
2012 Advanced Environmental Health/Advanced Food Technology Standing Review Panel

Evidence Review for:

The Risk of Adverse Health Effects Due to Alterations in Host-Microorganism Interactions and the Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System

Final Report

I. Executive Summary and Overall Evaluation

The 2012 Advanced Environmental Health/Advanced Food Technology Standing Review Panel (from here on referred to as the SRP) met for a site visit in Houston, TX on November 14 - 15, 2012. They specifically reviewed two documents: the new Evidence Report for the Risk of Adverse Health Effects Due to Alterations in Host-Microorganism Interactions (from here on referred to as the Host-Microbe Evidence Report); and the newly updated Evidence Report for the Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System (from here on referred to as the Food Evidence Report).

The SRP appreciated the time and effort that the AEH and AFT disciplines put into their review documents and presentations. The SRP felt that while the Host-Microbe Evidence Report documented the potential for serious risks from host-microbe interactions, more attention was needed towards assessing the magnitude and likelihood of the risks (relative risks), specifically risks related to fungal organisms. Spaceflight changes in the human microbiome should also be incorporated into the Host-Microbe Evidence Report. Specifically, radiation, in addition to microgravity, should be experimentally assessed for its effects on the microbiome. Caution was expressed as to how many diseases can effectively be controlled by pre-launch isolation. It is recommended that interactions be assessed with multiple additional disciplines found in the Integrated Research Plan (IRP), including nutrition, pharmacology, immune response, radiation exposure, and in-flight medical capabilities. Underlying all of this, it is felt that the overall qualifications of two of the Host-Microbe Evidence Report authors, beyond the highly qualified Dr. Ott, were limited and that literature reviews needed to be expanded.

The SPR believes that the Food Evidence Report sufficiently documented the relevant risks from host-microbe interactions, but the magnitudes of these risks might be underestimated in the Human Research Program (HPR) Requirements Document (PRD). The possibility of change in crewmember sensory perception leading to altered acceptability of foods needs to be explicitly addressed. The data on degradation kinetics of foods were felt to be insufficient, and a more extensive literature review was recommended. Additionally it was recommended that further studies should separate out degradation that occurs during preservation from degradation that occurs during storage. The SRP strongly recommended renewed emphasis on the use of the reduced temperatures and oxygen characteristic of space to facilitate achievement of the required five-year shelf life of the recommend variety of foods. Interactions with environmental health, nutrition, immune system, space radiation, and water quality were specifically recommended. The literature review was felt to need augmentation in multiple specific areas. The AFT

scientists were felt to have an excellent background to address these issues.

In summary, the SRP identified four common limitations between both the AEH and AFT 2012 Evidence Reports. These are listed below:

1. The need to augment literature reviews, especially outside of NASA
2. The need to integrate with other risks
3. The need to address the magnitude (likelihood) of the risks
4. The need to address immune and olfactory changes in the nasal compartment

II. Review of the Evidence for the Risk of Adverse Health Effects Due to Alterations in Host-Microorganism Interactions

1. Evaluate the 2012 Host-Microbe Evidence Report using the following criteria:

A. Does the 2012 Host-Microbe Evidence Report provide sufficient evidence that the Risk is relevant to long-term space missions?

The potential for high-impact (severe) events related to host-microbe interactions is clear in the 2012 Evidence Report; however, the magnitude (likelihood) of the risks is not discussed. In addition, the specific risks need to be more clearly stated, along with recommended approaches to evaluate the degree of risk. Risks associated with fungal exposure are not discussed. Risks related to devastating infections in space could easily be as great as “lack of oxygen”. Both could be fatal.

B. Is the risk properly stated in the HRP Program Requirements Document?

The risk is properly stated but reference to fungal disease is not present, and no indication of relative risk is presented. Knowledge of the human microbiome before and during spaceflight is also essential. For example, what are the chances that latent infectious agents will be carried onto the vehicle (e.g., norovirus, tuberculosis)? How are changes in immune response likely to affect these latent infections?

C. Is the text of the short description of the Risk provided in the HRP PRD clear?

Fungal risks are not mentioned.

The SRP is not convinced that the first sentence (“While hazard control systems and processes prevent the presence of many medically significant microorganisms during spaceflight missions...”) is true, especially the word “many”. Only a few diseases are common enough to be controlled by pre-launch isolation.

D. Does the evidence make the case for the knowledge-type gaps presented?

It does make the case for the knowledge gaps mentioned in the Host-Microbe Evidence Report, but the SRP thinks the knowledge gaps list is incomplete.

E. Are there any additional knowledge-type gaps in knowledge that should be considered for this specific Risk?

The SRP thinks that the initial research plan for human microbiome changes is good, but is a baby step. More studies, both human and animal, need to be done, as well as possibly *in vitro* studies that include the effect of radiation on the microbiome.

Experiments on the effects of radiation on the human microbiome in space beyond low Earth orbit need to be started soon. Well described *in vitro* models of the human microbiome could be used. (Kim B-S, Kim JN, Cerniglia CE. In Vitro culture conditions for maintaining a complex population of human gastrointestinal tract microbiota. J Biomed Biotechnol 2011; 2011: 838040 Epub 2011 Jul 24; Thomas LV, Ockhuizen T. 2012 New insights into the impact of the intestinal microbiota on health and disease: a symposium report. Br J Nutr, 107, pp S1-S13).

Animal models with humanized microbiomes could also be used. (Gootenberg DB, Turnbaugh PJ Companion Animals Symposium: Humanized animal models of the microbiome. J Anim Sci 2011; 89: 1531-1537).

1. The human microbiome should be exposed to sublethal doses of radiation designed to simulate the type of radiation encountered in space beyond low Earth orbit to the extent this type of radiation is understood and can be recreated in a laboratory.
2. Fungal exposure and risk needs to be evaluated.
3. Risk of changes to individual infectious agents under microgravity is covered, but not the direct effects of radiation on infectious agents.
4. The risk of hidden carriage of pathogens by crewmember, and residuals on surfaces should be evaluated, including viruses. For example, is the current pre-flight isolation period sufficient for a flight to Mars?
5. What changes occur in nasopharyngeal immunity due to fluid redistribution?

F. Does the Evidence Report address relevant interactions between this Risk and others in the HRP PRD/IRP (Integrated Research Plan, Rev. D)?

No. The SRP thinks the AEH discipline should also evaluate relevant interactions with the following Risks found in the Integrated Research Plan, Rev. D.: the Risk Factor of Inadequate Nutrition, the Risk Factor of Role of Clinically Relevant Unpredicted Effects of Medication; the Adverse Health Effects Due to Altered Immune Response; the Risk of Degenerative Tissue or other health effects from radiation exposure; and the Risk of Unacceptable Health and Mission Outcomes due to Limitations of In-flight Medical Capabilities.

G. Are the qualifications of the author(s) appropriate for identifying the evidence necessary to characterize the given Risk?

Mark Ott, Ph.D. is highly qualified, but from the CVs, it appears that neither of the other two authors have the relevant qualifications as evidenced by no infectious disease training and no publications in microbiology. More importantly, the SRP feels that the relevant literature reviews were not done.

H. Is there information from other disciplines that need to be included in the Evidence Report?

1. Immunology
2. Food science
3. Radiation health science

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4. Nutrition
 5. Pharmacology
 6. In-flight medical capabilities

I. Is the breadth of the cited literature sufficient?

No, the SRP felt the literature review was deficient. Factors affecting the human microbiome are not adequately referenced, nor are potential effects of immune response changes on the Risk for serious disease.

J. What is the overall quality and readability of the Evidence Report?

The overall quality and readability of the Host-Microbe Evidence Report is good.

III. Review of the Evidence for the Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System

1. Evaluate the 2012 Food Evidence Report using the following criteria:

A. Does the 2012 Food Evidence Report provide sufficient evidence that the Risk is relevant to long-term space missions?

The SRP thinks that the Food Evidence Report provides more than sufficient evidence that the AFT Risk is relevant and emphasizes that the current food system is inadequate for a long-term (five year) space mission. This conclusion is based on key observations:

- Food is currently considered the sole source of nutrition for the crew.
- Only a small number of currently available foods meet the five-year shelf life expectation.
- The challenges to reduce mass, volume, waste and disposal need additional attention.

B. Is the risk properly stated in the HRP Program Requirements Document?

Based on the magnitude of the challenges to the AFT scientists, the SRP recommends that the Risk be rewritten to more clearly state the magnitude (likelihood) of the gaps to be addressed.

C. Is the text of the short description of the Risk provided in the HRP PRD clear?

No, the SRP does not think the text of the short description of the Risk is clear. The statements presented as **Context** in Table 3 of the HRP PRD provide a more accurate and complete outline of the challenges that need to be addressed.

D. Does the evidence make the case for the knowledge-type gaps presented?

Currently, the AFT identifies four knowledge-type gaps, but a plan to reduce the number to three has been presented. This change will be accomplished by elimination of AFT2. The SRP endorses this change since AFT2 is redundant with both AFT1 and AFT3.

E. Are there any additional knowledge-type gaps in knowledge that should be considered for this specific Risk?

The SRP has concluded that the following knowledge gaps may exist:

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1. The influence of extended periods in a space environment may influence the sensory perception of crewmembers and specifically for odor/aroma. Changes in perception would impact the overall acceptability of the foods provided. This issue may be addressed in the University of Minnesota project, but the aims of that study do not clearly indicate that this issue is included.
 2. The data on degradation kinetics for food quality attributes presented in the Food Evidence Report are not sufficiently specific to provide a basis for recommendations on product shelf life or as a basis for future studies.
 - a. A more extensive review of current literature would provide additional and relevant data for many of the quality attributes of concern.
 - b. Future studies on quality degradation should separate the portion of degradation that occurs during a preservation process from the portion occurring during storage.
 - c. Kinetic constants should be used to identify specific quality attributes and storage parameters with direct impact on the limits to product shelf life.
 3. Renewed emphasis on the use of reduced temperatures [refrigerated foods (4C), frozen foods (-20 to -40C)] to extend the shelf life of foods is needed. The use of the low temperatures in the space environment will significantly reduce product quality degradation rates, as well as reduce the need for additional packaging to extend product shelf life. Creation of these low storage temperatures should be accomplished by using the naturally low temperatures in space, along with appropriate changes in vehicle design to create space for refrigerated and frozen foods. Given the challenges to achieving five-year shelf life for food, along with providing expanded variety of foods to the crewmembers, it seems evident that reduced temperatures offer the best option. In addition, this option provides the opportunity to reduce the types and magnitudes of packaging for the foods being stored on the vehicle. This approach should include considerations of using vacuum for storage of food products with sensitivity to oxygen.

F. Does the Evidence Report address relevant interactions between this Risk and others in the HRP PRD/IRP (Integrated Research Plan, Rev. D)?

The SRP could not identify references to interactions between the AFT Risk and the Integrated Research Plan in the Food Evidence Report. Several opportunities seem evident in the following disciplines: immune function, nutrition, and infection diseases. A more specific opportunity is the potential for control of food contamination originating from crewmember illness.

G. Are the qualifications of the author(s) appropriate for identifying the evidence necessary to characterize the given Risk?

The SRP concluded that the qualifications and experiences of the current AFT scientists are outstanding when considering characterization of the Risk.

H. Is there information from other disciplines that need to be included in the Evidence Report?

As suggested in the SRP response to Question F, there seem to be opportunities for the AFT Project to gain inputs from other disciplines such as environmental health, nutrition, immune systems, space radiation, water quality, and similar disciplines within the HRP.

I. Is the breadth of the cited literature sufficient?

The SRP has expressed concerns about the breadth and depth of literature referenced in the Food Evidence Report. There are disparities in the databases used to generate background for the research reported. Specific areas include a lack of references for kinetic parameters for evaluating shelf life estimates based on quality attributes, references on non-thermal methods for product surface sanitation, and attention to the influence of the freezing process on frozen food quality.

J. What is the overall quality and readability of the Evidence Report?

The SRP found the Food Evidence Report to be very readable. The Conclusions section is the weakest part of the Food Evidence Report, and should place more emphasis on the key outcomes mentioned in the Executive Summary. The Conclusions should include more comprehensive treatment of outcomes mentioned in the nearly 25 pages of the Food Evidence Report.

2. *Provide comments on any important issues that are not covered by the criteria in #1 above.* The SRP thinks that the combined experiences of Dr. Perchonok, Dr. Douglas and Dr. Cooper should be supplemented to avoid an experience gap as a transition in leadership for the AFT discipline continues.

IV. 2012 Advanced Environmental Health/Advanced Food Technology SRP Evidence Review: Statement of Task for the Risk of Adverse Health Effects Due to Alterations in Host-Microorganism Interactions and the Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System

The 2012 Advanced Environmental Health/Advanced Food Technology (AEH/AFT) Standing Review Panel (SRP) is chartered by the Human Research Program (HRP) Chief Scientist to review the evidence base for the Risk of Adverse Health Effects Due to Alterations in Host-Microorganism Interactions (Microhost Risk) and the Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System (Food Risk). The 2012 AEH/AFT SRP will generate a report of their analyses of the Microhost and Food Evidence Reports, including any recommendations on how to improve the Microhost and Food Evidence Reports, and submit it to the HRP Chief Scientist.

In 2008, the Institute of Medicine reviewed NASA's Human Research Program evidence in assessing the Risks identified in NASA's Human Research Program Requirements Document (PRD). The 2012 evidence for the Risk of Adverse Health Effects Due to Alterations in Host-Microorganism Interactions was not reviewed by the IOM in 2008 and the Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System has not been reviewed since the last IOM review and there have been significant changes to this evidence. The 2012 AEH/AFT SRP is being asked to review the latest versions of the Microhost and Food Evidence Reports.

The 2012 AEH/AFT SRP is charged to:

1. Evaluate the 2012 Microhost and Food Evidence Reports based on each of the following criteria:
 - A. Does the Evidence Report provide sufficient evidence that the Risk is relevant to long-term space missions?
 - B. Is the Risk properly stated in the HRP Program Requirements Document (PRD)?
 - C. Is the text of the short description of the Risk provided in the HRP PRD clear?
 - D. Does the evidence make the case for the knowledge-type gaps presented?
 - E. Are there any additional knowledge-type gaps in knowledge that should be considered for this specific Risk?
 - F. Does the Evidence Report address relevant interactions between this Risk and others in the HRP PRD/IRP (Integrated Research Plan, Rev. D)?
 - G. Are the qualifications of the author(s) appropriate for identifying the evidence necessary to characterize the given Risk?
 - H. Is there information from other disciplines that need to be included in the Evidence Report?
 - I. Is the breadth of the cited literature sufficient?
 - J. What is the overall quality and readability of the Evidence Report?
2. Provide comments on any important issues that are not covered by the criteria in #1 above.

Additional information regarding this review:

1. After the 2012 AEH/AFT SRP members have received the review materials and had the opportunity to look over the documents, the panel members will participate in a conference call to discuss any issues, concerns, and expectations of the review process to start the review prior to the meeting.
 - A. Discuss the 2012 AEH/AFT SRP Statement of Task and address questions about the SRP process.
 - B. Identify any issues the 2012 AEH/AFT SRP would like to have answered prior to or during the meeting.
2. Attend a meeting at NASA JSC on November 14 - 15, 2012 to discuss the Evidence Reports with the Space Human Factors and Habitability (SHFH) Element. At this meeting, prepare a draft report that addresses each of the evaluation criteria listed in the panel charge (A-J) including any recommendations on how to improve the Evidence Reports. Debrief the HRP Chief Scientist and a representative from the SHFH Element on the salient points that will be included in the final report and specifically the items in the panel charge.

Prepare a draft final report (within one month of the site visit debrief) that contains a detailed evaluation of the Microhost and Food Evidence Reports specifically addressing items #1 and #2 of the SRP charge. The draft final report will be sent to the HRP Chief Scientist and he will forward it to the appropriate Element for their review. The SHFH Element and the HRP Chief Scientist will have 10 business days to review the draft final report and identify any misunderstandings or errors of fact and then provide official feedback to the SRP. The SRP will have 10 business days to address any issues and finalize the 2012 SRP Final Report. The 2012 SRP Final Report will be submitted to the HRP Chief Scientist and copies will be provided to the SHFH Element that sponsors the AEH and AFT disciplines and also made available to the other HRP Elements. The 2012 SRP Final Report will be made available on the Human Research Roadmap public website (<http://humanresearchroadmap.nasa.gov/>).

V. 2012 Advanced Environmental Health/Advanced Food Technology Standing Review Panel Roster

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