
**Human Research Program
Human Health Countermeasures Element
Bone and Muscle Risk
Standing Review Panel (SRP)
Final Report**

November 2009

I. Executive Summary & Overall Evaluation

The Bone and Muscle Risk Standing Review Panel (SRP) met at the NASA Johnson Space Center (JSC) on October 4-6, 2009 to discuss the areas of current and future research targeted by the Human Health Countermeasures (HHC) Element of the Human Research Program (HRP). Using evidence-based knowledge as a background for identified risks to astronaut health and performance, NASA had identified gaps in knowledge to address those risks. Ongoing and proposed tasks were presented to address the gaps. The charge to the Bone and Muscle Risk SRP was to review the gaps, evaluate whether the tasks addressed these gaps and to make recommendations to NASA's HRP Science Management Office regarding the Panel's review. The Bone and Muscle Risk SRP consisted of scientists who are experts in muscle, bone, or both and could evaluate the existing evidence with sufficient knowledge of the potential effects of long duration exposure to microgravity. More important, although expertise in basic science is important, the SRP was requested to evaluate the practicality of the proposed efforts in light of the realistic demands placed on the HRP. In short, all tasks presented in the Integrated Research Plan (IRP) should address specific questions related to the challenges faced by the astronauts as a result of prolonged exposure to microgravity. All tasks proposed to fill the gaps in knowledge should provide applied, translational data necessary to answer the specific questions.

Several presentations were made to the SRP during the site visit and the SRP spent sufficient time to address the panel charge, either as a group or in separate sessions for the Bone and Muscle Risk subgroups. The SRP made a final debriefing to the HRP Program Scientist, Dr. John B. Charles, on October 6, 2009.

Taking the evidence and identified risks as givens, the SRP concluded that 1) integration of information should lead to a more comprehensive approach to identifying the gaps, 2) not all tasks addressed the gaps as stated in the IRP, 3) better access should be given to the SRP to existing data to include in its review, and 4) there were some missing gaps and tasks. As a result the SRP recommended 1) combining certain gaps, which in some cases were addressed with identical tasks, 2) additional gaps and tasks to address some of the gaps, 3) deleting some gaps and tasks to better focus the efforts of NASA's HRP in prioritizing their efforts, and 4) prioritizing gaps to address significant issues needing resolution in the short term while maintaining an awareness of long-term goals.

The SRP commended the efforts by the HHC Element to integrate knowledge gaps and design tasks to address the higher order questions. This integration did not apply to the Bone and Muscle Risk alone, but the musculoskeletal system as its functions integrate with issues in

nutrition, exercise, the nervous system regarding sensorimotor integration, and the hormonal system with regard to the integrated function of all physiological systems. The following report conveys the SRP's recommendations as a result of its deliberation during meetings and communications at the site visit in October 2009.

II. Critique of Bone Gaps and Tasks

RISK OF ACCELERATED OSTEOPOROSIS

B1: Is bone strength completely recovered with recovery of BMD?

The SRP recommends revising this gap to: Is there an increased lifetime risk of fragility fracture/osteoporosis in astronauts; Is bone strength completely recovered post flight, and does BMD reflect it; What are risk factors for poor recovery of BMD/bone strength?

Current Tasks:

- Monitoring of Bone Loss Bio-Markers in Human Sweat a non-invasive, time efficient means of monitoring bone resorption markers under micro and partial gravity loading conditions – Clarke
- Recovery of Bone Quantity and Quality upon Simulated Spaceflight as a Function of Exposure Frequency, Genetics, and Gender –Judex
- Bone Countermeasure Study – TBD
- Epidemiological Analyses of Risk Factors for Bone Loss and Recovery Related to Long Duration Space Flight – Amin
- Bone Recovery Study – TBD
- Contributors to Long-Term Recovery of Bone Strength following Exposure to Microgravity – Hogan

Missing Tasks Identified by the SRP:

1. Epidemiology study of fracture incidence in retired astronauts. Recommend that this be integrated with B29. (Note: The SRP recognizes that this may be ongoing in the Longitudinal Study of Astronaut Health (LSAH), but recommend it should be explicitly stated as addressing this important gap).
2. Use of existing databases to identify potential risk factors for poor recovery (data mining).

B3: What pharmaceuticals against bone loss are best used and how? MO5: Determine how can osteoporosis treatments be employed?

The SRP agrees that this is a relevant gap.

Current Tasks:

- Bisphosphonates as a countermeasure to space flight induced bone loss, SMO-021 – LeBlanc
- Space Radiation and Bone Loss: Lunar Outpost Mission-Critical Scenarios and

Countermeasures –Bateman

- Maintaining Musculoskeletal Health in the Lunar Environment – Bloomfield

Missing Tasks Identified by the SRP:

1. Need to evaluate other new drugs that have a better safety profile, acceptance, efficacy, and convenience. This may include animal and bed rest studies. (Note: Evaluations of such pharmaceuticals need to be integrated with renal stone assessment and risk).
2. Need to study the interactions among pharmaceuticals and exercise interventions.

B10: What is the time course of bone loss during flights >90 days on ISS and during Lunar Outpost missions?

The SRP recommends revising this gap to emphasize the following gaps in knowledge:

- *Is there a plateau in the loss of bone mass?*
- *What happens to bone loss during flights longer than 90 days and longer than 180 days?*
- *Can bone turnover markers be used to monitor bone loss?*
- *Is there a non-invasive test for measuring bone loss in flight?*
- *Are there gender differences in the time course of bone loss?*

Current Tasks:

- Monitoring of Bone Loss Bio-Markers in Human Sweat - a non-invasive, time efficient means of monitoring bone resorption markers under micro and partial gravity loading conditions - Clarke
- Recovery of Bone Quantity and Quality upon Simulated Spaceflight as a Function of Exposure Frequency, Genetics, and Gender – Judex
- Bone Countermeasure Study – TBD
- Epidemiologic Analyses of Risk Factors for Bone Loss and Recovery Related to Long Duration Space Flight – Amin
- Dietary Intake Can Predict and Protect Against Changes in Bone Metabolism During Space Flight and Recovery (ProK) – Smith

Missing Tasks Identified by the SRP:

1. Nutritional Status Assessment. SMO-016E (Nutrition SMO) and markers of bone formation and resorption.
2. *In vivo* bone measurements in flight-multiple time points across times of interest.
3. Development/validation of technology for monitoring bone loss.
4. Study whether bone and muscle deterioration is ameliorated by exposure to partial gravity environments.

B11: What are the effects of radiation on bone?

The SRP agrees that this is a relevant gap.

Current Tasks:

- Space Radiation and Bone Loss: Lunar Outpost Mission-Critical Scenarios and Countermeasures – Bateman

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- Maintaining Musculoskeletal Health in the Lunar Environment – Bloomfield

Missing Tasks Identified by the SRP:

None identified by the SRP.

B15: Can exercise hardware and protocol be designed to provide loads necessary to maintain bone health?

The SRP recommends revising this gap to: What exercise protocols are necessary to maintain skeletal health and can exercise hardware be designed to provide these?

Current Tasks:

- Integrated Countermeasure Study – TBD (Solicited in NRA 2009)
- Integrated Resistance and Aerobic Training Study (iRATS) – Ploutz-Snyder
- A Quantitative Test of On-Orbit Exercise Countermeasures for Bone Demineralization Using a Bed Rest Analog - Cavanagh
- Monitoring Bone Health by Daily Load Stimulus Measurement during Lunar Missions - Cavanagh
- An Integrated Musculoskeletal Countermeasure Battery for Long-Duration Lunar Missions - Lang

Missing Tasks Identified by the SRP:

None identified by the SRP.

N5: Can a single test monitor net bone calcium changes?

The SRP recommends revising this gap to: What is (are) the optimal test(s) to monitor bone turnover/calcium kinetics?

Current Tasks:

- Rapid Measurements of Bone Loss Using Tracer-Less Calcium Isotope Analysis of Blood and Urine - Anbar

Missing Tasks Identified by the SRP:

1. Integration of Nutrition SMO

N7: What are the potassium, magnesium, and phosphorus changes in relation to cardiovascular issues and bone loss?

The SRP agrees that this is a relevant gap.

Current Tasks:

- Nutrition Status Assessment. SMO O16E (Nutrition SMO) – Smith

Missing Tasks Identified by the SRP:

None identified by the SRP.

N14: What nutritional countermeasures can be used to mitigate bone loss?

The SRP recommends revising this gap to: What integrated nutritional, exercise, and pharmaceutical countermeasures can be used to mitigate bone loss?

Current Tasks:

- Dietary intake can predict and protect against changes in bone metabolism during space flight and recovery (ProK) – Smith

Missing Tasks Identified by the SRP:

1. Interactions among exercise, nutrition, and pharmaceutical countermeasures in altered weight bearing environments (bed rest, microgravity, partial gravity).
2. Integration of Nutrition SMO (especially Vitamin D).

MO5: Determine how can osteoporosis treatments be employed?

The SRP recommends revising this gap to: What integrated interventions should be used to prevent bone loss?

Current Tasks:

- Space Radiation and Bone Loss: Lunar Outpost Mission-Critical Scenarios and Countermeasures – Bateman
- Maintaining Musculoskeletal Health in the Lunar Environment – Bloomfield

Missing Tasks Identified by the SRP:

1. Need studies to evaluate dosing and modes of delivery and efficacy of various anti-osteoporosis medications, and their interaction with reduced mechanical loading due to micro- or partial gravity.

NEW GAP:

What are the risk factors for accelerated bone loss?

Suggested tasks for this new gap:

- Data mining for factors correlated with individual extent of bone loss, e.g. gender, activity, changes in weight, mission duration, numbers of missions, baseline parameters.

RISK OF BONE FRACTURE

B2: What new technologies are available for in-flight fracture diagnosis?

The SRP agrees that this is a relevant gap.

Current Tasks:

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- Assess Vertebral Compression Fractures (MRID)

Missing Tasks Identified by the SRP:

Additional tasks are needed to address this.

B10: What is the time course of bone demineralization during flights >90 days on ISS and during Lunar Outpost missions?

The SRP recommends revising the gap to emphasize the following gaps in knowledge:

(Note: The SRP recommends avoiding the term "demineralization". Use "bone loss").

- *Is there a plateau in the loss of bone mass?*
- *What happens to bone loss during flights longer than 90 days and longer than 180 days?*
- *Can bone turnover markers be used to monitor bone loss?*
- *Is there a non-invasive test for measuring bone loss in flight?*
- *Are there gender differences in the time course of bone loss?*

Current Tasks:

- Monitoring of Bone Loss Bio-Markers in Human Sweat - a non-invasive, time efficient means of monitoring bone resorption markers under micro and partial gravity loading conditions - Clarke
- Recovery of Bone Quantity and Quality upon Simulated Spaceflight as a Function of Exposure Frequency, Genetics, and Gender – Judex
- Bone Countermeasure Study – TBD
- Epidemiologic Analyses of Risk Factors for Bone Loss and Recovery Related to Long Duration Space Flight – Amin
- Dietary Intake Can Predict and Protect Against Changes in Bone Metabolism during Space Flight and Recovery (ProK) – Smith

Missing Tasks Identified by the SRP:

1. Nutrition SMO and markers of bone formation and resorption.
2. *In vivo* bone measurements in flight-multiple time points across times of interest.
3. Development/validation of technology for monitoring bone loss.

B29: What is the risk of vertebral compression fractures?

The SRP agrees that this is a relevant gap.

Current Tasks:

- Assess Vertebral Compression Fractures (MRID)

Missing Tasks Identified by the SRP:

1. Integration with other follow-up archives (available x-rays and lateral spine DXA).

NEW GAP #1:

What are the loads applied to bone in flight and during EVA activities and do they increase fracture risk in the light of expected bone loss?

Suggested tasks for this new gap:

- Need tasks to address this new gap.

NEW GAP #2:

Is there a risk of impaired fracture healing in reduced gravity and, if so, are there countermeasures or augmentation approaches to enhance fracture healing?

Suggested tasks for this new gap:

- Need tasks to address this new gap.

III. Critique of Muscle Gaps and Tasks

RISK OF IMPAIRED PERFORMANCE DUE TO REDUCED MUSCLE MASS, STRENGTH AND ENDURANCE

RISK OF REDUCED PHYSICAL PERFORMANCE CAPABILITIES DUE TO REDUCED AEROBIC CAPACITY

M2: What is the current status of in-flight and post-flight exercise performance capability? What are the goals/targets for protection with the current in-flight exercise program?

The SRP agrees that this is a relevant gap.

Current Tasks:

- Evaluation of Maximal Oxygen Uptake (VO_{2max}) and Submaximal Estimates of VO_{2max} Before, During and After Long Duration International Space Station Missions – Moore, A.
- Hypovolemia as A Model Of Space Flight: Cardiovascular Exercise Effects – Lee, S.

Comments regarding the Current Tasks by the SRP:

The measurement of maximal oxygen consumption will enable the assessment of exercise performance capability during flight. This maximal capability is influenced by several variables and the measurements in flight will provide valuable data as this capability influences the performance of many other physiological systems. The tasks will provide information on the third factor that limits the understanding of crewmember fitness. The two tasks, however, do not address the second half of the M2 gap; that is, the goals/target for protection with the current in-flight exercise program.

An additional concern expressed by one SRP member is that a true VO_{2max} measure (i.e. a plateau in VO_2 with increasing workload) is not a performance assessment. It is an assessment of oxygen delivery capacity. The individual VO_{2max} measures of a large population can distinguish a difference in performance with correlation of approx. 0.8 but that only explains 64% of the variance. Indeed, the correlation between the VO_{2max} of elite endurance athletes ranging from 72 ml O_2 /kg/min to 84 ml O_2 /kg/min is not significantly correlated with their individual performance and has a correlation coefficient of 0.3. Similarly, with the narrow range of VO_{2max} of the astronaut population, 50 ml O_2 /kg/min +/- 5ml O_2 /kg/min the prediction of performance for running would be low and for an EVA task would also be low. It is recommended that the final assessment of tasks consider this point.

M3: What tasks will be required for Exploration missions?

Current Tasks:

- Critical Mission Task (CMT) Assessment

Missing Tasks Identified by the SRP:

None identified by the SRP.

M4: What are the physiologic costs of Exploration mission tasks?

Current Tasks:

- Critical Mission Task (CMT) Assessment

Comments regarding the Current Tasks by the SRP:

These data, some of which already exist, can potentially be used to set threshold criteria relate to physiological cost and mechanical demands.

M6: Can a standardized performance measure of readiness for Exploration mission tasks be developed?

The SRP recommends that M3, M4 and M6 be restated, integrated into one gap, and included in a larger set of considerations for EVA tasks on ISS, tasks related to performance on the lunar surface, and on the surface of Mars. Tasks common to the various environments and tasks specific to each environment should be identified and evaluated and a series of studies is needed to estimate physiological cost and the mechanical loading on the human body. When this is accomplished, precedents can be set, thresholds defined, and valid input to interventions designed to maintain the required fitness levels can be developed.

Current Tasks:

- Critical Mission Task (CMT) Assessment

Missing Tasks Identified by the SRP:

1. The SRP further recommends that the biomechanical analysis measure the loads placed on the body in selected tasks to understand the kinetic demands on the human system and to provide information suitable for input to studies related to bone and muscle loading.
2. Knowledge of these loads will serve to validate the actual exercise accomplishments of each astronaut and can also be used to provide reaction force measurements, which is requisite information to the understanding of bone loads during selected tasks.
3. These tasks to be developed will emulate the task requirements of EVA activities, locomotion on the lunar surface, and on the surface of Mars.

M7: Can the current in-flight performance be maintained with reduced exercise volume?

M8: What is the minimum exercise regimen needed to maintain fitness levels for tasks?

M9: What is the minimum set of equipment needed to maintain those (M8) fitness levels?

Current Tasks:

- Flywheel Prescription Optimization – TBD
- Integrated Resistance and Aerobic Training Study (iRATS) – Ploutz-Snyder
- A New Harness for Use with Exercise Countermeasures – Validation of Improved Comfort and Loading with the Center for Space Medicine (CMS) Harness - Perusek
- Integrated Countermeasure Study – TBD (Solicited in NRA 2009)
- New Hardware Development – TBD
- Integrated Endurance and Resistance Exercise Countermeasures Using a Gravity-Independent Training Device - Adams
- Hydration Effects on Muscle – TBD
- Gender Effects on Muscle – TBD

SRP Recommendations:

There are eight proposed tasks to address the gaps M7, M8, and M9. Only two of these studies (iRATS and Integrated Countermeasure Study) address the gaps directly. Four other tasks (New Harness, Flywheel Optimization, New Hardware Development, and the Multi-Mode Exercise Device) involve hardware development and the last two tasks (hydration and sex differences) are not directly related to any of the gaps.

As these gaps are intended to provide information about the need to exercise during a six-month stay on the moon, it is not obvious how any of these tasks will explicitly provide this information. These tasks will provide data on exercise prescription and will develop new hardware, but will not inform us about the physiological demands of the tasks to be performed on the moon, whether or not the decline in performance of the

astronauts will impair their ability to perform these tasks, or how much exercise is needed to maintain an adequate fitness level to complete the tasks.

The SRP recommends that M7, M8, and M9 be combined into one gap with the primary hypothesis that shorter more intense bouts of resistance exercise together with exercise related to the development/maintenance of aerobic capacity will maintain bone and muscle integrity (i.e., decrease the rate of bone and muscle loss) and aerobic capacity better than using a protocol of lower intensity resistance exercise using more repetitions over a longer period of exercise time. M8, as stated/modified, would serve as the major gap with tasks related to M7 and M9 being addressed concurrently. The tasks identified above (i.e., the Adams Flywheel) would be done in parallel with other tasks proposed and these projects do not necessarily have to be done in series unless specifically identified by the PI. These efforts would have a significant impact on training methods related to, for example, the EVA task issues discussed above, save crew time on the ISS devoted to exercise, and provide a stimulus to develop the best, most comprehensive exercise protocols for fitness maintenance. If some of these studies, tasks, could be done in parallel this also would save time in reaching the stated goal of establishing a minimal exercise regimen needed to maintain fitness levels for tasks identified as critical to mission success.

We also give this gap our highest priority in the muscle group.

NEW GAP:

The SRP recommends that a new gap be developed to address sex differences and hydration.

Suggested tasks for this new gap:

- Need tasks to address this new gap.

M10: What is the correct set of ground-based studies (bed rest and others) to optimize exercise prescriptions for Lunar Outpost and Mars?

This gap will provide important data on issues related to bone, muscle, and cardiovascular changes as a result of exposure to a microgravity environment. This gap is also closely related to the previous series of gaps, M7 – M9, and could be a subset of studies under the general hypothesis stated in M8.

Current Tasks:

- Flywheel Prescription Optimization – TBD
- Integrated Resistance and Aerobic Training Study (iRATS) – Ploutz-Snyder
- A New Harness for Use with Exercise Countermeasures – Validation of Improved Comfort and Loading with the Center for Space Medicine (CMS) Harness - Perusek
- Integrated Countermeasure Study – TBD (Solicited in NRA 2009)
- New Hardware Development – TBD

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- Integrated Endurance and Resistance Exercise Countermeasures Using a Gravity-Independent Training Device - Adams
 - Hydration Effects on Muscle – TBD
 - Gender Effects on Muscle – TBD
 - Lunar EVA Study – TBD
 - Lunar Analog Pilot Study
 - An Integrated Musculoskeletal Countermeasure Battery for Long-Duration Lunar Missions - Lang

SRP Recommendations:

This gap asks about the correct set of ground-based studies to optimize exercise performance. These tasks all examine various aspects of exercise prescription, but none seeks to evaluate and validate the ground-based models. If the gap is real, it will need tasks to validate the models.

The SRP proposes previous data be reviewed through a meta-analysis to determine the match between outcomes from space flight and available ground-based models. For example, the SRP feels there may be an outcome that matches outcomes for leg muscles but not the trunk muscles. Furthermore, there appears to be minimal attention given the role of the upper extremities related to strength and endurance as well as attention given the etiology of low back pain reported by the astronauts post mission.

Some tasks have begun (e.g. iRATS) and others related to, for example, the development of new hardware are important.

Additionally, the SRP feels issues related to fatigue are not properly addressed in any of these tasks and propose this be a consideration in the development of future tasks.

SM7: Can an integrated post-flight functional task performance test be used on returning ISS crew members to obtain performance decrements?

This gap is considered to be extremely important and is rated #2 in importance by the SRP. The “translatability” of this information (i.e., its relevance to understanding performance decrements in returning crew members) will have a significant impact on interventions designed to mitigate losses in bone, muscle, and motor coordination. General health related issues in returning astronauts also has significance in maintaining their quality of life as they age into disability. Understanding the impact of extended exposure to microgravity is critical to improvement of countermeasures and interventions designed to maintain quality of life.

Current Tasks:

- Physiological Factors Contributing to Postflight Changes in Functional Performance - Functional Task Test (FTT) - Bloomberg
- Bed Rest Functional Task Test - Bloomberg
- Hypovolemia Factors of Influence Studies – TBD
- Gender Factors of Influence Studies – TBD
- Level of Fitness Factors of Influence Studies – Ploutz-Snyder

Missing Tasks Identified by the SRP:

None identified by SRP.

N9: Can nutritional countermeasures mitigate muscle loss?

The SRP recommends revising this gap to: Can nutrition and exercise countermeasures mitigate muscle loss?

This gap, as stated, needs to include exercise and nutritional countermeasures. This is a critical issue and rated highly by the SRP. Nutritional considerations are significant, but must be studied in concert with exercise and pharmaceutical interventions.

Current Tasks:

- Redox Modulation of Skeletal Muscle Function in Microgravity- Reid

Missing Tasks Identified by SRP:

1. Tasks that include exercise and nutritional countermeasures.

The SRP recommends that the N7 gap be included under the Muscle Risks:

N7: What are the potassium, magnesium and phosphorus changes in relation to cardiovascular issues and bone and muscle loss?

N15: Can nutrition/nutrients mitigate O2/radiation risks?

The SRP agrees that this is a relevant gap.

Current Task:

- Redox Modulation of Skeletal Muscle Function in Microgravity- Reid

Missing Tasks Identified by the SRP:

None identified by SRP.

CV2: What is VO₂max in-flight and immediately post-flight?

Current Tasks:

- Evaluation of Maximal Oxygen Uptake (VO_{2max}) and Submaximal Estimates of VO_{2max} Before, During and After Long Duration International Space Station Missions – Moore, A.
- Hypovolemia as a Model of Space Flight: Cardiovascular Exercise Effects – Lee, S.

SRP Recommendations:

The SRP agrees with these efforts, as it is critical information related to the evaluation

of the compromises to VO_2 capabilities/losses as a result of exposure to microgravity. Knowledge of the time course of changes, in flight, will prove valuable to understanding maintenance of crew fitness levels. We recommend the first $\text{VO}_{2\text{max}}$ test be conducted as soon as possible once on board.

IV. Discussion on the Strengths and Weaknesses of the Integrated Research Plan (IRP)

Strengths of the IRP

- Systematic approach to integrate disciplines.
- Active interest in breaking down silos.
- Logical approach to define task demands, i.e. working tasks during the various stages of the mission, i.e., EVA, work on the lunar surface.
- Focus on performance, with an appreciation for underlying mechanisms.
- Focus on best-evidence available to apply to the safety and performance of the crew.
- Work to date to integrate elements.
- Achievements in dietary and exercise measures.
- Interest in more centralized organization, fundamental top-down questions.
- Experienced staff.
- NASA has begun an excellent and much needed strategic planning effort to focus on research, data collection and integration, and resources. This process is an opportunity to breakdown silo thinking and allows integration of human physiology and performance.

Weaknesses of the IRP

- A major limitation is the small number of subjects who are engaged in different activities, excluding the possibility of randomized, controlled trials.
- There needs to be some resolution between crew medical privacy and the need for data. Need better access to de-identified data.
- Definition of "Space Normal" has been hampered due to HIPPA and informed consent.
- The relevance of ground-based models to predict in-flight physiology and responses to countermeasures needs to be clearer. There is a gap in evidence of system-specific appropriateness of ground-based studies of microgravity and of countermeasures.
- Absence of a strategy to unify and exploit databases: desirable to plan thorough data mining, use of archived samples, and use of advanced computational approaches to test for trends even with multiple variables.
- Importance of data beyond six months related to bone and muscle loss.
- The time frame for individual projects seems long. The IRP should place limitations on this.
- The major weakness of the IRP is the absence of a conceptual framework that integrates the priority (payoff) and urgency. Although the originators of the IRP may have this, it was not evident to the SRP. One method would be

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- to create orthogonal axes (each ranging from -10 to 10) with priority scaled on one axis and urgency on the second. Each gap would be rated for priority and urgency. This would help prioritize bed rest or mission studies and focus resources – high priority and high urgency would be first.
- The time frame for ground-based bed rest studies seems unrealistic for addressing relevant gaps. Several studies are scheduled over six years due to limits on facilities and available beds. If the gap is important, then the answer should be attained in a timely manner. For example, a pharmaceutical test that requires more than four years to test may be outdated by the time it is ready for space flight.
 - A unified database that contains all current and as much historical data as possible is not available for data mining across studies or across disciplines.

V. Discussion of Element Specific Questions in Addendum and/or Any Other Issues or Concerns the Panel Chooses to Address.

1. Are there obvious, unrealistic aspects in the IRP schedule?
 - The proposed projects have a very long time line making accomplishing these tasks very difficult and statistically very complex.
 - Some gaps and tasks seemed to be set because the projects were already in progress. A need to consolidate some gaps was identified and stated in this review. As a result of the proposed consolidation tasks should be set to answer higher priority questions.
2. Is the portfolio of tasks sufficiently complete to acquire an adequate description of the risks? For example, will “Space Normal” be adequately defined?
 - No. This may prove to be very difficult and of course, specific to specific projects.
 - As included in this report, several new tasks will have to be developed to address some of the more consolidated gaps.
3. Is the portfolio of tasks using or developing the appropriate technologies?
 - Yes, for the most part. The technologies identified seem appropriate but in light of the SRP comments new technologies may need to be developed.
4. Is the portfolio of tasks developing a sufficient number of countermeasures?
 - Discussion by the SRP and subsequently the individual Risk SRP Chairs indicated the tasks seemed to be countermeasure heavy, i.e., hardware development. The SRP recommends that more attention be given the gaps and then the tasks, not *vice versa* as perceived from the IRP.

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5. Is the portfolio well balanced among risk description, countermeasure development and technology development activities?
 - See #4.
 6. Are the appropriate analogs being used?
 - The SRP had no discussion on this matter.
 7. Is it reasonable to begin countermeasure work prior to completing the description of risks?
 - Some things can proceed in parallel but given the identification of risks, focus needs to be on the gaps, maybe at a higher more integrated level, and then the tasks. Using this line of thinking, development of countermeasures should be more focused on more integrated questions and hence better focus on countermeasure development.

VI. Bone and Muscle Risk SRP Charge

The SRP is chartered by the Human Research Program (HRP) Program Scientist at the NASA Johnson Space Center (JSC). The purpose of the SRP is to review and provide analysis on the status and progress of HRP Elements and Projects. Your report will be provided to the HRP Program Scientist and will also be given as a courtesy to the HHC Element and Projects at JSC.

The SRP should (to the fullest extent practicable):

1. Evaluate the ability of the Integrated Research Plan (IRP) to satisfactorily address the risks by answering the following questions:
 - A. Have the proper Gaps have been identified to address the Risks?
 - i) Are all the Gaps relevant?
 - ii) Are any Gaps missing?
 - B. Have the proper Tasks been identified to fill the Gaps?
 - i) Are the Tasks relevant?
 - ii) Are any Tasks missing?
2. Identify the strengths and weaknesses of the IRP, *and* identify remedies for the weaknesses, including answering these questions:
 - A. Are the risks addressed in a comprehensive manner?
 - B. Are there obvious areas of potential integration across disciplines that are not addressed?
3. Address (as fully as possible) the questions provided in the charge addendum and to comment on any additional information provided to the Panel that is not addressed in #1 or #2 above.
4. Expect to receive review materials at least five weeks prior to the site visit.
5. Participate in a SRP teleconference to discuss any issues, concerns, and expectations of the review process approximately three weeks prior to the face-to-face meeting
 - A. Discuss the SRP charge and address questions about the SRP process
 - B. Identify any issues the SRP would like to have answered prior to the site visit
6. Attend the SRP meeting and tour at NASA/JSC
 - A. Attend Element and risk panel presentations, question and answer session, and briefing
 - B. Prepare a draft report including recommendations from the SRP that will be briefed to the Program Scientist by the SRP chairperson or panel. The report should address #1 and #2 above, the questions in the charge addendum, and any other information considered relevant by the SRP.
7. Prepare a final report (within one month of the site visit) that contains a detailed evaluation of the risks and provides specific recommendations that will optimize the scientific return to the HRP. The final report should provide a comprehensive review of Item #1 and #2 above, address the questions in the addendum to the charge, and any additional information the SRP

would like to provide.

8. Consider the possibility of serving on a non-advocate review panel of a directed research proposal or on a solicited research peer review panel; or otherwise advise the Program Scientist.

Addendum to charge: (Element Specific Concerns):

1. Are there obvious, unrealistic aspects in the IRP schedule?
2. Is the portfolio of tasks sufficiently complete to acquire an adequate description of the risks?
 - a. For example, will “space normal” be adequately defined?
3. Is the portfolio of tasks developing the appropriate technologies?
4. Does the portfolio contain a sufficient number of countermeasure development tasks?
5. Is the portfolio properly balanced among risk description, countermeasure development and technology development activities?
6. Are the appropriate analogs being used?
7. Is it reasonable to begin countermeasure work prior to complete description of risks?

VII. Bone and Muscle Risk SRP Roster

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