Human Research Program
Human Health Countermeasures Element
Nutrition Risk
Standing Review Panel
Final Report

November 2009

I. Executive Summary & Overall Evaluation

The Nutrition Risk Standing Review Panel (SRP) reviewed and discussed the specific gaps and tasks for the Human Health Countermeasures (HHC) Element related to nutrition identified in the Human Research Program (HRP) Integrated Research Plan. There was general consensus that the described gaps and proposed tasks were critical to future NASA mission success. The SRP acknowledged the high scientific quality of the work currently being undertaken by the Nutritional Biochemistry group under the direction of Dr. Scott Smith. In review of the entire HRP, four new gaps were identified that complement the Element's existing research activities. Given the limitations of ground-based analogs for many of the unique physiological and metabolic alterations in space, future studies are needed to quantify nutritional factors that change during actual space flight. In addition, future tasks should seek to better evaluate the time course of physiological and metabolic alterations during flight to better predict alterations during longer duration missions. Finally, given the recent data suggesting a potential role for increased inflammatory responses during space flight, the role of inflammation needs to be explored in detail, including the development of potential countermeasures and new ground based analogs, if this possibility is confirmed.

II. Critique of Gaps and Tasks

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

GAPS:

N9: Can nutritional countermeasures mitigate muscle loss?

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

The SRP believes that the existing gaps addressing the muscle risk are relevant. We recommend that these gaps remain as written.

However, the SRP believed that two additional gaps and their associated tasks would greatly augment the two existing gaps for this Muscle Risk. The underlying question from the SRP for this risk is: Is it more than just the unloading of the muscles in microgravity? The SRP was

especially interested in understanding the role of inflammation on impaired performance due to reduced muscle mass, strength and endurance. In addition, the SRP strongly recommends the need for in-flight time course measurements using non-invasive tests. The SRP believes that none of the ground-based analogs can effectively capture the metabolic changes. Time course measurements should also be used for extrapolating to longer term missions. The shape of the curve from these measurements could provide valuable information.

Two new gaps and their associated tasks are strongly recommended by the SRP that would help address this Muscle Risk.

Suggested New Muscle Gap #1:
What is the true etiology of muscle loss, the understanding of which is knowledge imperative for the development of effective countermeasures?

Suggested tasks for this new gap:

- Establish the potential role of inflammation and/or unloading in order to see if new experimental paradigms are necessary. Collect metrics that define the presence of an inflammatory response including effects on muscle protein synthesis and breakdown and measures of the systemic inflammatory response including at a minimum high sensitivity C-reactive protein, serum IL-6 and serum soluble TNF receptor.

- If chronic inflammation is established to be a factor in loss of lean tissue in space travel, establish a ground-based model for chronic inflammation.

Suggested New Muscle Gap #2:
What is the time course of changes during space flight in muscle protein turnover and muscle mass, physiologic performance, systemic inflammation and other relevant biomarkers for conditions of interest, which is knowledge essential for extrapolating to longer duration space flights?

Suggested task for this new gap:

- Establish protocols for longitudinal in-flight measurements. This might be assisted by pre-flight assessments of exercise capacity, body composition and nutritional status.

RISK OF ACCELERATED OSTEOPOROSIS

GAPS:

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

N14: What nutritional counter-measures can be used to mitigate bone loss?

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

The SRP believes that the existing gaps addressing the osteoporosis risk are relevant. We recommend that these gaps remain as written. The SRP does not recommend that any additional nutritional gaps are needed to address this risk.

RISK OF BONE FRACTURE

GAPS:

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

N14: What nutritional counter-measures can be used to mitigate bone loss?

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

The SRP believes that the existing gaps addressing the risk of bone fracture risk are relevant. We recommend that these gaps remain as written. The SRP does not recommend that any additional nutritional gaps are needed to address this risk.

RISK OF RENAL STONE FORMATION

GAPS:

N14: What nutritional counter-measures can be used to mitigate bone loss?

N13: Can renal stone risk be decreased using nutritional counter-measures?

The SRP believes that the existing gaps addressing the risk of renal stone formation are relevant. We recommend that these gaps remain as written. The SRP does not recommend that any additional nutritional gaps are needed to address this risk.

RISK OF CARDIAC RHYTHM PROBLEMS

GAPS:

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

The SRP believed that the existing nutrition gap addressing the risk of cardiac rhythm problems are. We recommend that this gap remain as written. The SRP does not recommend that any additional nutritional gaps are needed to address this risk.

RISK FACTOR OF INADEQUATE NUTRITION

GAPS:

N1: Are nutrients in food are stable during space flight?

N2: What is the optimal dose of vitamin D supplementation?

N3: How do nutritional status/ nutrition requirements change during spaceflight?

N6: What impact does flight have on oxidative damage?

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

N4: Do counter-measures impact nutrition?

The SRP believes that the existing gaps addressing the risk of inadequate nutrition are relevant. We recommend that these gaps remain as written. The SRP does not recommend that any additional nutritional gaps are needed to address this risk, however, the SRP has recommended that an additional task be added to Gap N3. The SRP believes that psychosocial and behavioral factors have a significant influence on nutrition intake and that the HHC group should investigate these factors as a cause of reduced nutritional intake in astronauts.

Suggested new task for N3 Gap:
Expand SMO-16 - Examine the psychosocial and behavioral factors that may influence reduced nutrition intake in Astronauts. This task should be coordinated with the Behavioral Health and Performance Element.

RISK OF INADEQUATE FOOD SYSTEM

GAPS:

AFT1: How can the food system deliver the required level of nutrition throughout the mission?

AFT2: How can the nutrition and acceptability of the food system be maintained throughout the mission?

The SRP believed that the existing gaps addressing the risk of inadequate food systems are relevant. We recommend that these gaps remain as written. However, the SRP has recommended that an additional gap be added to this risk. The SRP strongly recommends that powder supplements and other fortifications intended for use as liquid supplements be considered to close the energy gap and provide a vehicle for potential nutritional supplementation.

Suggested New AFT Gap:
Can powder supplements or fortifications intended for use as a liquid supplement be used to close the energy gap and provide a vehicle for potential nutritional supplements?

RISK OF COMPROMISED EVA PERFORMANCE AND CREW HEALTH DUE TO INADEQUATE EVA SUIT SYSTEMS

EVA 3 (new): What suit characteristics, systems, and consumables are required to optimize crew performance, health & safety?

The SRP believed that the existing gap addressing the risk of EVA performance and crew health is relevant. We recommend that this gap remain as written. The SRP does not recommend that any additional nutritional gaps are needed to address this risk.

III. Discussion on the strengths and weaknesses of the IRP

The IRP document was difficult to navigate. The gaps might have been better justified by a few lines of explanation, and the tasks flowing out of them placed right afterwards in the text rather than scattered through the text. The experiments to implement the tasks were explained in a fragmentary manner.

The SRP feels that the IRP would benefit from a formal integration of Nutrition Risks with the Behavioral Health and Performance Element. Nutrition affects mood and behavior, and mood and behavior affect food consumption and food choices. Expertise in these interrelationships could be brought to bear and the SRP expects it would yield important insights that would lead to more effective strategies for supplying the best food to the astronauts and making it more likely they will eat well.

IV. Discussion of element specific questions in addendum and/or any other issues or concerns the panel chooses to address.

During the course of excellent presentations from the NASA contingent, it became obvious that a systemic inflammatory response could well be playing a prominent role in the hypocaloric intake and metabolic alterations observed in NASA astronauts. This could play an important and definitive role in the changes in nutritional status and physical performance observed during space travel and potentially have a considerable impact on changes in bone metabolism. Factors such as anorexia, inadequate intake unless encouraged to consume additional food, the presumed increase in skeletal muscle protein catabolism, and the effect of microgravity to cause the expression of the nuclear transcription factor NFKB observed *in vitro* all support such a conclusion. Consideration of this distinct possibility to document the presence of inflammation during space flight makes this effort imperative. If systemic inflammation plays a prominent role, then experience with clinical models of mild chronic inflammation would suggest that alternative countermeasures e.g. correction of nutritional intake by the use of liquid nutritional supplements made from powders might be useful. Development of a ground-based model of chronic inflammation would be helpful to explore other means of dealing with the net protein catabolism consequent to space travel including nutritional supplements employing novel ingredients, hormonal manipulation, and pharmacologic agents. Concurrently, pre-flight and in-flight longitudinal metabolic profiling will be imperative to extrapolate to longer term missions.

1. Are there obvious, unrealistic aspects in the IRP schedule?
   - The SRP had no comment on this question.

2. Is the portfolio of tasks sufficiently complete to acquire an adequate description of the risks? For example, will "space normal" be adequately defined?
   - Because of the limitations of the ground based models to fully replicate the conditions of space travel, more in-flight studies, particularly time-course studies, will be important to fully document the unique effects of space travel. These approaches will be necessary to begin to understand the long term impact of space travel on

nutritional status, astronaut health and performance, and develop countermeasures when necessary.

3. Is the portfolio of tasks developing the appropriate technologies?
   - The gaps currently identified are appropriate but we have provided additional gaps and tasks because we feel that emerging data suggest that inflammation plays a role in the observed changes in nutritional status and pathophysiologic changes in muscle and bone.

4. Does the portfolio contain a sufficient number of countermeasure development tasks?
   - The SRP had no comment on this question.

5. Is the portfolio properly balanced among risk description, countermeasure development and technology development activities?
   - The SRP had no comment on this question.

6. Are the appropriate analogs being used?
   - The present analogs (Antarctica, NEEMO and bed rest, etc.) are appropriate to model various aspects of space flight. However, inflammation has been recently identified as a potential factor in the adverse impacts of space travel and it is not adequately addressed by the present models. Thus, there is a need for more in-flight measurements and the development of new ground-based analogs to address this issue.

7. Is it reasonable to begin countermeasure work prior to complete description of risks?
   - We agree that it is reasonable to begin countermeasure work prior to complete description of the risks.

V. Nutrition 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 have 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 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? 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?

VI. Nutrition Risk SRP Roster

Panel Chair:

Bruce Bistrian
Harvard Medical School
Beth Israel Deaconess Medical Center
Department of Medicine
1 Deaconess Road
Boston, MA 02215
Ph: 617-632-8545
Email: bbistria@bidmc.harvard.edu

Panel Members:

Roger Fielding
Tufts University
Nutrition, Exercise, Physiology & Sarcopenia (NEPS)
711 Washington Street
Boston, MA 02111-1524
Ph: 617-556-3016
Email: roger.fielding@tufts.edu

Marc Hellerstein
University of California at Berkeley
Department of Nutritional Sciences
309 Morgan Hall
Berkeley, CA 94702-3104
Ph: 510-643-2550
Email: march@nature.berkeley.edu

John Hoffer
McGill University
Department of Medicine
3755 Cote Ste Catherine
Montreal, QC H3T 1E2
CANADA
Ph: 514-340-8222 x5276
Email: l.hoffer@mcgill.ca

Gordon Jensen
Pennsylvania State University
Department of Nutritional Sciences
110H Chandlee Laboratory
University Park, PA 16802
Ph: 814-865-0108
Email: GLJ1@psu.edu