2015 Dust Risk Standing Review Panel

Research Plan Review for:
The Risk of Adverse Health and Performance Effects of Celestial Dust Exposure

Final Report

I. Executive Summary and Overall Evaluation

The 2015 Dust Risk Standing Review Panel (from here on referred to as the SRP) participated in a WebEx/teleconference with members of the Space Human Factors and Habitability (SHFH) Element, representatives from the Human Research Program (HRP), NASA Headquarters, and the NASA Research and Education Support Services (NRESS) on November 12, 2015 (list of participants is in Section VII of this report). The SRP reviewed the updated research plan for The Risk of Adverse Health and Performance Effects of Celestial Dust Exposure (from here on referred to as the Dust Risk), as well as the Evidence Report for this Risk.

Overall, the SRP was very pleased with the progress made on the Dust Risk.

II. Critique of Gaps and Tasks for the Risk of Adverse Health and Performance Effects of Celestial Dust Exposure

A. *Have the proper Gaps been identified to mitigate the Risk?*
    a. *Are all the Gaps relevant?*
    b. *Are any Gaps missing?*
B. *Have the gap targets for closure been stated in such a way that they are measureable and closeable?*
    a. *Is the research strategy appropriate to close the Gaps?*
C. *Have the proper Tasks been identified to fill the Gaps?*
    a. *Are the Tasks relevant?*
    b. *Are there any additional research areas or approaches that should be considered?*
    c. *If a Task is completed, please comment on whether the findings contribute to addressing or closing the Gap.*
D. *If a Gap has been closed, does the rationale for Gap closure provide the appropriate evidence to support the closure?*

Gaps and Tasks:

- The SRP thinks the Gaps are relevant and appropriate to mitigate the Risk.
- The SRP thinks there may be one missing Gap; specifically the concern for long-term pulmonary health effects is still an issue, given the physical-chemical similarities of lunar dust to fibrosis-inducing agents such as quartz. Therefore, the potential for fibrosis in extraterrestrial dust exposures on extended missions was considered by some SRP members to be a missing research Gap.
- The SRP thinks the stated Gaps are measureable and closeable with the possible exception of the exposure guideline permissible exposure limit (PEL) Gap.
- Although the stated Gaps appear to be measurable and closeable (with the exception of Gap AEH 5), one member of the SRP was concerned that because the Gaps were developed over time, they have become somewhat jumbled or overlapping in their presentation in the Report and this hinders the SRP in determining if the research strategy will result in measureable progress or closeable solutions for all Gaps.

- The SRP thinks the tasks are relevant but are mostly very general.
- In terms of an additional Risk, one member of the SRP suggested that an elementary gavage study may be warranted since it is likely that these inhaled and deposited dusts will be cleared by the lung to the gastrointestinal (GI) tract. Whether this might occur in chronic celestial dust exposure scenarios is unclear at this time.
- The SRP thinks the tasks associated with understanding Lunar Dust Toxicity (Lunar Dust D/O - Cellular Studies to Support Pulmonary Toxicology Evaluation of Lunar Dust; Dermal Studies of Lunar Dust and Ocular Studies of Lunar Dust; Lunar Dust-ITI - Pulmonary Toxicity Studies of Lunar Dust in Mice and Rats; Lunar Dust - Cell - Study of Lunar Dust and Lunar Simulant Activation, Monitoring; Solution and Cellular Toxicity Properties; and, Human Lung Low g - Clearance of Particles Depositing in the Human Lung in Low-Gravity) contribute substantially to the understanding of the toxicity of extraterrestrial dusts by establishing a theoretical framework for toxicological assessment.
- The SRP thinks the Lunar Airborne Dust Toxicity Assessment Group (LADTAG) final report of February 7, 2014 provides the appropriate evidence to support the closure of the Lunar Dust Toxicity Gaps (with the exception of Gap AEH 5).

AEH 1: What are the unique properties of lunar dust that affect physiology? (Closed)

Tasks:
- Geology, Geochemistry and Lithology Science Support Activities – Completed Task
- Study of Lunar Dust and Lunar Simulant Activation, Monitoring, Solution and Cellular Toxicity Properties – Completed Task

AEH 2: What is the toxicity of lunar dust in the respiratory system? (Closed)

Tasks:
- Cellular Studies to Support Pulmonary Toxicology Evaluation of Lunar Dust, Dermal Studies of Lunar Dust and Ocular Studies of Lunar Dust – Completed Task
- Pulmonary Toxicity Studies of Lunar Dust in Mice and Rats – Completed Task
- Study of Lunar Dust and Lunar Simulant Activation, Monitoring, Solution and Cellular Toxicity Properties – Completed Task
- Clearance of Particles Depositing in the Human Lung in Low-Gravity – Completed Task

AEH 4: What is the dermal and ocular toxicity of lunar dust? (Closed)

Tasks:
- Cellular Studies to Support Pulmonary Toxicology Evaluation of Lunar Dust, Dermal Studies of Lunar Dust and Ocular Studies of Lunar Dust – Completed Task

AEH 5: What are the permissible exposure limits for inhalation of lunar dust? (Closed)
- The SRP does not think the rationale for closing this Gap provides the appropriate evidence to support the closure. The setting of exposure guidelines is a fluid process as new data (e.g., newly discovered immune, cardiovascular, or fibrotic effects) become available. While it is understood that a PEL is necessary to devise and build engineering

controls in a mission that is several years in the future, it is important to reconsider PELs as new data are presented. Regardless, the SRP does not think this Gap should be closed.

- One member of the SRP felt that particle deposition is a Gap which is considered as a modifier of effect, but it is not clear if the impact of modifiers such as physiologic stress, health status (including hydration for example), changes in ambient air quality (fractional gas content), and patterns of exposure (e.g., peak vs monotonic exposure levels) should be included in the standard PEL approach.

Tasks:

- Cellular Studies to Support Pulmonary Toxicology Evaluation of Lunar Dust, Dermal Studies of Lunar Dust and Ocular Studies of Lunar Dust – Completed Task
- Geology, Geochemistry and Lithology Science Support Activities – Completed Task
- LADTAG Lunar Dust Health Standard – Completed Task
- Pulmonary Toxicity Studies of Lunar Dust in Mice and Rats – Completed Task
- Study of Lunar Dust and Lunar Simulant Activation, Monitoring, Solution and Cellular Toxicity Properties – Completed Task
- Clearance of Particles Depositing in the Human Lung in Low-Gravity – Completed Task
- Extraterrestrial dust – Carbonaceous Asteroids – Deleted Task

DUST 11: What is the potential for acute toxicity of lunar dust (all relevant endpoints), and acute/chronic cardiovascular toxicity of lunar dust? (Formerly AEH 11)

- The SRP thinks this Gap is relevant and appropriate.

Task:

- Acute Lunar Dust Toxicology – Planned Task

AEH Watch Item/NSBRI Research: What are the effects of lunar gravity on permissible exposure limits for inhalation of lunar dust? (Closed)

Tasks:

- Aerosol Deposition in the Lung in Fractional Gravity: Risk Mitigation for Lunar and Martian Habitats – Completed Task
- Clearance of Particles Depositing in the Human Lung in Low-Gravity – Completed Task
- Variability in flow distribution within the lung and its effects on deposition and clearance of inhaled particles in normal and reduced gravity (NSBRI Postdoctoral Fellowship) – Completed Task

DUST 12: We need to determine if technologies are available or need to be developed to evaluate celestial dust toxicity and/or volatile composition in situ.

- This SRP thinks this Gap is relevant but some of the tasks are unclear.

Tasks:

- Robotic Precursor – Planned Task
    - The SRP thinks that this task may be important but that it should be outsourced to extramural researchers. Such high-through put systems are useful if there are

hundreds or thousands of samples which does not apply to existing or future extraterrestrial dust samples. These high throughput systems remain largely invalidated given their infancy in development. They are expensive to develop and while they may be worth pursuing, there is no level of confidence yet regarding their utility in risk quantification decision trees for a limited number of celestial dusts.

- Organ on a chip (Pilot) – Planned Task
    - The SRP thinks this task is a clever approach for toxicity testing, but is beyond the scope of NASA at this time. This is a rapidly developing field and while a comparison of single cell to organ-like cell combinations/interactions is important in identifying and ranking the toxicity of celestial dust samples, it would best be left to extramural research efforts.
    - If these models mature, it will be relatively easy and less expensive to use them at that time. The approach of organ on a chip has some advantages over the more simple high-throughput methodology in that they do encompass an additional level of physiologic reality with multiple pathways and cell-cell interactions. On a practical note, the SRP thinks it is also important to consider the fact that most of these systems are designed for water- or media-soluble testing materials whereas particles pose special challenges which add to the complexity of their use.

DUST 13: We need to determine if there are significant differences in respiratory, cardiovascular, ocular, or dermal toxicity of dusts from different exploration targets or if existing permissible exposure limits can be applied.

- The SRP thinks this Gap is relevant. Although in a formative stage, the issues noted are indeed important and the SRP agrees that NASA should be examining cardiorespiratory and ocular/dermal impacts as well as pulmonary effects. With assessments of existing knowledge of Apollo reports etc., additional toxicological work would be proposed on an as-needed basis. Among the issues which would seem to be particularly relevant would be dose-response and patterned exposures – short or long term – that may play into the toxicologic risk.
- The task of in vivo exposure studies has allowed the PEL Gap to be closed but it should be re-considered for additional endpoints, if necessary, as outlined in Dust 13.

Tasks:

- Celestial Dust Ground – Planned Task
- Dust Data Mining – Planned Task
- Martian Dust Technical Interchange Meeting (TIM) – Planned Task

DUST 14: If relative toxicity is unknown and/or significant differences in toxicity do exist, we need to understand the acute and chronic toxicities of the celestial dust and/or volatiles in order to establish permissible exposure limit.

- The SRP thinks this Gap is relevant and appropriate.

No Tasks

III. Discussion on the strengths and weaknesses of the IRP and identify remedies for the weaknesses, including answering these questions:

A. Is the Risk addressed in a comprehensive manner?
- The Risk was presented in a comprehensive manner, although one member of the SRP suggested that the Risk could be addressed in an even more comprehensive manner if the Gaps were better defined/stated.

B. Are there areas of integration across HRP disciplines that are not addressed that would better address the Risk?
- Based on the materials presented, it is evident to the SRP that certain combinations of exposure appear to present the possibility of synergistic effects. The effect of prolonged lower gravity environments (Section 4.3.6 of the Human Research Program Integrated Research Plan) on celestial dust exposure is cited as posing potential allergenic problems that may be exacerbated by spaceflight. Several recent studies have provided evidence of immune dysregulation during spaceflight (Mehta et al., 2007, 2013; Crucian et al., 2008, 2009, 2011, 2013), which may show an increased potential for resulting acute hypersensitivity. Potentially higher radiation exposure (Sections 4.5.2 and 4.5.3), both alone or in combination with lower gravity environments may also effect the immune system when there is an exposure to Martian dust as mentioned in Gap Dust-11 and the two should therefore be considered as possibly synergistic. Therefore, the SRP thinks the dust discipline should consider more integration with the Exploration Medical Capability Element, the Human Health Countermeasures Element (the design of the EVA suit to be more easily cleaned without producing exposure and reduced radiation exposure which could in turn reduce immunological function; the cardiovascular discipline, due to the acute cardiovascular risk from dust), and the Space Radiation Element.
- The SRP thinks the dust discipline should also collaborate with other disciplines in the Space Human Factors and Habitability Element. Specifically, the Space Human Factors Engineering Project can address measures to reduce dust intrusion into living areas through design of the living area, design of entry and exit procedures.

IV. Evaluation of the progress on the Dust Risk Research Plan since the 2014 SRP meeting

- The SRP is pleased with the progress on the Dust Risk Research plan since it was presented to the Advanced Environmental Health/Advanced Food Technology SRP during the 2014 WebEx/teleconference.

V. Additional Comments

- Developing the ability to amend or better adapt dust control procedures is another unrecognized countermeasure necessary to assure that the human crew receives the maximum protection. This is particularly true in case the toxicology underestimates the risk of a ‘new’ celestial dust or if engineered dust controls are not as effective as

presumed. Therefore, dust monitoring would seem to be advisable for both airborne and dermal exposure situations as part of the ground station and for the return trip for the capsule environment. Also, reducing dust intrusion into living areas through design of the living area, re-design of entry and exit procedures, and the design of the extravehicular activity (EVA) suit to be more easily cleaned (without generating additional particle exposures or reducing radiation protection) could in turn reduce adverse pulmonary and ocular effects.

VI. 2015 Dust Risk SRP Research Plan Review: Statement of Task for the Risk of Adverse Health and Performance Effects of Celestial Dust Exposure

The 2015 Dust Risk Standing Review Panel (SRP) is chartered by the Human Research Program (HRP) Chief Scientist. The purpose of the SRP is to review the Risk of Adverse Health & Performance Effects of Celestial Dust Exposure section of the current version of the HRP's Integrated Research Plan (IRP) which is located on the Human Research Roadmap (HRR) website (http://humanresearchroadmap.nasa.gov/). Your report, addressing each of the questions in the charge below and any addendum questions, will be provided to the HRP Chief Scientist and will also be made available on the HRR website.

The 2015 Dust Risk SRP is charged (to the fullest extent practicable) to:

1. Based on the information provided in the current version of the HRP's IRP, evaluate the ability of the IRP to satisfactorily make progress in mitigating the Risk by answering the following questions:

   A. Have the proper Gaps been identified to mitigate the Risk?
   i) Are all the Gaps relevant?
   ii) Are any Gaps missing?

   B. Have the gap targets for closure been stated in such a way that they are measureable and closeable?
   i) Is the research strategy appropriate to close the Gaps?

   C. Have the proper Tasks been identified to fill the Gaps?
   i) Are the Tasks relevant?
   ii) Are there any additional research areas or approaches that should be considered?
   iii) If a Task is completed, please comment on whether the findings contribute to addressing or closing the Gap.

   D. If a Gap has been closed, does the rationale for Gap closure provide the appropriate evidence to support the closure?

2. Identify the strengths and weaknesses of the IRP, *and* identify remedies for the weaknesses, including, but not limited to, answering these questions:
   A. Is the Risk addressed in a comprehensive manner?
   B. Are there areas of integration across HRP disciplines that are not addressed that would better address the Risk?
   C. Other

3. Based on the updates provided by the Element, please evaluate the progress in the research plan since the last SRP meeting.

4. Please comment on any important issues that are not covered in #1, #2, or #3 above, that the SRP would like to bring to the attention of the HRP Chief Scientist and/or the Element.

Additional Information Regarding This Review:

1. Expect to receive review materials at least four weeks prior to the WebEx conference call.

2. Participate in a WebEx conference call on November 12, 2015 at 11:30 am ET.
   A. Discuss the 2015 Dust Risk SRP Statement of Task and address questions about the SRP process.
   B. Receive presentations from the HRP Chief Scientist (or his designee), the Space Human Factors and Habitability (SHFH) Element, and participate in a question and answer session, and briefing.

3. Prepare a draft final report (approximately one month after the WebEx conference call) that contains a detailed evaluation of the current IRP specifically addressing items #1, #2, and #3 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 review the draft final report and identify any misunderstandings or errors of fact and then provide official feedback to the SRP within two weeks of receipt of the draft report. If any misunderstandings or errors of fact are identified, the SRP will be requested to address them and finalize the 2015 SRP Final Report as quickly as possible. The 2015 SRP Final Report will be submitted to the HRP Chief Scientist and copies will be provided to the SHFH Element that sponsors the dust discipline and also made available to the other HRP Elements. The 2015 SRP Final Report will be made available on the HRR website (http://humanresearchroadmap.nasa.gov/).

VII. Dust Risk SRP Research Plan Review WebEx/Teleconference Participants

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VIII. 2015 Dust Risk Standing Review Roster

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