessary. The indicators for veterinary intervention to alleviate discomfort, distress, or pain should be described. The ways in which veterinary staff may intervene should be described.

Point 4 - Provisions to minimize discomfort, distress, pain, and injury

Procedures or circumstances that may result in more than momentary discomfort, distress, pain, or injury should be identified. Methods to alleviate discomfort, distress or pain should be described. If

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pharmacological agents are used, the agent(s) should be specified by name or class. Any additional (e.g., non-pharmaceutical) means to avoid discomfort, distress, pain, or injury should be described briefly. The manner, circumstances and duration of all post-surgical provisions and care should be described. If special housing is necessary following surgery or manipulations, the VASR should describe these provisions and the duration and type of monitoring provided. If procedures (e.g., pharmacological or surgical) might lead to severe discomfort, distress, pain, or injury, indicators for humane endpoints and euthanasia (e.g., severe infection, respiratory distress, failure to eat, tumor size) should be described. All of these issues are particularly important for survival surgeries. If multiple surgeries are proposed, these must be well justified and provisions to avoid any potential complications must be described. Describe how restraining devices will be used, if applicable.

Point 5 - Euthanasia

The method(s) of euthanasia must be described and must comply with the *AVMA Guidelines on Euthanasia*. If the method(s) do not comply with AVMA recommendations, the rationale and scientific justification for use of the method(s) must be provided. The indicators for euthanasia (i.e., termination of experiment or humane endpoints) should be stated. It is not sufficient to state simply that humane methods consistent with the recommendations of the *AVMA Guidelines on Euthanasia* or the Institutional Animal Care and Use Committee (IACUC) will be used.

References

Guidance in this document is based on NASA and PHS Policy, and federal requirements. The NASA and PHS Policy incorporate the standards in the *Guide for the Care and Use of Laboratory Animals* and require that euthanasia be conducted according to the *AVMA Guidelines on Euthanasia*. Additional background information and references are available on the Office of Laboratory Animal Welfare website (<http://grants.nih.gov/grants/olaw/olaw.htm>).

NASA Policy and Requirements

<http://quest.nasa.gov/neuron/events/habitat/NASAprin.html>

PHS Policy

<http://grants.nih.gov/grants/olaw/references/phspol.htm>

Guide for the Care and Use of Laboratory Animals

http://www.nap.edu/openbook.php?record_id=5140

AVMA Guidelines on Euthanasia

http://www.avma.org/issues/animal_welfare/euthanasia.pdf

C. Worksheet to Assist in Addressing the Required Five Points of the VASR

Performance site(s):

The five points must be addressed for all performance sites.

___ If the applicant's institution is not where animal work will be performed, are all collaborative performance site(s) identified?

___ If more than one performance site is planned, are descriptions of animal care and use for each site

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provided?

Point 1 - Describe the animals and their proposed use; address the following for all species to be used:

- Species
- Strains
- Ages
- Sex
- Number of animals to be used
- A concise, but complete, description of proposed procedures (i.e., sufficient information for evaluation)

Point 2 - Provide justifications for:

- The use of animals
- Choice of species
- Number of animals to be used (cite power calculations, if appropriate)

Point 3 - Provide a general description of veterinary care, including veterinary support that is specifically relevant to the proposed procedures. Indicate the following:

- A brief account of veterinary staff and their availability
- The regular schedule of monitoring of animals by veterinary staff
- Any additional monitoring and veterinary support that may be required to ensure humane care, if relevant to the procedures proposed (e.g., post-surgical)
- Indicators for veterinary intervention to alleviate discomfort, distress, or pain, if relevant

Point 4 - Describe procedures to minimize discomfort, distress, pain, and injury. Indicate the following:

- Circumstances relevant to the proposed work, when animals may experience discomfort, distress, pain, or injury
- Procedures to alleviate discomfort, distress, pain, or injury
- Identify (by name or class) any tranquilizers, analgesics, anesthetics, and other treatments (e.g., antibiotics) and describe their use
- Provisions for special care or housing that may be necessary after experimental procedures
- Plans for post-surgical care, if survival surgeries are proposed
- Indicators for humane experimental endpoints, if relevant
- Describe the use of restraint devices, if relevant

Point 5 - Describe methods of euthanasia:

- Describe the method(s) of euthanasia and rationale for selection of method(s)
- Indicate if the method is consistent with AVMA Guidelines on Euthanasia
- Provide a scientific justification for the choice of method if not AVMA recommended

D. Example of a complete VASR

(This VASR worksheet has been modified from the original. It addresses all five points concisely.)

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Vertebrate Animals

Aims 1-3 will be addressed *in vitro*; Aim 4 will be addressed using a mouse model of ocular infection.

- 1) Female Balb/c mice will be used to determine if virions treated with enzyme can cause viral keratitis, and to test the *in vivo* efficacy of the test articles. The studies will require 700 mice, 4 to 6 weeks old. Based on prior experience, 70 groups, each including 10 mice will be required over five years to achieve adequate statistical power. Ocular infection is accomplished by scratching the cornea of anesthetized mice with a sterile needle and exposing the scarred portion of the cornea to inoculum. Test articles are applied directly to the scarified cornea as liquid or cream. Following inoculation and recovery, mice are monitored for 30 days. With the mice under anesthesia, the eyes will be examined at intervals, microscopically, and are flushed with medium containing 2% serum to determine viral titers. Thirty days post-infection, with the mice under deep anesthesia, the trigeminal ganglia are removed aseptically for viral assay, followed immediately by euthanasia.
- 2) The proposal is to study mechanisms for the prevention of ocular disease caused by viral infections, a leading cause of blindness in the U.S. Mice are needed for these experiments because no alternative *in vitro* model incorporates all elements of the mammalian ocular immune system; too little is known about this system for the development of computer simulations. Mice are a well-accepted model for studying viral keratitis, assessing the virulence of viral strains and testing the efficacy of antivirals. Mice provide several advantages: a) The murine ocular immune system is similar enough to that of humans to allow extrapolation of the results; b) Their small size allows the use of smaller amounts of drugs for testing; c) The entire mouse genome is known and easily manipulated genetically, allowing extension of the work in future genetic studies. Female mice will be used due to compatibility issues. Balb/c mice will be used because they have intermediate resistance to infection. ABC-4 knockout and ABC-4 test-strains will be used. For the enzyme study, we will use 4 treatment groups: enzyme-1, enzyme-2, enzyme-3, and mock treated virus. We will also use different amounts of inoculum for each condition allowing a more accurate calculation as to the effect of the digestions on infectivity. For the test-article peptide study, we will use two formulations (one aqueous and one hydrophobic), test four different concentrations and also vary the treatment protocol. Two groups will receive a single dose of drug in each of the two formulations prior to the addition of virus to assess prophylactic activity. These groups will not receive any additional enzyme treatments. Two groups will be infected with virus and beginning 4 h post-infection, we will treat with each formulation and concentration four times daily for seven days.
- 3) All mice are housed in the Animal Resources Center of the University. Animal housing rooms are under temperature and humidity control. The mice will not be subjected to water or food restrictions, and bedding material is placed in each cage. The facility is staffed by four full time veterinarians and six veterinary technicians; the veterinary staff is on-site and a clinical veterinarian is available at all times. Animal care staff conducts routine husbandry procedures (e.g., cage cleaning, feeding, and watering) and checks animals daily to assess their condition. Laboratory staff monitors mice when treatments are given, disease is scored, or samples are collected for titring. The veterinary staff monitors mice in their home cages weekly. If animals exhibit any indication of infection or distress, the veterinary staff confers with laboratory personnel to recommend appropriate antibiotics, analgesics, or other

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pharmaceuticals. The veterinary staff may intervene or recommend euthanasia based on animal welfare concerns.

- 4) Mice will be anesthetized with isoflurane (3-5%) during the infection process, when treatments are administered and titer samples are collected. This eliminates the need for restraint devices and topical anesthetics that would interfere with the infection and disease process. For post-procedural pain relief, we will administer buprenorphine twice daily for the duration of the experiments (i.e., approximately two weeks post-inoculation). Death is not an endpoint for the studies; the Balb/c strain was chosen because of its resiliency and resistance to this particular virus. Our goal is to avoid severe infections leading to death. Though unlikely, if an animal reacts severely, it will be euthanized, based on humane indicators (e.g., failure to groom or feed). These experiments involve no post-surgical survival animals.
- 5) All mice will be euthanized by cervical dislocation under isoflurane anesthesia. Isoflurane ensures that the mice are unconscious, while dislocation ensures quick death. This minimizes animal distress, is effective and efficient; it is consistent with the recommendations of the *AVMA Guidelines on Euthanasia*.