Human Research Program Integrated Research Plan

Human Research Program

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Human Research Program
Integrated Research Plan

Submitted By:

Original signature on file	07/31/2020
Lisa Milstead	Date
Integration Engineer	
Program Science Management Office	
Human Research Program	

Concurred By:

Original signature on file	08/06/2020
Steven H. Platts, Ph.D.	Date
Chief Scientist (Acting)	
Human Research Program	

Approved By:

Original signature on file	08/12/2020
William H. Paloski, Ph.D.	Date
Program Director	
Human Research Program	

DOCUMENT CHANGE/ REVISION LOG

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Change/ Revision	Date	Description of Change	Pages Affected
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Revision B	6/24/2010	Revision B approved by HRPCB per SLSDCR-HRPCB-10-009-R2	All
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Revision E	7/29/2013	Revision E approved by HRPCB per SLSDCR-HRPCB-13-007 and SLSDCR-HRPCB-13-008	All
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Revision I, PCN-1	11/29/2017	Revision I, Page Change Notice-1, approved by HRPCB per SA-00459	4.3.12, Appendix A, HRR Content, and Appendix C, List of Acronyms
Revision I, PCN-2	3/27/2018	Revision I, Page Change Notice-2, approved by HRPCB per SA-00678	Appendix A, HRR Content
Revision J	7/30/2018	Revision J, approved by HRPCB per SA-00943	All
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1 INTRODUCTION

Crew health and performance are critical to successful human exploration beyond low Earth orbit (LEO). The Human Research Program (HRP) is essential to enabling extended periods of space exploration through research and technology development (R&TD) activities that are aimed to mitigate risks to human health and performance. Human spaceflight risks include physiological and performance effects from hazards such as radiation, altered gravity, and hostile environments, as well as unique challenges in medical support, human factors, and behavioral health support. The HRP delivers human health and performance countermeasures, knowledge, technologies and tools to enable safe, reliable, and productive human space exploration. Without HRP results, National Aeronautics and Space Administration (NASA) will face unknown and unacceptable risks for mission success and post-mission crew health.

1.1 Purpose

The Integrated Research Plan (IRP) describes HRP's approach and R&TD activities intended to address the needs of human space exploration. As new knowledge is gained, the required approach to R&TD may change.

The IRP serves the following purposes for the HRP:

- provides a means to ensure that the most significant risks to human space explorers are being adequately mitigated and/or addressed;
- shows the relationship of R&TD activities to expected deliverables;
- shows the interrelationships among R&TD activities that may interact to produce deliverables that affect multiple HRP Elements, Portfolios, Projects or research disciplines;
- accommodates the uncertain outcomes of R&TD activities by including milestones that lead to potential follow-on activities;
- shows the assignments of responsibility within the program organization and, as practical, the proposed acquisition strategy;
- shows the intended use of research platforms such as the International Space Station (ISS), NASA Space Radiation Laboratory (NSRL), and various spaceflight analog environments including the Human Exploration Research Analog (HERA);
- shows the budgeted and unbudgeted R&TD activities of the HRP, but does not show <u>all</u> budgeted activities, as some of these are enabling functions, such as management, facilities, and infrastructure, and others are internal/discretionary tasks.

1.2 Scope

The IRP documents the tasks necessary to fill the gaps associated with each risk listed and details where (e.g., the ISS or a ground analog) and who (e.g., investigators within a specific HRP organization) will accomplish the task and what is being produced (e.g., risk uncertainty reduction, candidate health or performance standard, or countermeasure strategy). The IRP includes research that can be conducted with the resources available to the HRP, as well as research that would be performed if additional resources were available. The timescale of human

space exploration is envisioned to take many decades. The IRP attempts to describe a plan of research looking forward many years into the future and illustrates the Program's research plan from early beyond Earth orbit (BEO) missions through exploration missions of extended duration. The fidelity of the IRP is quite high in the near term (2020-2024), but decreases with time. The IRP will be regularly revised and updated based on exploration mission development, achievement of key milestones, and consideration of new evidence gained.

The IRP was originally baselined as HRP-47065, Human Research Program Integrated Research Plan, in 2008. In 2010, the detailed technical content (formerly Appendix A) transitioned to the Human Research Roadmap (HRR): http://humanresearchroadmap.nasa.gov/.

1.3 Responsibility and Change Authority

This document, as well as the accompanying HRR, is under Configuration Management control of the Human Research Program Control Board (HRPCB). Changes to this document will result in the issuance of change pages or a full re-issue of the document.

2 DOCUMENTS

The relationship of the HRP documents in Section 2 with the IRP is illustrated in Figure 1. A more detailed explanation of the flow depicted in Figure 1 is provided in Section 3.

2.1 Applicable Documents

The following documents of the specified revision or the latest revision if not identified, are applicable to the extent specified herein.

Document Number	Document Title
HRP-47052	Human Research Program Requirements Document (PRD)
HRP-47069	Human Research Program Unique Processes, Criteria, and Guidelines (UPCG)
Various	Evidence Reports

2.2 Reference Documents

The following documents contain supplemental information to guide the user in the application of this document. These reference documents may or may not be specifically cited within the text of the document.

Document Number	Document Title
HRP-47051	Human Research Program Plan
HRP-47053	Human Research Program Science Management Plan
NASA-STD-3001,Vol. 1 and Vol. 2	Space Flight Human-System Standards, Volume 1 Crew Health and Volume 2 Human Factors, Habitability and Environmental Health
NASA/SP-2010-3407	Human Integration Design Handbook (HIDH)

2.3 Order of Precedence

All specifications, standards, exhibits, drawings or other documents that are invoked as "applicable" in this specification are incorporated as cited. All documents that are referred to within an applicable document are considered to be for guidance and information only.

In the event of a conflict between the text of this specification and an applicable document cited herein, the text of this document takes precedence.

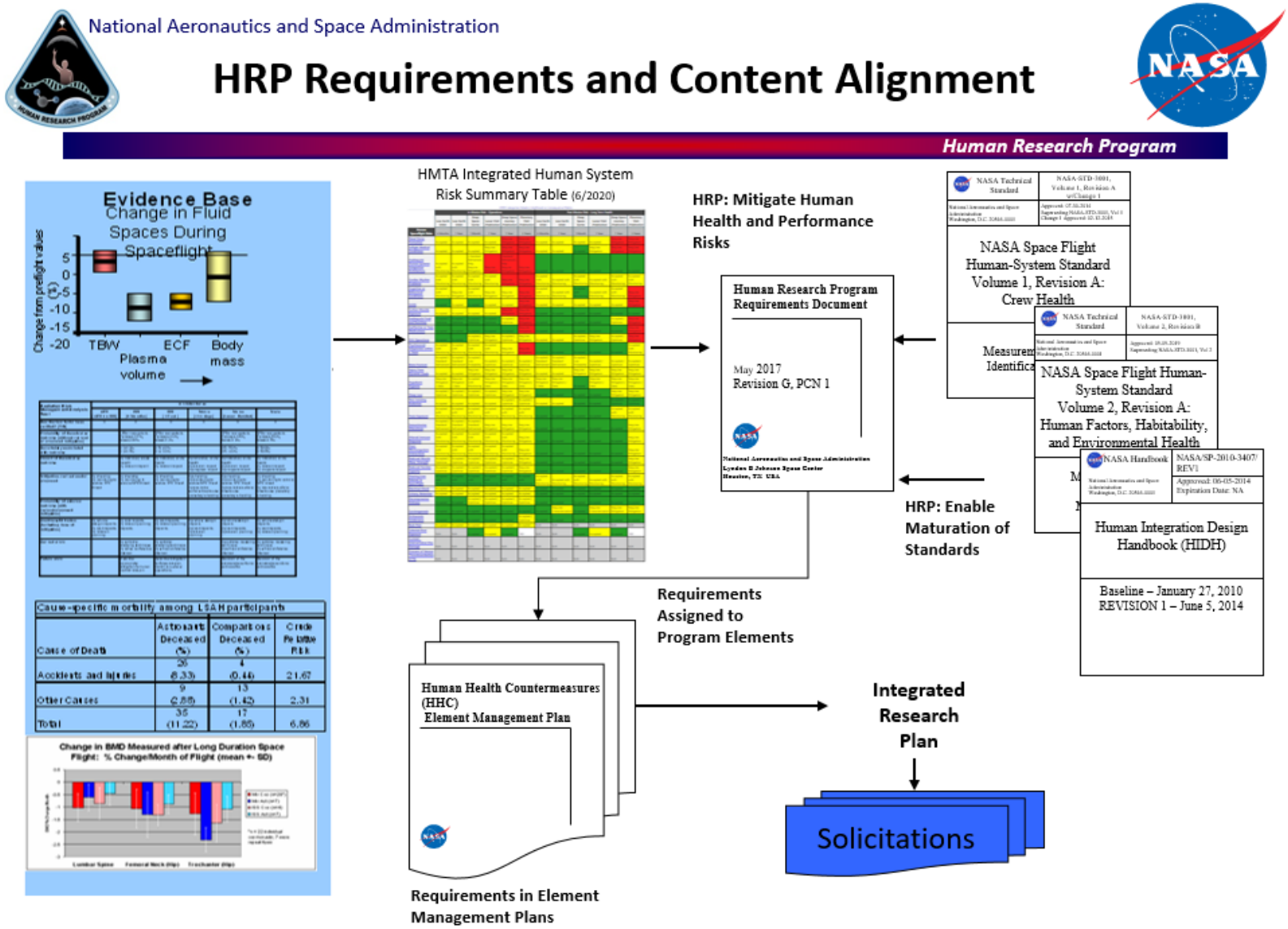


Figure 1. HRP Requirements and Content Alignment

3 CONTEXT OF THE IRP

3.1 Risk Research Portfolio

The Human Systems risks fall within the purview of the Office of the Chief Health and Medical Officer (OCHMO). The OCHMO established the Human Systems Risk Board (HSRB), chaired by the Johnson Space Center (JSC) Human System Risk Manager, to ensure a consistent, integrated process for managing human system risks that are critical to successful human exploration beyond LEO. Risks in the HRP research portfolio shall be identified by the HSRB as risks requiring research and documented as requirements in the HRP-47052, Human Research Program Requirements Document.

3.2 Program Requirements

HRP-47052 defines, documents, and allocates the requirements to each of the HRP Program Elements: Exploration Medical Capability (ExMC), Human Factors and Behavioral Performance (HFBP), Human Health Countermeasures (HHC), Research Operations and Integration (ROI) (as an implementing Element, no risks assigned), and Space Radiation (SR). These HRP requirements are derived to satisfy the exploration mission requirements from Human Exploration and Operations Mission Directorate (HEOMD) and the OCHMO as found in NASA-STD-3001, Space Flight Human-System Standards, Volume 1 Crew Health and Volume 2 Human Factors, Habitability and Environmental Health. In addition, NASA/SP-2010-3407, Human Integration Design Handbook (HIDH), was published as a compendium of human space flight history, lessons learned, and design information for a wide variety of disciplines to serve as a companion document to NASA-STD-3001, Volume 2. The HRP has two main responsibilities regarding these standards. In some cases, a NASA-STD-3001 requirement is written in generic terms to ensure its applicability to a wide range of mission environments (such as microgravity in orbit, lunar surface habitation, or transit to Mars). HRP research can serve to inform the standard, refine the requirement, and help define processes or methods (cutting edge or state of the art) to meet the requirement. Where emerging evidence or knowledge may indicate that the standards are not written in a way that captures a complete set of relevant considerations, additional research may be conducted to facilitate an update.

The requirements in the Program Requirements Document (PRD) are divided into three categories: requirements related to human system standards, requirements related to human health and performance risks, and requirements related to provision of enabling capabilities. Each Element, with the exception of ROI, incorporates its respective PRD requirements into its specific Element Management Plan. These Elements subsequently derive a research plan to address the requirements. ROI implements the requirements identified by the other HRP Elements for research and technology demonstration tasks that require the use of the ISS or ground analogs, as appropriate.

3.3 Human Research Program Architecture

The development of HRP content has been formulated around the architecture of:

3.3.1 Evidence

Reviews of the accumulated evidence from medical records, spaceflight operations and research findings are compiled into HRP Evidence Reports. These findings provide the basis for identifying the highest priority human risks in space exploration and are a record of the state of knowledge for each risk in the PRD. The Evidence Reports are available to the scientific community and general public at the following link: http://humanresearchroadmap.nasa.gov/evidence/. The Evidence Reports receive outside independent review and are updated as needed. If new evidence indicates that a risk should be retired or that a new risk should be added, the HRP will, after thorough review with the HSRB, take the appropriate action to modify the PRD and update the Evidence Reports accordingly.

3.3.2 Risks

The HSRB, chaired by the JSC Human System Risk Manager, identifies risks relevant to the Chief Health and Medical Officer (CHMO) and to the health and human performance aspects of the exploration program based on current evidence. Each risk is assigned a risk rating by the HSRB which is used as a tool to communicate to Agency management the seriousness of a risk to crew health and performance when applied to the mission architecture and/or mission characteristics defined for each Design Reference Mission (DRM). The risk ratings are maintained by the HSRB and serve as one of several inputs to determine the priority of each human risk, helping HRP Management make program decisions and allocate program resources. The HRP uses the HSRB forum to communicate updates to the risks resulting from HRP R&TD activities. The HRP utilizes the HSRB to identify risks requiring research. The PRD allocates these risks as requirements to quantify, mitigate, or monitor these human system risks to the appropriate Element within the HRP. The PRD, however, does not establish priority for the risks.

The HRP uses the IRP to describe the approach and R&TD activities intended to address the needs of human space exploration. The risks-gaps-tasks-deliverables detail in the IRP is required to ensure completeness in addressing the risks. The forecasted schedule to mitigate risks is captured in a strategy chart called the Risk Approach Plan. This chart includes a Path to Risk Reduction (PRR) bar to depict an overall timeline and significant risk milestones, along with research logic descriptions and flow chart to show the research strategy being used to improve the risk ratings.

In the past, the HRP documented some risks at a more-detailed level than the HSRB. These sub-risks were documented as standalone risks in the HRR. As part of the 2020 IRP revision (revision L), the risks documented in the HRR now align with the HSRB. Traceability

information to show the transition from the past sub-risks to the current combined risks is given on the affected risk pages in the HRR.

3.3.3 Gaps

For each risk requiring research, HRP identifies gaps in knowledge about the risk and the ability to mitigate the risk. The degree of uncertainty in understanding the likelihood, consequence and/or timeframe of a particular risk as well as its criticality to the mission(s) are the major factors that drive the priority of the research gaps listed in the IRP. Gaps should represent the critical questions that need to be answered in order to significantly reduce the risk. Gaps could change over time based on research progress, current evidence, and mission planning scenarios. In some cases, a gap can address multiple risks. During FY20 the HRP Elements completed a strategic re-planning exercise on the research plans for many of the HRP Risks in the HRR. The new strategies required significant gap updates for many of the HRP Risks. The 2020 IRP revision (revision L) includes these new gap structures. Traceability information to show the transition from the old gaps to the current gaps is given on the affected gap pages in the HRR.

3.3.4 Tasks

The IRP defines the tasks that will provide the deliverables required to fill the gaps. The HRP Elements identify specific research tasks that are targeted at better characterizing a risk or developing mitigation capabilities to reduce the risk to an acceptable level. A major criterion for selection of a specific task is how well the proposed research provides deliverables toward closure of the gap. A task can range from activities that define research requirements or operational needs, such as data mining and literature reviews, to a three to four year grant project selected from proposals that have been submitted in response to the annual HRP NASA Research Announcement (NRA). Even though not specifically a R&TD activity, a data mining task can provide results which are pivotal in defining further steps in the research path, and a hardware evaluation can further the engineering approach to risk mitigation.

Tasks are solicited through an NRA, the Small Business Innovation Research (SBIR) program, NASA Request for Proposals (RFP), etc., or are directed by HRP scientists. The HRP's intent is that most studies are procured through competitive means, i.e., NRA, RFP, etc. In some cases, due to timeliness of data, or close interconnectedness with operations or other NASA entities, the HRP will direct that a specific study be done. Criteria for these decisions are given in HRP-47069, Human Research Program Unique Processes, Criteria, and Guidelines. The current or planned procurement method for each task in this research plan is identified. Identification of any investigation as a directed study within the IRP does not signify a commitment on the part of the HRP to implement that study as a directed study without further consideration by the Chief Scientist as specified in HRP-47069.

It is the HRP's policy that all investigations sponsored by the program will undergo independent scientific merit review. This includes proposals submitted in response to NRAs, all directed study proposals, and all unsolicited proposals.

3.3.5 Deliverables

Each task or progression of tasks is designed to ultimately culminate in deliverables or products that range from risk characterization to prototype technology or countermeasures. External customers for the products delivered by HRP typically include: the NASA OCHMO (both Human System Risk Board (HSRB) and Health & Medical Technical Authority (HMTA)), System Capability Leadership Team (SCLT), Crew Health & Safety (CHS), and Human Health and Performance Directorate (HHPD).

Deliverables provided to external customers are usually the result of the integration and synthesis of evidence and deliverables from a line or lines of research. These deliverables are linked to tasks with Maturation listed as the procurement mechanism in the HRR. Common deliverables include risk characterization, recommendations for new or updated standards (e.g., Permissible Exposure Limits), requirements (e.g., Net Habitable Volume for a spacecraft), countermeasures, and technologies. Specifications for some deliverables are agreed upon with customers of the HRP products.

Common deliverables include recommended standards (e.g., Permissible Exposure Limit [PEL]), requirements (e.g., flight rule), risk characterization, countermeasures, and technologies. After deliverables are provided, the R&TD results are assessed for applicable updates to the evidence base as it impacts risks, gaps and tasks in order to achieve risk reduction goals as laid out in the PRR.

3.4 Research Platforms

The HRP utilizes various research platforms and data sources to address gaps in knowledge. Data mining involves gathering and analyzing data from historical spaceflights via the Lifetime Surveillance of Astronaut Health (LSAH), previous research data in the Life Sciences Data Archive (LSDA), spaceflight operational data (e.g., landing performance and simulator performance data), and other sources to identify possible correlation with physiologic or psychological function, and relevant data from ground studies (NASA-sponsored and otherwise).

The HRP utilizes the ISS and other flight platforms as they become operational to conduct research requiring the unique environment of space. The spaceflight data primarily identify and/or quantify physiological and behavioral changes to the human system occurring in the microgravity environment. The ISS is utilized to validate potential countermeasures, as an analog for long-duration exploration missions, and to gather data to define space normal as given in Section 3.5.

The use of the ISS platform, in several cases, is critical to obtaining the required knowledge to build products supporting longer, more challenging missions. The Shuttle retirement in 2011, the uncertainty in replacement transport vehicles to ISS, and the planned retirement of the ISS in 2024 levy significant constraints on available flight resources. However, since not all research that requires the ISS can be accomplished by 2024, the HRP will continue to plan use of the ISS as a viable research platform should the vehicle retirement be extended beyond the 2024 timeframe or an alternate LEO or analog platform can be found. Where possible, the HRP will utilize ground-based analog environments to perform the research required to fill gaps in

knowledge, preserving the limited flight resources for only those that cannot be addressed elsewhere. HRP utilization of the ISS is managed by the ROI Element.

There are several analog environments utilized by the HRP, some owned and operated by HRP, some by NASA, and others operated by other agencies. Each analog environment is assessed for its characteristics and the fidelity with which relevant portions of the flight environment are represented (e.g., isolation & confinement, extreme environments). No ground-based analog can serve to simulate the flight environment completely; thus each analog selected for use is based on its important flight-like characteristics specific to the task objectives. The use of several analogs may be required to fill a gap. Throughout the IRP, tasks requiring the use of specific analogs are identified. The ROI Element coordinates utilization of some ground-based research analogs to complement space research. HRP utilization of the NSRL is managed by the SR Element.

3.5 Functional Definition of Space Normal

Space normal is defined for this document as the normal human response to prolonged spaceflight. As NASA prepares to send crewmembers on extended exploration missions, questions arise regarding the impacts of the spacecraft and surface exploration environment on the health, safety, and performance of the explorers. The normal human response to prolonged microgravity exposure during (and after) orbital spaceflight missions has received considerable research attention, but little is known about the human physiological responses to prolonged fractional gravity exposure. It would be useful to know ahead of time whether any of the effects could be severe enough to cause functionally significant decrements in crew health, safety, or performance during these missions, so that appropriate countermeasures could be provided from the outset.

All organ systems are affected by the environmental factors associated with spaceflight, although the time frame and degree of negative impact on astronaut health and performance is highly variable. The spectrum of consequences to human health and performance ranges from catastrophic through steady loss or decrement, to short-term transitional adjustment, to benign with no meaningful impact. Currently, the HRP approach for each physiological condition or organ system of concern is to:

1. document the acclimated state;
2. recommend revisions to crew health standards if that state is medically unacceptable;
3. if unacceptable, then determine physiological mechanisms of action; and
4. develop countermeasures as appropriate.

The acclimated state is understood to represent space normal, the newly adapted normal baseline physiological state. A rigorous definition of space normal must consider the presence or absence of pre-existing clinical conditions and legacy countermeasures, as well as variability in incident SR, ambient atmospheric pressure, temperature and composition; acoustics; lighting; etc., in addition to the absence of apparent gravity. In particular, all experiments currently defining space normal on ISS are conducted in the presence of an exercise prescription that has varied from mission to mission and astronaut to astronaut over the first decade of ISS operations.

With an accepted definition of space normal, HRP would be in a position to recommend whether or not to allow acclimation to spaceflight conditions, and if so, to what degree: acclimation followed by treatment just prior to or after Earth return; acclimation accompanied by in-flight monitoring and countermeasures implementation at a predetermined degree of decrement; or no acclimation permitted whatsoever.

3.6 Hardware and Countermeasure Development Cycles

Many HRP deliverables contribute to hardware development. NASA hardware development proceeds through several stages, with reviews occurring between the stages. The exploration program goes through these stages as it designs the next crew capsule, a lunar lander, and the next generation space suit. Common reviews seen in the HRP documentation are as follows:

- System Requirements Review (SRR): At the beginning of the project, establishes what the system will and will not do.
- Preliminary Design Review (PDR): At 10% design completion, is primarily to critique the architecture of the design and critical decisions made in the design.
- Critical Design Review (CDR): At 90% design completion, is primarily to make a last set of changes before the design is finalized.

To make sure that all the organizations within NASA and its associated contractors are working from the same set of plans, NASA uses a rigorous “configuration management” system to obtain, review and implement changes to key documents. A change is initiated by a formal document called a Change Request (CR). A CR often solicits input from many stakeholders. That input is often provided in the form of a Review Item Discrepancy (RID). A RID is essentially a request to change part of a document and includes the rationale. The owner of the document decides whether or not to make the change. The HRP often provides RIDs to CRs concerning exploration program documents. This is the NASA process that allows HRP results to change NASA’s plans for exploration vehicles.

Design solutions and technology typically must be defined to a Technology Readiness Level (TRL) 6 by the PDR. TRLs are defined in Appendix B.

The HRP nominally begins a countermeasure development at Countermeasure Readiness Level-4 (CRL-4) and develops the selected countermeasure to CRL-7 or -8. At this point, the HRP transfers the countermeasure to the implementing organization for incorporation. For some Elements, SR for example, countermeasure development must begin at much lower CRLs and are thus developed to CRL-6 prior to transition. CRLs are defined in Appendix B.

4 RESEARCH APPROACH

The IRP describes a plan of research that addresses both human physiology, human performance and the interconnected system of the human and spacecraft in a highly integrated manner. It is often not possible to address the risks simply as stand-alone units. The knowledge or mitigation

gaps often appear in multiple risks. Many of the specific research tasks address multiple gaps across risks.

In the following sections, the PRD risks are listed by HRP Element. Sections 4.1 through 4.4 provide a high-level view of the research approach to the risks. More detailed research findings, including citations, can be found in each risk's Evidence Report on the HRR. The HRP Elements are arranged in the following order:

1. Exploration Medical Capability
2. Human Factors and Behavioral Performance
3. Human Health Countermeasures
4. Space Radiation

Detailed information about gaps and tasks for each risk is located in the HRR: http://humanresearchroadmap.nasa.gov/.

The interactions between the risks, gaps, and tasks are not readily shown in a printed book. In the HRR database, the user will be able to search for such items as gaps associated with a risk, the tasks associated with a given gap, the cross-integration of a task across multiple gaps or risks, and deliverables associated with a gap or task.

4.1 Exploration Medical Capability

4.1.1 Risk of Adverse Health Outcomes & Decrements in Performance due to Inflight Medical Conditions (Short Title: Medical)

A human mission to Mars is a challenge outside of the bounds of human experience, but within the grasp of our technology and imagination. It is critical to both draw lessons from prior spaceflight experience and to recognize the limits of that experience. Each medical system designed for earlier human spaceflight was developed for a close-proximity, Earth-centered mission that enjoyed the advantages of real-time tele-medical support, consumable resupply, and medical evacuation when necessary. Operating outside low Earth orbit, without these advantages, requires a closer alignment between vehicle engineering and medical system development.

In a real sense, success in a human Mars mission will depend on a comprehensive and mission-enabling astronaut healthcare system as well as an understanding of how such a system will be integrated and implemented within an exploration mission. All other design requirements and research within exploration medicine will be driven by the above goals; thus, these goals form the conceptual cornerstone that defines the medical system design and the supporting research pathway. Using this framework, the ExMC Element works to envision the medical needs for a human Mars mission, to identify operational barriers to meeting those needs, and to implement a research pathway in the support of stakeholder needs and interests.

The medical challenges expected in a Mars mission are unlike any prior human spaceflight experience. As a result, provision of medical care within the limitations of such a mission requires a paradigm shift in the understanding and acceptance of risk, the ethical framework of

exploration missions, and the trading of medical capabilities against other vehicle components within a vehicle architecture limited by mass, volume, power, data, and many other factors unique to long-distance spaceflight. Medical system requirements and vehicle design must be integrated to minimize the risks to crews, and flexible and minimized technologies must factor heavily in system design to elevate a medical capability without sacrificing other systems components. It is imperative that the medical system balance these constraints to ensure that crew health and performance is maintained and mission risks are minimized.

The ExMC Element is specifically concerned with establishing evidenced-based methods of monitoring and maintaining astronaut health. Essential to completing this task is the advancement in techniques that identify, prevent, and treat health threats that may occur during space missions. These techniques, in turn, must be supported by an evidence-based medical data architecture appropriate for long-duration, exploration-class missions. This exploration medical system will need to be designed for use in a progressively Earth independent manner, so that astronauts can function autonomously to maintain their own crew health and performance.

ExMC is applying systems engineering principles and practices to accomplish its integrative goals. The systems engineering activities apply a structured and disciplined technical approach to support development of a medical system addressing clinical, behavioral health, human factors, physiological performance, and task performance needs. The systems engineering activities also enable effective coordination and integration with exploration mission engineering, operational, and technology development efforts by communicating with products (e.g., requirements, interface descriptions) typically used in those communities. Tools to support quantitative evaluation of medical risk, trade space analyses of clinical capabilities, development of technical requirements, and system implementation options will be necessary.

4.1.2 Risk of Renal Stone Formation (Short Title: Renal)

Historical spaceflight data have revealed both in-flight and post-flight instances of renal stones. While none have led to loss of crew life, there have been in flight medical conditions leading to either evacuation or early termination of mission. Renal stone formation in microgravity has been well studied and modeled. Recent results from simulations starting with the chemistry of renal stone formation and ending with associated risk have provided validated models quantifying the risk of clinically significant renal stones during exploration as a function of hydration, nutritional countermeasures, and gravitational environment. Current research efforts are aimed at 1) integrating in-flight strategies to reduce stone formation into exploration medical system designs, 2) progressively autonomous ultrasound monitoring and biochemical diagnostics for early detection of stones, and 3) treatment interventions, such as moving renal stones through the application of ultrasound waves.

4.1.3 Risk of Ineffective or Toxic Medications During Long-Duration Exploration Spaceflight (Short Title: Pharm)

NASA’s current Low Earth Orbit (LEO) operations involve frequent resupply missions that may be problematic for some long duration missions and impossible for deep space exploration missions. As such, ensuring a safe and effective pharmacy for exploration missions is an important challenge. At this time, it is unclear how, and to what extent, 1) the spaceflight

environment changes drug stability and 2) alterations of human physiology or the medications themselves affect drug pharmacokinetic and pharmacodynamic properties. The potential for drug instability compounded by altered drug response may pose a risk to exploration crews. Current research efforts are underway to propose a safe and effective exploration spaceflight formulary able to maintain a ≥ 3 year shelf-life. The proposed ExMC research includes: analysis of medication packaging and storage solutions; studies that will provide validation for chemical / physical pharmaceutical stability; degradation product toxicity and drug safety profiles; and better characterize pharmacokinetics, pharmacodynamics, and pharmacotherapeutic properties of medications in spaceflight.

4.1.4 Risk of Adverse Health & Performance Effects of Celestial Dust Exposure (Short Title: Dust)

The impact of exposure to dust from extraterrestrial sources (celestial dusts) could lead to respiratory, cardiac, ocular, or dermal harm during exploration surface missions, resulting in immediate or long-term health effects. NASA needs to sufficiently characterize the consequences of exposure to these dusts so vehicles and habitats are designed to maintain concentrations of airborne dust within safe limits while future operations planning minimizes the dust impacts on human health and performance. NASA rodent based research results coupled with expert review have established a permissible exposure limit (PEL) for lunar dust that has been converted into a NASA standard. This lunar dust NASA standard is being used to develop engineering controls for lunar surface missions that keep astronaut exposures below the PEL. Current research is focused on determining the allergenicity of lunar dust exposure and future work will be performed on Mars surface samples once acquired.

4.1.5 Risk of Bone Fracture due to Spaceflight-induced Changes to Bone (Short Title: Fracture)

Spaceflight-induced bone changes are largely targeted to regions of the skeleton that experience larger deficits in mechanical loading in microgravity, i.e. weight-bearing sites on Earth. Hence, these skeletal sites may be more at risk for fracture during mission operations. The risk for fracture associated with falls is minimal during missions in microgravity because impact loads are essentially non-existent. Mechanical loads to bone will increase in the gravitational environment of celestial bodies and with the performance of mission activities during surface exploration, such as the construction of habitats, ambulation in extravehicular suits, jumping from ladders or structures, conducting vehicle egresses, or off-nominal spacecraft landings. Computational modeling, performed in support of the Integrated Medical Model, suggests that mechanical loads to bone during a fall on the Moon or Mars are unlikely to lead to fracture. As a result, there is no active research regarding spaceflight clinical fracture management at this time as the risk is considered “accepted” for all Design Reference Missions. However, there is still ongoing research to further characterize bone changes during long-duration missions. These efforts may influence countermeasures inclusion in future exploration missions and/or allow for the updating of computational models.

4.2 Human Factors and Behavioral Performance

4.2.1 Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (Short Title: BMed)

HFBP research addresses the risk of adverse cognitive and behavioral conditions and psychiatric disorders developing during or following a spaceflight mission. Hazards affecting behavioral health and performance include isolation and confinement, altered gravity, distance from earth, hostile & closed environment, and exposure to the space radiation environment. Given the need to assess and mitigate performance outcomes – regardless of the stressor – the "Risk of Acute (In-flight) and Late Central Nervous System (CNS) Effects from Radiation Exposure", is now embedded within the BMed Risk.

Early detection and mitigation of stress or other risk factors during spaceflight is imperative to deter development of behavioral or psychiatric conditions which could seriously harm and negatively impact the individual or the crew, and pose serious consequences for accomplishing mission objectives or jeopardizing these missions altogether. For long-duration space exploration, early detection and delivery of countermeasures to crew with increased autonomy, reduced communication capabilities, and limited resupply is essential to the health of spaceflight crewmembers. Toward this end, HFBP is developing methods for monitoring behavioral health during a long duration exploration mission, and adapting/refining various tools and technologies for use in the spaceflight environment. These measures and tools will be used to monitor, detect and treat early risk factors that contribute to adverse cognitive and behavioral conditions, as well as psychiatric disorders. HFBP will utilize analogs and, where appropriate, spaceflight, to test, further refine, and validate these measures and tools for future missions. HFBP also develops countermeasures for maintaining behavioral health and enhancing performance during long duration isolated, confined, and highly autonomous missions; provides recommendations for spaceflight medical operations; and, provides updates for human health and performance standards, and habitability and human factors standards.

The magnitude of physical and biological stressors will vary by mission phases but will simultaneously, perhaps synergistically, and cumulatively act on the human system with the potential to adversely impact operationally-relevant crew performance. Three high priority risk factors—space radiation, isolation, and altered gravity exposure—may synergistically impact the CNS, and subsequently, crew cognitive and behavioral health and performance, on long-duration missions. To that end, HFBP leads the development of a fully integrated research approach referred to as the CNS/BMed/Sensorimotor (CBS) Integrated Research Plan, which brings together needed research across two risks:

- Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (BMed)
- Risk of Impaired Control of Spacecraft/Associated Systems and Decreased Mobility Due to Vestibular/Sensorimotor Alterations Associated with Spaceflight (SM)

Complementing behavioral performance measures, the CBS Integrated Research Plan identifies a need to assess brain physiology, neurovascular unit integrity, molecular signaling, and biomarker changes, in order to generate data sets that can be incorporated into computational models to

represent and predict changes in operationally-relevant "brain performance pathways" (BPP). The emphasis on BPP's reflects an integrative, applied research emphasis on the functionally distinct regions in the brain which map to areas activated by the demanding sensory, cognitive, and motor activities required for the training and sustainment of the readiness to perform operationally-relevant tasks. The BPPs provide the conceptualization for the functional integration of these regions with the social-emotional, sensorimotor, and cognitive networks that allow for a coherent integration and activation of systems needed for sensation, cognition, memory, motor control, and affect that motivates and/or maintains that performance.

The CBS Integrated Research Plan integrates scientific research from 3 discipline areas (space radiation, sensorimotor and behavioral health) to operationalize a risk-assessment approach to define crew health and performance related to: Operational performance and fitness for duty standards relative to each risk within the framework of Performance Outcome Levels (POL), and Permissible Exposure Limits (PEL) (established by assessing the relative risks to operationally relevant performance associated with exposures to combinations of spaceflight hazards). The plan aims to deliver standards and guidelines development (including POLs and PELs). This requires complementary, translational approaches to identify the mechanisms, pathways, and components that contribute to operational performance risks by:

- Appreciation of the multifactorial nature of spaceflight hazards, exposures, and dose-effect responses (i.e. differential variability due to differences in vulnerability to hazards).
- Use or development of consistent/valid animal translational models (and back-translational approaches), along with human biomarkers and measures to assess the function of some mechanisms discovered in animal models, used to develop a multidimensional set of validity criteria that is then generalized to relevant human risk.
- Leveraging translational and computational modeling to integrate traditional and novel data (e.g., animal model analogues of brain-behavior risk translated to human performance).
- Strategic leveraging of transdisciplinary expertise in more transparent approaches focused on integration of approaches, data and technology to attain greater confidence in risk assessments.

4.2.2 Risk of Performance and Behavioral Health Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team (Short Title: Team)

This risk focuses on developing and maintaining high-performing and well-functioning spaceflight teams, which includes both flight crew and ground support as part of the larger multi-team system. While relatively few empirical spaceflight studies have been conducted regarding the impact of interpersonal and intrapersonal factors on performance, a growing body of evidence from spaceflight analog environments suggests that team-level issues could jeopardize long-duration exploration missions. Reports from spaceflight missions prior to ISS (e.g., MIR), reveal that several missions may have been terminated earlier than planned and saw a decrement in performance due to friction between crewmembers. Additionally, some veteran NASA astronauts have reported conflict during previous missions, while ineffective team skills have reportedly led to performance decrements and/or more training (Stuster 2010; 2016). Conversely,

good team skills have benefited both team cohesion and performance in space. Understanding the potential impacts of inter- and intra-personal issues from both spaceflight and high-fidelity analog environments is important for identifying countermeasures to aid flight and ground support during future high-autonomy missions (e.g., cislunar space and Mars).

A series of HFBP-funded literature reviews and interviews of crew and operations personnel identified the most likely and most serious threats to crew cohesion, crew performance, and crew-ground interaction that might be expected for long-duration exploration missions. Follow-on studies are currently collecting data in spaceflight and high-fidelity analogs (e.g., NASA's HERA, Antarctic stations) with the goals of: identifying the critical drivers of team and multi-team systems functioning; validating objective measures for monitoring crew cohesion and processes; composing teams with the right mix of knowledge, skills, abilities, and personalities; coordinating across the multi-team system under communication delays, and during changing levels of autonomy; informing human factors designs in habitability, and in interactions with robotics, computers, and automated systems; and developing approaches to enhance team training related to teamwork skills and multi-cultural crews. Deliverables build upon the current highly successful in-flight support services and countermeasures to mitigate risks associated with increased isolation, confinement, duration, and communication delays. These measures and countermeasures are assessed for feasibility and acceptability in appropriate analog environments, to include in-flight studies examining the cohesion and performance of ISS crews.

4.2.3 Risk of Performance Decrements and Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, and Work Overload (Short Title: Sleep)

Objective and subjective evidence indicates that during ISS and Shuttle missions, sleep is reduced and circadian rhythms are misaligned. As measured by actigraphy and accompanying sleep logs, the average nightly sleep duration of crewmembers for both short and long duration missions is around six hours, with astronauts sleeping significantly longer on Earth, indicating a sleep debt accrued on orbit.

Ground evidence demonstrates that performance impairments can occur when sleep is attained in quantities similar to that attained by astronauts in flight. In addition, preliminary results from a flight study on the ISS demonstrates that reaction time is impaired as a function of reduced sleep. Future spaceflight data mining efforts may also yield insight into the relationship between sleep duration and circadian phase, with other outcomes (e.g., immune health, operational performance).

HFBP research aims to further characterize and quantify this risk by implementing studies on ISS using standardized measures to evaluate performance relative to fatigue and performance. Planned data mining efforts seek to further investigate contributors to sleep loss, fatigue, circadian desynchronization, and work overload by evaluating environmental factors, individual vulnerabilities, and mission timelines relative to sleep. The role of sleep and circadian phase in other outcomes (i.e., BMed and Team studies) will also be further evaluated through analog research.

Such investigations help to inform the optimal countermeasure strategy for mitigating the health and performance effects of sleep loss and related issues in flight. As an example, ground-based

studies indicate that strategically timed light exposure can help maintain circadian alignment, and/or facilitate schedule shifting, performance and alertness. Current efforts aim to determine the operational protocols and technical requirements for lighting systems on the ISS, as well as future exploration vehicles. Other countermeasures that are currently being investigated include sleep-wake models of performance that may inform real time scheduling decisions as well as optimal ways to individualize countermeasure regimens. The effectiveness of other potentially relevant countermeasure strategies, such as stress management, diet, and exercise, may also be assessed.

4.2.4 Risk of Adverse Outcome Due to Inadequate Human Systems Integration Architecture (Short Title: HSIA)

The Human Systems Integration Architecture (HSIA) represents an integrated Human Factors portfolio. The conceptual framework for HSIA proposes to address the integration of onboard capability and crew roles and responsibilities necessary to enable crew to respond effectively and efficiently int eh required increasing autonomous mission operations framework. The Human System Risk Board (HSRB) approved the HSIA risk in 2019. The HSIA represents the integration of five individual human factors risks that were aligned according to the risk areas of: vehicle design/habitability, human computer interaction, human automation and robotics integration, training, and task design presented an integrated representation of the risks termed the HSIA to the HSRB. In the HSIA risk area, the research is focused on the challenges of Exploration missions, i.e., beyond Low Earth Orbit (LEO). Ground laboratories, analogs, and the International Space Station (ISS) are utilized to answer research questions necessary to ensure that future Exploration crewmembers, who will be dealing with many unknowns, communication delays, and increasing autonomy, will be able to adequately perform their tasks and complete their missions. Characterizing the human factors risks into this one higher level HSIA structure enables research to be completed that is aligned to measurable outcomes to meet the needs of future operations by identifying knowledge and countermeasure gaps.

Future deep space missions will present new challenges for crew, and increased risks to human performance due to the stress, fatigue, radiation exposure, and isolation that characterize these missions. In addition, crew will no longer be able to depend on real-time support from Mission Control Center (MCC) due to distance from the Earth, but will have to work increasingly autonomously, performing critical tasks that were previously carried out by Flight Controllers. This greater crew/vehicle autonomy will depend, in part on advanced, on-board automated systems but also on new approaches to training, teaming and crew selection. Most importantly, it will depend on a successful integration of intelligent vehicle capabilities with crew capabilities into the physical vehicle / habitat design.

We must understand the types of tasks that astronauts will likely be performing autonomously, as well as the human-system integration standards and guidelines needed in order to provide tools and mitigations that ensure success in performing those tasks on an autonomous mission. An HSIA approach addresses the integration of onboard capability and crew roles and responsibilities necessary to enable adequate response to safety critical situations in the required increasingly autonomous mission operations framework. Enabling a flight crew of 4 to perform the job that has traditionally been done by a ground crew of 40+ will require a fundamental

rethinking of crew-vehicle integration and operations as well as crew-ground collaboration. A flight crew of 4 will need to function more autonomously in response to anticipated reduction in communication quantity and quality as well as unanticipated blackouts instead of depending on frequent real-time communications with a large MCC ground support team of diverse specialties to provide directions. This increased autonomy will force them to rely heavily or exclusively on the information systems available to them within the vehicle or habitat.

The impact of the increased autonomy will be felt particularly in dealing with unanticipated, off-nominal situations. Our current operational models therefore (tied to ground control) must evolve as mission operations become increasingly earth independent. Decreasing real-time ground support for the execution of complex operations during future exploration missions will require the flight crew to respond to potentially safety-critical anomalies with no established procedures on their own. A delay or absence of ground support during unanticipated contingencies can become a significant hazard and increase the risk of jeopardizing crew and vehicle safety if there are not sufficient onboard capabilities to assist with troubleshooting and contingency management. The attainment of increased crew autonomy therefore lies in the ability to complement and enhance crew capabilities so that the 4-person flight crew can, on their own, perform the kind of anomaly response that had previously been done mostly by MCC, and complete these activities in the face of the expected communication delays or unexpected blackouts. This undoubtedly impacts the areas of human computer interaction, human automation and robotics integration, training, and task design, and vehicle/habitat designs along the integrated representation of the risks encompassed by the HSIA.

It is important to highlight that complex, engineered systems, automated/autonomous or not, will experience unanticipated safety critical malfunctions. These malfunctions can be due, in part or in whole, to human error and/or space environment impacts, but can also be independent of these. Humans are the critical problem-solving components of complex engineered systems and while Artificial Intelligence (AI), Intelligent/Autonomous Systems can help the human decision maker, especially with pattern analysis, the AI systems will not be able to provide actual problem-solving. It is therefore critical that c*apabilities be wrapped around the human(s) in order to address the safety critical issues related to the HSIA risk.*

4.2.5 Risk of Injury from Dynamic Loads (Short Title: Occupant Protection)

Future spacecraft systems may include launch-abort systems and parachute-assisted, capsule landings. Because of these potential design features, dynamic loads transmitted to the human may result in higher forces than currently experienced during spaceflight. The current standards and requirements do not adequately document the acceptable limits of forces and/or direction of force vectors which can be transmitted to the human without causing injury. Injuries may impair or prevent a crew-member from unassisted evacuation of the spaceflight vehicle after landing. Development of Agency-level human health and performance standards appropriate to occupant protection from dynamic loads, as well as development of the method(s) of meeting those standards in the design, development, and operation of mission systems, would reduce the likelihood of this risk so that crew injury or Loss of Crew (LOC) may be avoided or reduced. In addition, the Columbia Crew Survival Investigation Report cited inadequate upper body restraint and protection as a potential lethal event, and recommended that future spacecraft suits and seat

restraints should use state-of-the-art technology in an integrated solution to minimize crew injury and maximize crew survival in off-nominal acceleration environments (lumbar IVD: L2-4/L3-4), and should incorporate conformal helmets and neck restraint designs similar to those used in professional auto racing (lumbar IVD: L2-7). Because all crewmembers must endure dynamic phases of flight, detailed understanding of the human body response to such environments is critical. Given that spaceflight deconditioning causes decreases in bone strength, decreases in muscle strength, and increases in bone fracture risk, the criticality of this understanding is greater with longer duration spaceflight missions.

The Occupant Protection Team at NASA has developed a forward plan to develop new standards for protecting the crew during dynamic phases of flight. In collaboration with external peers in industry, academia and other government agencies, the Team will develop and validate the standards using a combination of data mining, testing, analysis, simulation and expert opinion.

4.3 Human Health Countermeasures

4.3.1 Risk of Performance Decrement and Crew Illness Due to Inadequate Food and Nutrition (Short Title: Food and Nutrition)

The space food system and the nutrition it delivers will be critical to the success of future crewed space exploration missions. During these long-duration, confined missions in the harsh environment of space, food and nutrition will be an essential countermeasure for maintaining the health and performance of astronauts. Outside of low-Earth orbit, constraints on resources and lack of food resupply will further constrain nutritional support of crew health, and increased radiation exposure will increase risks of oxidative stress and resulting tissue damage.

The current ISS food system consists of processed and prepackaged foods that are required to be stable at room temperature for multiple years prior to consumption. While the nutritional quality of the ISS food system has improved in recent years (e.g., reduced sodium), space food still does not meet many basic nutritional guidelines. For example, the ISS food system is limited in sources of omega-3 fatty acids and has limited selection of fruits and vegetables: food types that have extensive health benefits on Earth. The Food Physiology study is designed to evaluate effects of providing more sources of these beneficial foods and evaluating effects on immune, microbiome, and nutritional outcomes. This is a first, critical element in documenting the benefits of nutrition.

Human history documents that exploration food system adequacy becomes more central to mission success as mission length and isolation increases. NASA expects Mars missions to take up to 3 years. Resupply may not be an option, and food may even be prepositioned before crew launch. Unknown crew assignments or late crew changes will eliminate the opportunity for crew to select their food preferences, and resource constraints may limit quantity and variety. Cold storage may not be available for food, but the food system will need to be safe, nutritious, and acceptable for at least five years. Recent studies have shown that the processed and shelf-stable foods used on the ISS will only retain acceptable quality and nutrition for one to three years under ambient storage conditions. Insufficient nutrition, whether due to inadequate food system content (e.g., calories, specific nutrients, bioactive compounds), nutrient degradation during

storage, or inadequate intake by the crew due to factors such as menu fatigue, lack of preference, or quality degration during storage may lead to body mass loss, muscle loss, and eventually nutritional deficiency(ies) that may impact crew health and performance

Beyond nutritional and quality challenges, food resource requirements are a significant burden for exploration missions. If food system requirements exceed the capabilities of the mission resources, the mission may not be feasible, or allocation of resources to other systems may be overly constrained. Nutritional content and food quality must remain key requirements in any food system strategy to reduce mass and volume.

Even on shorter-duration Gateway and Lunar missions, there will be no resupply vehicles to deliver fresh foods to the crew, as on ISS, and mass and volume will be more limited. "Meal Replacement" bars have been developed to help reduce mass and volume but ground testing has revealed that even over short durations (less than 30 days) these have negative effects on dietary intake, health, performance, and morale.

Studies are underway to determine how formulation, processing, packaging, and storage strategies can help increase the shelf life of a prepackaged food system and/or reduce mass and volume requirements. Alternative strategies, such as inclusion of bioregenerative salad crops, introduce new resource challenges (e.g., food safety, reliability), but offer potential solutions to nutrition and variety challenges. Delivery of personalized nutrition through automated bulk processing may also have potential to supplement the food system. Ongoing collaborative studies are investigating the potential of food system improvements to enhance physiological and psychological health. These efforts could lead to the design of more efficient, targeted dietary interventions. Results from these studies will help to determine an optimal food system strategy and will identify areas where additional research is required to improve shelf life or food system composition.

The most basic role of food and nutrition is to prevent nutrient deficiency. On Earth, the variety of foods we consume can help stave off frank deficiencies, although the typical western diet is still limited in some nutrients (e.g., vitamin D). Individuals who limit their intake of certain foods or food categories increase their risk of nutrient deficiencies—for example, vegetarians need to be mindful of meeting protein, iron, and vitamin B12 requirements; people who avoid fruits and vegetables are at greater risk of vitamin deficiencies; people who avoid lactose are at risk of calcium and potassium insufficiency, and individuals who are trying to lose weight by reducing calories or following defined diet protocols often have micronutrient deficiencies.

Although nutrition plays a significant role in long-term health and in mitigating disease incidence (including cardiovascular disease, cancer, osteoporosis, muscle loss and sarcopenia, dementia and cognitive decline), traditional dietary recommendations (e.g., Dietary Reference Intakes) are simply designed to prevent deficiencies, not chronic disease. That is because much less is known about the effects of diet and nutrition on performance and disease incidence than we do about how to prevent nutrient deficiency. For exploration missions outside of low-Earth orbit, while we must not only stave off deficiency, we must understand how food and nutrition

interact with the human system to optimize health and performance. Nutrition becomes even more important in space, where environmental factors (e.g., radiation, carbon dioxide (CO_2)), a closed environment, and stress can all affect intake and metabolism, physiology, biochemistry, health and performance. Nutrition can positively (or negatively) affect cardiovascular and ophthalmologic physiology (and pathophysiology), immune system function, bone and muscle loss, response to exercise and extravehicular activity (EVA), and more. Dietary intake helps maintain hydration and reduce renal stone risk. Food choices and nutritional status affect mood and improve a crewmember's performance and team cohesion. Optimal nutrition also improves exercise performance, maintains circadian rhythms, and promotes sleep. However, many of these outcomes have not been evaluated in relationship to the space food system, and baseline data in these areas will become increasingly important as risk trades are made between human health and vehicle systems based on resources available on future exploration missions.

Crewmembers must be adequately nourished before, during, and after missions. While preventing nutrient deficits inflight is crucial, optimizing dietary intake and nutritional status before flight will maintain crew health and enable mission success, and proper nutrition will also be important in postflight rehabilitation and return to flight status. Food and nutrition serve as an obvious behavior/performance countermeasure – before, during, and after flight.

An important element of nutritional assessment is to monitor inflight dietary intake. In 2016, a custom developed iPad App was deployed to ISS—the ISS Food Intake Tracker (ISS FIT); this software allows crews to record food consumption and the App provides the crew with real-time nutrition feedback. In addition to providing information on food use and inventory, ISS FIT can also helps crewmembers select meals in preparation for specific tasks (e.g., EVAs, preparation for return to a gravitational field). The response from crewmembers has been outstanding, and highlights the importance of providing tools to both enhance autonomy, and provide greater insight into actual intakes. While we have only scratched the surface so far, we have identified relationships between food intake and changes in nutritional status, as well as relationships between nutrient intake and oxidative stress. A key gap that remains is being able to relate nutrition with other clinical outcomes. This is hindered by the limited insight into these issues, and the lack of interaction between science and operational teams.

Research over the past 10-15 years has yielded many findings. Two projects, the "Nutritional Status Assessment: SMO-016E (Nutrition/SMO-016E)" and "Biochemical Profile" projects yielded numerous insights regarding the role of nutrition in human adaptation to spaceflight. One key finding was that these experiments provided biochemical evidence for susceptibility of some (but not all) individuals to the risk of vision and ocular pathologies during spaceflight. These projects ultimately documented a genetic predisposition for some astronauts to develop these issues: a finding that the ISS Program Scientist declared the most compelling human research from ISS in 2016. Subsequent studies identified differences in response to carbon dioxide exposure in some individuals based on these same genetics, and most recently documented an association of genetics with the incidence of optic disc edema in bed rest subjects. This research highlights the need for individual assessments on the role of genetics on nutritional requirements, which will be required for successful exploration missions and could potentially have profound

implications for terrestrial medicine. Countermeasures have been proposed based on this line of research, and these need to be tested.

Another Nutrition Supplemental Medical Objective (SMO) finding was that iron stores increase early in spaceflight and then return to pre-flight concentrations by the end of a six month mission. Increased iron stores during flight were associated with increased oxidative damage to deoxyribonucleic acid (DNA), and also correlated with bone loss. Crewmembers that consumed more iron had a greater iron response during flight (and a greater oxidative damage, and regional bone loss). Given that the ISS food system provides more than 3x the defined iron requirement per day, this is an area where food provisions could clearly help mitigate risks.

Additionally, data from the Nutrition SMO also showed that high levels of urinary calcium resulting from bone loss have clogged the ISS Urine Processor Assembly (UPA) and this resulted in the recommendation that astronauts increase their fluid intake. The ISS Program used the data to make decisions regarding operational limits for the ISS UPA, providing estimated savings of more than 80 L of water *not launched* every year since 2012.

Despite the successes of the Nutrition SMO and the follow-on Biochem Profile, this effort was stopped in 2018. Biochemical measures collected as part of the Standard Measures and 1-Year-Mission projects have replaced a portion of the original suite of biochemical measures that were encompassed in Biochem Profiles, and as we fly more crew on missions longer than 6 months, fly more diverse crews, and test different countermeasures inflight, we will have some biochemical data to help us understand the implications of these differences.

While all concede that food will be flown for exploration missions, there is little concession that we need to understand optimal composition of that food. The food system for low Earth orbit mission was designed simply to meet cost constraints (e.g., by largely using commercially available items), and delivered a less than optimal food system. The role for nutrition in terrestrial health and disease prevention is evident. We need to document the extent to which we can mitigate the negative effects of spaceflight on human adaptation and performance.

Food and nutrition are the only countermeasure that we can be absolutely positive will be onboard exploration missions. It is HRP’s goal to evaluate and define food and nutrition strategies that will optimize crew health during these exploration missions, helping to ensure mission success while imparting long-lasting benefits on crew health and performance.

4.3.2 Risk of Spaceflight Induced Cardiovascular Disease (Short Title: CVD)

The HRP risks presented in this document mirror those managed by the HSRB. This section is an exception, as it is a merger of 2 older HRP/HSRB risks (“Risk of Cardiovascular Disease and Other Degenerative Tissue Effects from Radiation and Secondary Spaceflight Stressors” and “Risk of Cardiac Rhythm Problems”), a merger that is still in early development phases at the HSRB level. Please note that the content in this section will be updated over the next few months as this merger matures.

4.3.3 Risk of Injury and Compromised Performance Due to EVA Operations (Short Title: EVA)

Astronauts perform spaceflight EVAs in confined spaces that must provide the same life support, nutrition, hydration, waste disposal, and consumables of an actual space vehicle, while allowing them to perform tasks within acceptable limits of human performance and comfort. The physiological and functional demands during EVA or EVA training can injure an astronaut, compromise their physical and/or cognitive performance, and may lead to incomplete mission objectives. Factors affecting EVA crewmember health and performance include EVA task design and concepts of operations (e.g., EVA frequency, duration); suit sizing and in-flight anthropometric changes; crewmember muscle, aerobic, sensorimotor and cognitive performance; availability of suit system and physiological sensor information (e.g., biofeedback, decision support systems); and suit design parameters (e.g., suit pressure, mass, center of gravity, joint mobility, nutrition, and hydration).

Multiple planned and ongoing research studies associated with these aspects of the EVA risk are included in the "Integrated EVA Human Research Plan", which is updated annually and currently located here: https://www.nasa.gov/sites/default/files/atoms/files/nasa-tp-2019-220232.pdf. The integrated plan is program agnostic and includes planned and ongoing EVA tasks and projects funded by multiple organizations. Multiple HRP-funded tasks were included in the original plan, but were later defunded by the Human Research Program and are now funded by other organizations. The latest update to the integrated plan is currently in review and will be renamed the "Crew Health & Performance EVA Roadmap".

4.3.4 Risk of Decompression Sickness (Short Title: DCS)

Space exploration missions will have different variables that affect decompression sickness (DCS) than Shuttle or ISS missions. This includes differences in cabin pressures, oxygen concentrations, EVA metabolic profiles, ground reaction forces, lower body musculoskeletal workloads, gravity levels, suit pressures, suit gas mixtures, and EVA durations and frequencies. DCS during a lunar or exploration mission could have severe impacts on an astronaut's health and on the success of the mission.

Space exploration is remote and standard treatment methods for DCS will be unavailable. NASA will predominantly mitigate the risk of DCS using preventative measures.

Research tasks associated with understanding, quantifying, and mitigating the risk of DCS during spaceflight were included in previous versions of the IRP but have since been defunded by the Human Research Program. Several of these tasks are described in the "Integrated EVA Human Research Plan" (Abercromby et al, 2019) and are now funded by other programs.

4.3.5 Risk of Adverse Health Event Due to Altered Immune Response (Short Title: Immune)

Recent investigations have found that certain aspects of immunity are dysregulated during spaceflight and the phenomenon persists for the duration of a six-month mission. To date, experts have characterized this phenomenon as consisting of altered peripheral leukocyte

distribution, diminished T cell and NK cell function, and dysregulated cytokine profiles. Immune dysregulation is credited with the reactivation of latent herpes viruses in astronauts, likely resulting from reduced function of cytotoxic T cells. Moreover, it appears that certain adverse medical events occur in select crewmembers – including atypical allergic symptoms, atopic dermatitis, or various infectious processes – may relate to immune dysregulation. Although these phenomena have not resulted in widespread clinical concerns during orbital missions, the data suggest that astronauts will have an elevated risk for more serious adverse medical events during deep space exploration missions. Immune dysregulation is likely to worsen during such missions due to synergy with increased levels of radiation exposure, stress, and circadian misalignment, and also because treatment options will be limited with no capability for rapid return to Earth. The immune system is complicated, consisting of many distinct types of cells, each with a unique function. Current investigations continue to characterize previously uninvestigated aspects of immunity in ISS astronauts including innate cellular function, DNA damage in immune cells, gene expression in leukocytes, and protein alterations. After characterization, the HRP will determine specific clinical risks for deep space missions, develop a monitoring strategy, and determine the need and nature of potential immune countermeasures. A recent published review details options for immune countermeasures, including nutritional supplements, augmented exercise, stress relief, and pharmacological interventions (Crucian et al, Frontiers, 2018). A specific countermeasures protocol, suitable for validation in both ground analog and spaceflight conditions, was published in 2019 by the same international team of authors (Makedonas et al, Frontiers, 2019). In parallel, researchers are also studying immune responses of subjects who are exposed to environments that are analogous to space – including 'winterover' (one-year duration) inhabitants of research stations in Antarctica – to aid in characterizing these in-flight phenomena and provide a terrestrial platform in which NASA could evaluate potential countermeasures.

4.3.6 Concern of Intervertebral Disc Damage upon and immediately after re-exposure to Gravity (Short Title: IVD)

Evidence has suggested that astronauts have a higher incidence of intervertebral disc (IVD) damage than the general population. On-going postflight surveillance of astronaut cohort however has not substantiated an increased incidence of IVD damage in astronauts. Further studies have attempted to characterize the effects of spaceflight on the vertebral unit (vertebral bodies/IVD/musculature), but likewise the data have not further informed the concern for IVD damage to elevate it to a risk. The HRP may need to expand its characterization to the entire back/spinal unit. These findings may better inform the need for in-flight countermeasures and provide the guidance to design re-entry and post-flight protocols, as well as future re-entry protocols for exploration spacecraft, as appropriate.

4.3.7 Risk of Impaired Control of Spacecraft/Associated Systems and Decreased Mobility Due to Vestibular/Sensorimotor Alterations Associated with Spaceflight (Short Title: Sensorimotor)

Exposure to microgravity induces adaptive central reinterpretation of visual, vestibular, and proprioceptive information. These changes are most prevalent during and after gravitational transitions, and lead to performance decrements during and after spaceflight. During these

adaptation and readaptation periods, disturbances in perception, spatial orientation, posture, gait, eye-head, and eye-head-hand coordination occur that disrupt an astronaut's ability to control vehicles and complex systems and to move around and perform tasks. The risk of impairment is greatest during and soon after gravitation transitions when performance decrements may have high operational impact (control of vehicles during landing, immediate egress, and extravehicular activities following landing). Alterations in sensorimotor performance are a concern for Mars missions as well as extended lunar missions when astronauts will be exposed to prolonged periods of microgravity during transit and will have to perform landing tasks when they arrive. Therefore, we are currently working to characterize this risk more completely, including decrements in posture and gait, manual control, spatial orientation, motion sickness, as well as investigating spaceflight-related changes (including radiation exposure) to brain structure, which might subsequently result in changes in cognition and performance of tasks. Published results indicate that functional tasks requiring a greater demand for dynamic control of postural equilibrium (standing from a prone position after a fall, obstacle avoidance during walking, moving objects from one location to another, jumping down from a low platform and climbing a ladder) showed the greatest decrement in pre to postflight performance. Recent Field Test study results also indicate that most, if not all, crewmembers following long duration spaceflight experience motion sickness symptoms. There are considerable variations between crewmembers, with some unable to complete a short Field Test battery at the landing site. Bed rest studies have revealed that aerobic and resistance exercise alone is not sufficient to mitigate decrements in postural stability induced by body unloading, indicating the need for targeted countermeasures for post-flight postural and gait disturbances. Near-term investigations are also being planned to characterize basic neurovestibular changes during and after longer duration missions (i.e. 1 year ISS). Currently, operational countermeasures are being developed to address balance and locomotor deficits as well as motion sickness post-flight. This includes preflight and inflight training exercises, post-flight rehabilitation, sensory augmentation, and combining non-pharmacological countermeasures with new anti-motion sickness drug formulations. Future plans also include defining standards that are tied to fitness for duty for exploration tasks and provide a quantitative index of readiness to perform key exploration tasks, as well as validating self-administered integrative countermeasure approaches suitable for autonomous exploration missions. HHC is working with HFBP and SR in support of the Integrated CBS plan (see section 4.2.1).

4.3.8 Risk of Impaired Performance Due to Reduced Muscle Mass, Strength & Endurance (Short Title: Muscle) and Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity (Short Title: Aerobic)

Prolonged exposure to spaceflight results in diminished exercise tolerance, decreased cardiac and sensorimotor function, reduced bone mineral density, and the loss of muscle mass and strength. NASA's vision for future exploration missions depends on the ability to protect astronauts' health and safety for performance of EVA, in both 0-G and during ambulation in partial gravity, and to allow astronauts to safely egress from vehicles in a variety of landing scenarios, including water landing upon return to Earth and undefined planetary/lunar landings. The amount of deconditioning and the time required to recover from microgravity exposure will influence the astronauts' ability to complete physically demanding tasks during an exploration mission,

including habitat construction and EVA, especially when the astronaut must work against a semi-rigid pressurized suit during EVA for up to 8 hours.

For 6-month ISS missions, if crew launch with regular adherence to an effective exercise schedule, have access to adequate exercise countermeasure systems, and perform exercise countermeasures as prescribed in-flight, then on average, they return above the task standard for aerobic fitness and muscle strength. Astronauts perform daily aerobic and resistance exercise during International Space Station (ISS) missions to maintain physical fitness; however, to date these exercise countermeasures have not been fully protective. Briefly, maximal aerobic capacity (VO_2pk), lower body muscle cross-sectional area and strength are decreased by approximately 10% to 15% after short-duration (~14 days) and long-duration (~6 months) ISS spaceflight and simulated microgravity exposure (i.e., bed rest). Since installment of the Advanced Resistance Exercise Device (ARED) on ISS in 2009, pre to post-flight reductions in knee extension and flexion strength are 7% and 12.5%, respectively, average ankle flexion and extension strength losses are ~12%. Importantly, there is considerable variability among crewmembers with respect to post-flight changes in fitness, with some crewmembers experiencing no or minimal losses and others with 30% decrements in VO_2pk or muscle strength. Muscle strength and aerobic fitness standard updates have been proposed for 0g EVA and vehicle egress. Additional data collection and funding is required to develop partial gravity EVA standards. These standards will provide information necessary for programs to develop requirements for systems and hardware (e.g., spacesuits, Environmental Control and Life Support System (ECLSS), exercise hardware) needed to maintain these performance capabilities.

4.3.9 Risk of Orthostatic Intolerance During Re-Exposure to Gravity (Short Title: OI)

About 20-25% of Space Shuttle crewmembers and more than 60% of the crewmembers who participate in long-duration missions (4-6 months) experience hypotension and presyncope during a10-minute 80° head-up tilt test on landing day. The current suite of countermeasures to mitigate orthostatic intolerance (OI) during re-exposure to gravity includes on-orbit exercise, suit cooling, end-of-mission fluid loading, recumbent posture during re-entry and landing, and lower body compression garments. Additionally, medical personnel provide ground support at the vehicle landing site and administer intravenous fluids, as needed, to mitigate blood volume loss. Some astronauts will continue to wear lower body compression garments for several days after landing to manage symptoms. Given the maturity of the mitigation solutions, research on this risk is being phased out and the mitigations are being transitioned to operational use.

4.3.10 Risk of Spaceflight Associated Neuro-ocular Syndrome (SANS) (Short Title: SANS)

Through 2019, twenty-eight crewmembers who participated in long-duration space missions have experienced structural and/or functional changes to their eyes that include optic-disc edema, globe flattening, choroidal folds, and hyperopic shifts. NASA has termed the risk of developing these ocular changes the *Spaceflight Associated Neuro-ocular Syndrome (SANS)*. Not all of these effects develop in affected crewmembers. The percentage of affected crewmembers varies for each sign: optic disc edema, 10/74 (14%); retinal and/or choroidal folds, 12/58 (21%); globe flattening, 17/58 (29%); and change in refractive error ≥0.75D, 10/58 (17%). Objective quantification of optic disc edema with optical coherence tomography suggests up to 69% of

USOS astronauts flying long-duration missions to the ISS show early signs of edema, suggesting that longer duration missions may impact a greater number of astronauts. It is thought that the ocular structural changes are triggered by the cephalad-fluid shift that crewmembers experience during weightlessness, but because not all crewmembers develop SANS, it is likely that some environmental, genetic, anatomical, or lifestyle related factors incur greater susceptibility or protection to SANS.

Hypotheses to explain deficits in visual acuity and structural changes in the eye include elevated pressure in the cephalad veins and increased resistance in outflow from the eye veins, increased intracranial pressure, localized elevation of cerebrospinal fluid pressure within the sheath of the orbital optic nerve, and impaired drainage in the cephalad lymphatic system. The goal of several ongoing and future research is to test these hypotheses.

Many of the symptoms of SANS that develop during spaceflight recover on return to 1G; however, some structural changes are permanent or do not fully recover. It is currently unknown whether these structural changes will cause long-term decrements in visual acuity, visual fields, or have other functional consequences. Follow up imaging and testing of affected and non-affected crewmembers is currently ongoing to determine if the rate of ocular functional decrements increases years after the initial physiologic insult.

4.3.11 Risk of Adverse Health Effects Due to Host-Microorganism Interactions (Short Title: Microhost)

While current preventative measures limit the presence of many of the medically significant microorganisms during a mission, infections cannot be completely eradicated. Evidence indicates that certain characteristics of microorganisms are altered when microbes are cultured in spaceflight. These alterations include changes in virulence, concentration, and diversity. Because of this evidence, the HRP plans to compare microbial diversity, microbial characteristics, and specific host-microorganism interactions in spaceflight and ground-based conditions in close collaboration with NASA’s Space Biology Program and by integrating the research between the microhost, food, and immune disciplines. This comparison will be used to determine the risk of microbiologically-induced adverse health effects during a spaceflight mission. Using this microbial risk assessment, the HRP will determine whether current operational and engineering controls used to mitigate these microbiological risks during human exploration of space are adequate or additional countermeasures should be developed.

4.3.12 Risk of Reduced Crew Health and Performance Due to Hypobaric Hypoxia (Short Title: Hypobaric Hypoxia)

Future human exploration missions will require a robust and flexible EVA architecture that existing operational denitrogenation protocols, suit egress/ingress methods and EVA suit hardware do not currently provide. This robust EVA architecture can be achieved through the combination of an intermediate staged atmosphere of 8.2 psia and 34% O_2 in the habitat, variable pressure EVA suits that are compatible with a 8.2 psia habitat pressure, and highly efficient EVA ingress and egress. Oxygen enrichment in the habitat is currently limited to 34% to reduce the risk of flammability, but this enriched environment is mildly hypoxic to humans. Astronauts will inhale partial pressure of O_2 (P_IO_2) of 128 mmHg. Astronauts have experienced this P_IO_2 in

space before – the Space Shuttle atmosphere was 10.2 psia / 26.5% O_2 (P_IO_2 = 127 mmHg) – but they were only exposed to this P_IO_2 for up to 10 days.

Decreased levels of O_2 to the body's organs and systems affects all physiological functions. However, the 8.2 psia and /34% O_2 environment induces only mild hypoxic stress, which healthy individuals can tolerate well on Earth. For example, millions of people live at altitudes higher than 4000 ft. and even more people experience mild transient hypoxia during airplane flights at 5000-8000 ft. However, additive effects of an 8.2 psia and 34% O_2 environment and other spaceflight factors, such as microgravity, elevated CO_2, mission stress, space radiation, and cycling between mild hypoxia and mild hyperoxia during EVA, might impair human health and performance, although this has not been established.

Should the 8.2 psia and 34% O_2 become the baseline for exploration missions, we need to understand how varying periods of exposure to this level of hypobaric hypoxic stress affects the astronaut. Using data from past shuttle flights that operated at a mild hypobaric hypoxic environment for short durations of time, we can evaluate how the increased hypobaric stress contributes to the overall physiological stress associated with this engineered environment, however, the data from Shuttle is limited and exploration scenarios could vary significantly from our Shuttle experience. In addition, an inflight surveillance program may need to be developed to understand if and how this mild hypobaric hypoxia affects astronauts for increased durations of time.

4.4 Space Radiation

4.4.1 Risk of Radiation Carcinogenesis (Short Title: Cancer)

One of the many environmental hazards in space flight is exposure to chronic, low dose-rate high energy particles that make up the space radiation environment. These exposures increase the likelihood of cancer morbidity and mortality to crew over their lifetimes. Due to lack of resource availability and impracticalities in spacecraft design, shielding crew from the high energy particles that comprise the space radiation environment (87% protons, 12% helium, 1% higher charge and energy [HZE] ions) remains imperfect, leaving crew members exposed to the space radiation field, particularly during deep space and interplanetary missions. To mitigate the risk of radiation carcinogenesis, the Space Radiation Element has implemented a multi-effort research strategy to reduce the risk of astronaut morbidity and mortality from cancer.

Ground-based analog studies conducted at the NASA Space Radiation Laboratory (NSRL) are used to better characterize the role of radiation quality and dose-rate in space radiation carcinogenesis. Recent commissioning of various galactic cosmic rays (GCR) simulation beams allows the Space Radiation Element to direct research efforts to understand potential interactions between radiation types in a mixed field exposure approximating the local space radiation environment inside a spacecraft during space flight. The interaction of other space flight stressors in modifying the risk of radiation carcinogenesis will be investigated. The information gained through these ongoing and future ground-based studies will help to characterize the carcinogenic risk from space radiation exposures as well as inform uncertainties in risk estimates.

The initiation and implementation of the NASA Specialized Center of Research (NSCOR) tasked groups to understand the different mechanisms of radiation carcinogenesis specific to the tissue types hypothesized to be major contributors to overall cancer risk including lung, breast, colon, the blood and lymphatic system (leukemia and lymphoma), liver, and brain. These efforts have led to the development of tissue-specific research models to support the identification of tissue-specific risk factors as well as contribute necessary information to aid in the early detection of pre-malignant disease and health monitoring through the identification of biomarkers.

New, data-driven computational models are under investigation to assess radiation carcinogenesis risk and translate ground-based radiation research results to astronauts. The baseline NASA radiation carcinogenesis risk model is primarily based on human epidemiological data from the Life Span Study of atomic bomb survivors (LSS). Other radiation exposed cohorts, including the Million Person Study (MPS), will be assessed and incorporated to inform risk of radiogenic cancers arising from exposures more similar to the astronaut population. Specifically, the National Council of Radiation Protection (NCRP) has been commissioned to examine the role of sex dependence on radiogenic cancer rates. To test this and other risk model assumptions (including transfer of risk across populations, use of average incidence and mortality rates for the U.S. population, role of attained age and age at exposure, and radiation quality and dose-rate effects) past, current, and future data will be assessed using advanced biostatistical and computational methods. Further, to more fully understand the uncertainties surrounding assessment of radiation carcinogenesis risk ensemble modeling approaches are being explored.

Advances in terrestrial cancer early detection and treatment modalities will be monitored utilizing the 2017 Potomac Institute report entitled “Projection of U.S. Cancer Mortality and Incidence Rates” as a baseline. Ongoing clinical trials and translational research in cancer prevention and treatment will continue to be monitored and supported where appropriate. Collaborative committees with federal and state agencies (National Cancer Institute (NCI), National Institute of Allergy and Infectious Diseases (NIAID), Cancer Prevention and Research Institute of Texas (CPRIT)) and cancer related professional societies (American Association for Cancer Research, American Society of Therapeutic Radiation Oncology, Radiation Research Society, etc.), and other stakeholders will monitor advancements in early detection and treatment outcomes. These advances will be utilized to inform best clinical practices for monitoring astronaut health during their career and into retirement. Interagency collaboration will also help develop infrastructure to support identification and validation of medical countermeasures to reduce carcinogenesis risk in appropriate biological models.

The Space Radiation Element will continue to sponsor studies utilizing a systems biology approach to provide a framework to integrate mechanistic studies of cancer risk across multiple levels of understanding (molecular, cellular, tissue, systems, and organismal levels). Limited informatics data sets (transcriptomics, genome sequencing, etc.), and the establishment of tissue archives will provide resources for future analysis to answer specific questions in a timely fashion. Tech watches to explore new approaches in terrestrial cancer research and model development will also be implemented to leverage the broader field of cancer research to support tissue-specific risk assessment.

Specific goals, deliverables, and recommended targets for closure efforts are outlined in the eight Cancer Gaps and questions can be directed to the Space Radiation Element Scientist, Deputy Element Scientist, and Discipline Leads.

5 CONTENT IN THE HUMAN RESEARCH ROADMAP

The IRP contains detailed research plan information in a standard format, including a graphical depiction via Risk Approach Plan charts and specific information fields. Through the HRR the information is accessible to the public.

5.1 Risk Page

Each HRR risk or concern item has a risk page with relevant information, including short title, risk statement, context, and mitigation strategy, as detailed below. A risk rating for DRMs, a link to the Risk Approach Plan chart, and a listing of the gap(s) that must be addressed before each risk is mitigated are also included on each risk page.

- Short Title: assigned to the risk as a matter of convenience and is used internally within HRP.
- HRP Risk Status: this field provides information on the current status of the risk (or concern) from the HRP perspective.
- Risk Statement: this is the HSRB-approved Risk Statement for each risk that concisely describes specific condition of relevance to human spaceflight missions and the negative outcomes that may potentially result.
- Context: this is the HSRB-approved Risk Context for each risk that briefly describes the what, when, where, how, and why of the risk or concern by stating the circumstances and scenario(s) considered, any known contributing factors, operational relevance, evidence or related issues to provide background information not captured in the risk statement.
- Mitigation Strategy: the approach strategy for the mitigation of the risk is outlined in this section. For instance, the strategy may be to first determine space normal physiology, then identify specific countermeasures.

Each Risk Approach Plan chart, which shows the forecasted timeline of high level risk milestones and a strategic flow of the research logic for improving risk ratings, is accessed through the PRR tab on each risk page. At this time, only the BMed, HSIA and Sensorimotor Risk Approach Plan charts are available in the HRR. The Risk Approach Plan Charts for the other risks are in development. The Risk Approach Plan Chart Overview, seen in Section 6, shows an example of the chart. Specific highlighted risk milestones shown in the top bar represent thresholds in movements of the risk ratings (e.g., red to yellow to green).

5.2 Gap Page

Each gap in knowledge or in the ability to mitigate each risk, as identified by the HRP Elements, is listed in the IRP. Each gap page includes a description of the gap, which typically contains the

initial state and approach, a target for closure, and a listing of the task(s) that are required to address the gap.

5.3 Task Page

Each task, as identified by the HRP Elements, required to address a gap is named in the IRP. In some cases, a task may address multiple gaps within a risk or gaps across multiple risks. Each task page typically contains information on the responsible HRP Element, Principal Investigator (PI), procurement method, the task's overall aims, resources needed (e.g., ground analog or flight), and deliverable(s). The level of detail in the task information may depend on the task's maturity level, with those tasks in the near future typically having higher fidelity and more complete information compared to tasks planned farther in the future.

In some cases, organizations outside the responsible Element, such as other HRP Elements, other divisions within NASA, the Translational Research Institute for Space Health (TRISH), or even an international partner, are responsible for implementation of specific tasks in the research plan. These collaborating organizations are identified within this section and the responsible Element will coordinate with the appropriate organization in these cases.

Each deliverable in the IRP is classified by category and subcategory. The deliverable categories and subcategories are listed in the table below and briefly described in the text that follows. This information is verbatim from HRP-47069, and is reprinted in the IRP as a matter of convenience for the reader.

TABLE 1. CATEGORY OPTIONS FOR DELIVERABLES

Category	Subcategory	Example Customers	Example Deliverables
Requirement or Guideline	Vehicle/Suit Design	Vehicle/Mission Definition & Development Program	Suit Design Requirements
	Flight Rule/ MRID/Practice Guidelines	Medical/Mission Operations	Procedures, Best Practices
Technology or Tool	Systems Solutions, Prototype Hardware or Software	Medical Operations, Vehicle/Mission Definition & Development Program	Food packaging technologies, In-flight Blood Analysis Technology, User interface prototype
	Clinical Care, Medical Informatics, Human Performance Data Collection Methods	Medical Operations, Vehicle/Mission Definition & Development Programs	Training Protocol for Effective Medical Operations, Questionnaires
	Computational Models, Software	Medical Operations, OCHMO, Vehicle/Mission Definition & Development Program	Radiation Risk Assessment models, Digital Astronaut models, Net habitable volume (NHV) model
	Database	Human Research Program, Medical Operations, Vehicle/Mission Definition & Development Program	Database created by gathering existing data
	Simulation	Medical Operations, Vehicle/Mission Definition & Development Program	Decision support tool, Integrated Medical Model
Countermeasure	Prescription	Medical Operations, OCHMO	Integrated Resistance and Aerobic Training Study
	Protocol	Medical Operations, OCHMO	Prebreathe Protocol for Exploration Systems
	Prototype Hardware or Software	Medical Operations, OCHMO, Vehicle/Mission Definition & Development Program	Prototype treadmill harness for use during exercise countermeasures, computer-based training for stress management
	Pharmaceutical or Nutritional Supplement	Medical Operations, OCHMO, Vehicle/Mission Definition & Development Program	Pharmaceutical recommendations resulting from Vitamin D Study
Standard	Update	OCHMO	Nutrition Standard Update
	New	OCHMO	Lunar Dust PEL
Risk Characterization, Quantification	Evidence	OCHMO, HSRB	NRA final report, Evidence Report, Conceptual Model
Study Results	Customer Requested Study or Analysis	Vehicle/Mission Definition & Development Program	Trade Study Analysis Results and Recommendations

Requirement or Guideline

The "Requirement or Guideline" deliverable is chosen when a task will result in information that is relevant to a requirement (or requirements set) or guideline owned by another Program or to another Element. For example, the task may end up informing the requirements on the lighting spectrum in the vehicle, or the results may apply to the radiation shielding design, or conclusions may be reached that apply to the food system from nutritional risk work. These deliverables often feed the design of the vehicle and its sub-systems. As inputs to requirements, they primarily are applied in the SRR timeframe.

Technology or Tool

The "Technology or Tool" deliverable covers a broad spectrum of developments that includes hardware, software, systems solutions, new processes, inventions, innovative methods, design tools, databases, computational models, or systems simulations. These deliverables support HRP research, as well as external customers.

Countermeasure

A "Countermeasure" deliverable is a specific protocol that is developed and validated to prevent or reduce the likelihood or consequence of a risk. Countermeasures may be medical, physical, or operational entities, such as a pharmaceutical or nutritional supplement, prototype hardware or software, or specific exercise routines, respectively. A countermeasure deliverable is usually specific and extensive enough to require validation in spaceflight. For instance, if a ground task results in a spaceflight task that is called a "flight validation study," it likely is a countermeasure. Note that in some cases the countermeasure will also affect mission operations (in areas like timelines). Some general direction on this, however, is that the countermeasure usually does not affect the design of the spacecraft, and is applied in the mission operations phase as a solution to a problem; thus, the countermeasure deliverables generally affect the mission operations PDR or CDR phases.

Standard

A "Standard" deliverable often begins as a Risk Characterization, Quantification activity. Preliminary information about a risk is often incomplete. HRP would not be in a position to recommend a standard update, but preliminary information would represent a significant step toward such a recommendation. Risk Characterization tasks can feed into other tasks that also have information for standards, or they can be combined with other "Standard" deliverables to result in a recommendation for a new or updated standard.

A "Standard" deliverable is mandated when the program is ready to provide the OCHMO with a new standard or a recommended update to an existing health or performance standard. A key test of the "Standard" as a deliverable is that the program is ready to write the text for the recommended standard update. Since the standards are applied in a broad spectrum for design and operations, these deliverables can be linked to any of the system design or mission operations milestones. They should be applied as early as possible in the design phase or mission operations development phase, so, most often, they are necessary prior to SRR.

Risk Characterization, Quantification

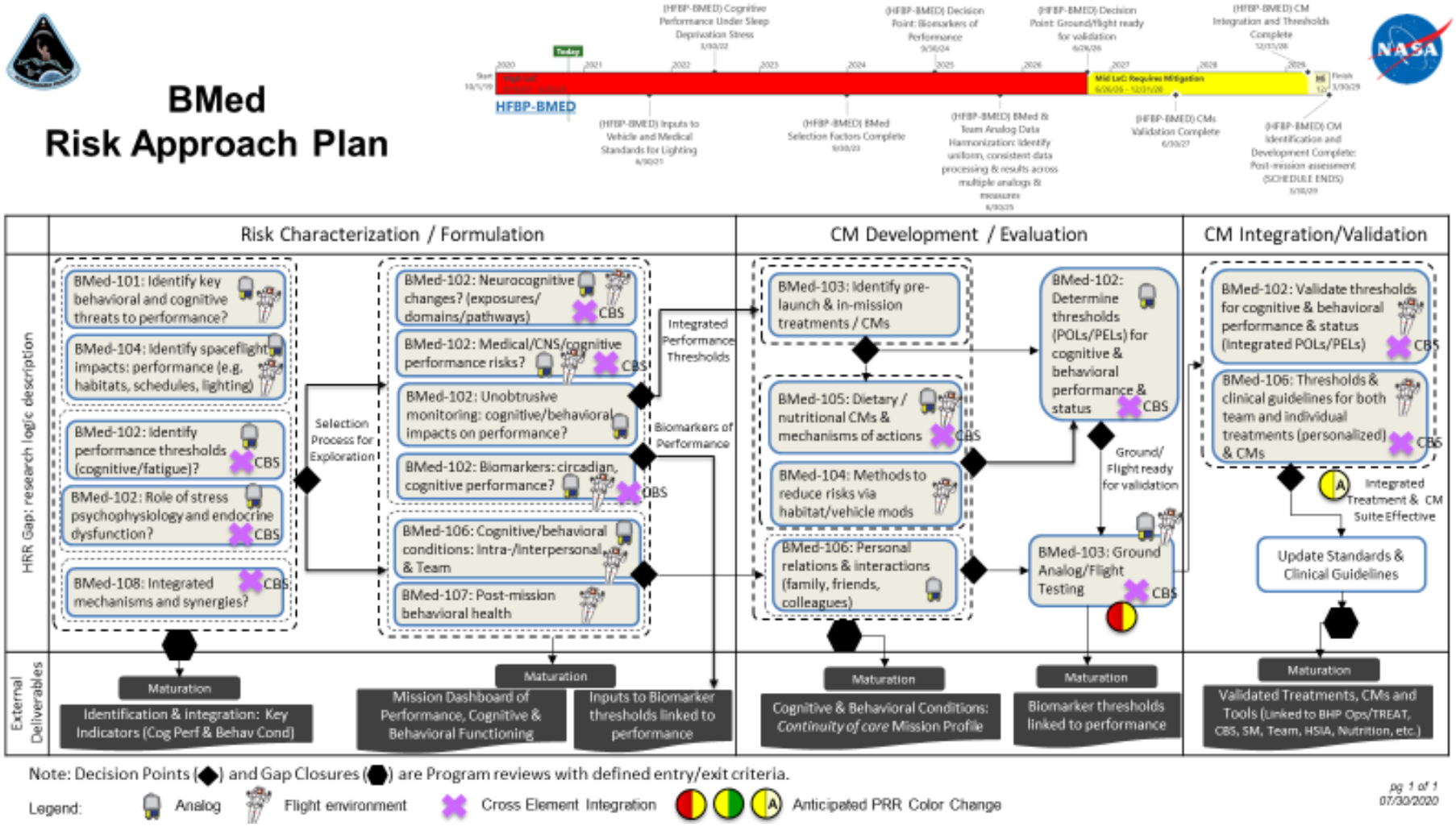
When a task results in information that must be considered by the HSRB, medical operations community and/or OCHMO, this deliverable is used. This deliverable is applicable when it impacts the rating of the likelihood or consequence of a risk. It is also applied when the results of the study are anticipated by the space medical operations community.

Study Results

A study or analysis is requested by an HRP customer or Element. This is often a trade study that includes analysis, results and recommendations. Data mining or literature review tasks typically produce this type of deliverable.

6 RISK APPROACH PLAN CHART

Risk Approach Plan Chart Example: Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders (BMed)



Verify that this is the correct version.

APPENDIX A - LINK TO HUMAN RESEARCH ROADMAP

Risk, gap and task information that was formerly contained in Appendix A is now located in the HRR:

https://humanresearchroadmap.nasa.gov/

HHC Infrastructure Gaps are not linked to any of the HRP risks; they may be found by searching "GAPS" for HHC1, 2, 3 or 5.

APPENDIX B - TECHNOLOGY READINESS LEVELS (TRL) AND COUNTERMEASURE READINESS LEVELS (CRL)

Definition of Technology Readiness Levels (TRL) & Countermeasure Readiness Levels (CRL)

[from HRP Science Management Plan, HRP-47053]

Countermeasure Readiness Level (CRL)		Technology Readiness Level (TRL)
Phenomenon observed and reported.	**CRL/ TRL 1**	Basic principles observed and reported: Transition from scientific research to applied research. Essential characteristics and behaviors of systems and architectures.
Hypothesis formed to understand phenomenon. Preliminary research & occupational surveillance studies completed to evaluate hypothesis & associated parameters.	**CRL/ TRL 2**	Technology concept and/or application formulated: Applied research. Theory and scientific principles are focused on specific application area to define the concept. Characteristics of the application are described.
Hypothesis refined with spaceflight or high fidelity terrestrial analog study(s)	**CRL/ TRL 3**	Analytical and experimental critical function and/or characteristic proof-of concept: Proof of concept validation. Active Research and Development (R&D) is initiated with analytical and laboratory studies.
Countermeasure hypothesis formed and tested in animal and cellular analogs.	**CRL/ TRL 4**	Component/subsystem validation in laboratory environment: Standalone prototyping implementation and test. Integration of technology elements.
Countermeasure hypothesis formed and tested in humans and terrestrial analogs.	**CRL/ TRL 5**	System/subsystem/component validation in relevant environment: Thorough testing of prototyping in representative environment. Basic technology elements integrated with reasonably realistic supporting elements.
Countermeasure tested & validated with humans in spaceflight. Proven to mitigate risk on limited number of subjects.	**CRL/ TRL 6**	System/subsystem model or prototyping demonstration in a relevant end-to-end environment (ground or space): Prototyping implementation on full-scale realistic problems. Partially integrated with existing systems.
Flight countermeasure qualified for particular vehicle/DRM through ground or flight testing.	**CRL/ TRL 7**	System prototyping demonstration in an operational environment (ground or space): System prototyping demonstration in operational environment. System is at or near scale of the operational system, with most functions available for demonstration and test.
Flight countermeasure integrated with operational systems and mission validated through test and demonstration in spaceflight.	**CRL/ TRL 8**	Actual system completed and "mission qualified" through test and demonstration in an operational environment (ground or space): End of system development. Fully integrated with operational hardware and software systems.
Countermeasure system thoroughly demonstrated and tested in its operational environment. Thoroughly proven operationally with numerous subjects to mitigate risk(s).	**CRL/ TRL 9**	Actual system "mission proven" through successful mission operations (ground or space): Fully integrated with operational hardware/software systems. Actual system has been thoroughly demonstrated and tested in its operational environment.

APPENDIX C - LIST OF ACRONYMS

A

AI	artificial intelligence
ARED	Advanced Resistance Exercise Device

B

BEO	beyond Earth orbit

C

CBS	CNS/BMed/Sensorimotor
CDR	Critical Design Review
CHMO	Chief Health and Medical Officer
CNS	central nervous system
CO_2	carbon dioxide
CPRIT	Cancer Prevention and Research Institute of Texas
CR	Change Request
CRL	Countermeasure Readiness Level
CSA	Customer-Supplier Agreement
CVD	cardiovascular disease

D

DCS	decompression sickness
DNA	deoxyribonucleic acid
DRM	Design Reference Mission

E

EVA	Extravehicular Activity
ExMC	Exploration Medical Capability

F

G

G	gravity
GCR	galactic cosmic rays

H

H_2O	water
HEOMD	Human Exploration and Operations Mission Directorate
HERA	Human Exploration Research Analog
HFBP	Human Factors and Behavioral Performance
HHC	Human Health Countermeasures
HIDH	Human Integration Design Handbook
HRP	Human Research Program
HRPCB	Human Research Program Control Board
HRR	Human Research Roadmap
HSIA	Human Systems Integration Architecture
HSRB	Human Systems Risk Board
HZE	High Charge and Energy

I

IRP	Integrated Research Plan
ISS	International Space Station
ISS FIT	ISS Food Intake Tracker
ISS UPA	ISS Urine Processor Assembly
IVD	intervertebral disc

J

JSC	Johnson Space Center

K

L

LEO	low Earth orbit
LSAH	Lifetime Surveillance of Astronaut Health
LSDA	Life Sciences Data Archive
LSS	Life Span Study
LOC	Loss of Crew

M

MCC	Mission Control Center
MPS	Million Person Study
MRID	Medical Requirements Integration Document

N

NASA	National Aeronautics and Space Administration
NCI	National Cancer Institute
NCRP	National Council on Radiation Protection
NHV	net habitable volume
NIAID	National Institute of Allergy and Infectious Diseases
NRA	NASA Research Announcement
NSCOR	NASA Specialized Center of Research
NSRL	NASA Space Radiation Laboratory

O

O_2	oxygen
OCHMO	Office of the Chief Health and Medical Officer
OI	orthostatic intolerance

P

PDR	Preliminary Design Review
PEL	permissible exposure limit

PI	principal investigator
P_IO_2	partial pressure of O_2
POL	performance outcome levels
PRD	Program Requirements Document
PRR	Path to Risk Reduction

Q

R

R&TD	research and technology development
REV.	Revision
RFP	Request for Proposal
RID	Review Item Discrepancy
ROI	Research Operations and Integration

S

SANS	spaceflight associated neuro-ocular syndrome
SBIR	Small Business Innovation Research
SMO	Supplemental Medical Objective
SR	Space Radiation
SRR	System Requirements Review
STD	Standard

T

TBD	to be determined
TRISH	Translational Research Institute for Space Health
TRL	Technology Readiness Level

U

UPCG	Unique Processes, Criteria, and Guidelines
USOS	US Orbital Segment

VWXYZ