# Human Research Program
# Space Radiation
# Standing Review Panel (SRP)
# Final Report

# February 2010

## I. Executive Summary & Overall Evaluation

The Space Radiation Standing Review Panel (SRP) met at the NASA Johnson Space Center (JSC) on December 9-11, 2009 to discuss the areas of current and future research targeted by the Space Radiation Program Element (SRPE) 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 Space Radiation 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 SRP's review. The SRP was requested to evaluate the practicality of the proposed efforts in light of the demands placed on the HRP.

Several presentations were made to the SRP during the site visit and the SRP spent sufficient time to address the SRP charge. The SRP made a final debriefing to the HRP Program Scientist, Dr. John B. Charles, on December 11, 2009.

The SRP noted that current SRPE strategy is properly science-based and views this as the best assurance of the likelihood that answers to the questions posed as gaps in knowledge can be found, that the uncertainty in risk estimates can be reduced, and that a solid, cost-effective approach to risk reduction solutions is being developed.

The current approach of the SRPE, based on the use of carefully focused research solicitations, requiring thorough peer-review and approaches demonstrated to be on the path to answering the NASA strategic questions, addressed to a broad extramural community of qualified scientists, optimally positioned to take advantage of serendipitous discoveries and to leverage scientific advances made elsewhere, is sound and appropriate.

The SRP viewed with concern statements by HRP implying that the only science legitimately deserving support should be "applied" or, in some instances that the very term "research" might be frowned upon. We understand the desire of management to ensure that research stay focused on mission objectives, but the terms used are code words fraught with different meaning for scientists. Such expressions, taken at face value, convey a profoundly flawed view of science, can easily lead down counterproductive paths, and have the potential to irretrievably corrupt NASA requirements. The SRP understands and endorses the mandate to keep research efforts focused on the mission needs. However, thoughtful application of knowledge gained by understanding the mechanisms and pathways of biological effects cannot be replaced.

The SRPE has done an excellent job in generating a community of scientists with the required expertise to address scientific questions essential to NASA. It is critical to maintain and expand this effort in the future as expertise in this area is slowly fading away. The SRPE has done an outstanding job of defining the key gaps, establishing relationships with other federal agencies and scientific societies and presenting the critical issues NASA faces.

The SRP is aware of the recent proposed changes in NASA's exploration plans. The proposed Human Research Program is highly relevant to any and all human space exploration and requires sustained effort as the results of one set of experiments are needed to continue to obtain the necessary knowledge and countermeasures to make human space travel as safe as possible. To start, stop and restart the proposed experiments would be costly in terms of knowledge, research teams and rate of progress. Despite what may be significant changes in NASA's overall research strategy we strongly urge the sustained investment in human research to avoid loss of information that will be critical to NASA's future.

## II. Critique of Gaps and Tasks in the *RISK OF RADIATION CARCINOGENESIS*

**Cancer 1: How can experimental models of tumor development for the major tissues (lung, colon, stomach, breast, liver, and leukemias) be developed to represent the major processes in radiation carcinogenesis and extrapolated to human risk projections?**

Current Tasks:

1) Links Between Persistent DNA Damage, Genome Instability, and Aging
2) Mouse models approach for intestinal tumorigenesis estimates by space radiation
3) Systematic Identification of Genes and Signal Transduction Pathways Involved in Radio Adaptive Response
4) HZE induced mammary cancer development processes in murine and humanized models, and their influence on radiation quality functions
5) Mitochondrial-Derived Oxidants and Cellular Responses to Low Dose/Low LET Ionizing Radiation
6) Space Radiation Risk Assessment
7) Effects of prolonged exposure to space radiation on carcinogenesis and neuroendocrine differentiation in human prostate models
8) NSCOR: Radiation Carcinogenesis
9) NSCOR: Space Radiation and Intestinal Tumorigenesis
10) The Role of Gap-Junction Communication and Oxidative Metabolism in the Biological Effects of Space Radiation
11) Telometric proteins in the radiation/DNA damage response
12) DNA Damage Responses Induced by HZE Particles In Human Cells (03-OBPR-07)
13) Mechanisms of the Repair of HZE Induced DNA Double-Strand Breaks in Human Cells
14) Mechanisms for induction of Bystander Effects by High Energy Particles in Cells and Tissues
15) Role of high-LET radiation-induced mitotic catastrophe in mutagenesis: implication for carcinogenesis
16) Comparative analysis of charged particle-induced autosomal mutations in murine tissue

and cells
17) A mechanistic investigation of space radiation induced carcinogenesis
18) Elucidating the relationship between the effects of various radiation qualities and cancer development processes using novel flow-based assays
19) Histone Acetyltransferases and the Cellular Response to DNA Damage
20) The Relation Between Mutagenesis and Genomic Instability After Particle Exposure In Vivo
21) The mechanism of excess relative risk on carcinogenesis induced by high-LET radiation
22) A role for homologous recombination in complex DSB repair after HZE particles
23) NSCOR: Lung Cancer Pathogenesis and HZE Particle Exposure
24) NSCOR: The contribution of non-targeted effects in HZE cancer risk (LBNL)
25) NSCOR: The contribution of non-targeted effects in HZE cancer risk (NYU)
26) Epigenetic effects of radiation on epithelial cell self-renewal
27) Dose rate effects on the mechanisms of space radiation induced delayed genomic instability
28) Dose-rate effects of protons on the induction of genomic instability in vivo
29) NSCOR: Solid Tumor Risk Estimation: Incorporating Intercellular Interaction Effects
30) Low Dose IR Activation of TGF-Beta 1-IGF-1-sCLU In Vivo: Mechanisms, Functions of a Changing Microenvironment
31) Risk assessment of space radiation enhanced colon tumorigenesis II
32) Space Radiation Risk Assessment

- The SRP has no specific comments about any one task however it is important to move closer to the human situation and recommends encouraging prospective grantees to consider the use of animal models that in some respect mimic the human situation. For example knockout mice for known human genes implicated in radiation-induced cancer, or humanized animal models.
- The description of gaps and tasks uses the term "model" in two different contexts. For this reason the SRP has rephrased the relevant descriptions to clarify the context. In one instance, "model" refers to subjects of an experimental design; in the other, "model" refers to the framework of a calculation.
- In experimental models, the processes responsible for the radiation response of the model organisms are thought to be sufficiently similar to comparable processes in other organisms. To the extent that such experimental models are a faithful analog, they may be used as surrogates for all organisms sharing common properties. Thus, the radiation response of experimental models can be expected to be similar to that of organisms that cannot be subjected to experimentation, such as humans. Examples range from transgenic mice, incorporating human genes in their DNA, to pigs, whose skin response to radiation is similar to human skin. The main drawback of experimental models is the limited degree to which similarity between species can be adduced.
- Theoretical models use mathematical descriptions of biological processes to predict the magnitude and probability of effects caused by radiation with defined physical properties. A sufficient number of statistically significant comparisons with experimental results can validate the model assumptions and lead to accurate theoretical predictions, thus allowing interpolation between experiments and, hopefully, extrapolation beyond experimental databases. The accuracy of model predictions depends on the accuracy with which

mathematical descriptions capture the details of biological processes. Theoretical models range from simple curve-fitting to epidemiological dose response data to sophisticated use of signal pathways in biochemical networks. The main drawback of theoretical models is the limited knowledge of biological processes involved in the response to radiation.

**Cancer 2: How can experimental models of tumor development for the other tissues (bladder, skin, esophagus, brain, etc) be developed to represent the major processes in radiation carcinogenesis and extrapolated to human risk projections?**

Current Tasks:

1) Space Radiation Risk Assessment
2) Effects of prolonged exposure to space radiation on carcinogenesis and neuroendocrine differentiation in human prostate models
3) NSCOR: Radiation Carcinogenesis
4) NSCOR: Space Radiation and Intestinal Tumorigenesis
5) DNA damage clusters in human cell transformation induced by single or multiple space radiation exposures
6) Radiation and gliomagenesis: a sensitive model system to evaluate the tumorigenic potential of HZE particles
7) Impact of Radiation Quality on Cancer Processes in 2D and 3D Esophageal Cell Models
8) Integrated experimental and computational study of radiation induced matrix remodeling in a human skin equivalent

- The SRP has no specific comments about any one task and is supportive of the decision to split the cancers into two groups in Cancer 1 and 2. It is important to encourage prospective grantees to consider the use of humanized animal models or knockout models for specific gene effect studies.

**Cancer 3: How can models of cancer risk be applied to reduce the uncertainties in radiation quality effects from SPE's and GCR?**

*The Space Radiation SRP suggests rewording the gap to:*
*How can experimental models of cancer risk be applied to reduce the uncertainties in radiation quality effects from SPE's and GCR?*

Current Tasks:

1) HZE induced mammary cancer development processes in murine and humanized models, and their influence on radiation quality functions
2) Space Radiation Risk Assessment
3) Effects of prolonged exposure to space radiation on carcinogenesis and neuroendocrine differentiation in human prostate models
4) NSCOR: Radiation Carcinogenesis
5) NSCOR: Space Radiation and Intestinal Tumorigenesis
6) The Role of Gap-Junction Communication and Oxidative Metabolism in the Biological Effects of Space Radiation
7) Telometric proteins in the radiation/DNA damage response

8) DNA Damage Responses Induced by HZE Particles In Human Cells (03-OBPR-07)
9) Mechanisms of the Repair of HZE Induced DNA Double-Strand Breaks in Human Cells
10) Mechanisms for induction of Bystander Effects by High Energy Particles in Cells and Tissues
11) Role of high-LET radiation-induced mitotic catastrophe in mutagenesis: implication for carcinogenesis
12) Comparative analysis of charged particle-induced autosomal mutations in murine tissue and cells
13) A mechanistic investigation of space radiation induced carcinogenesis
14) Elucidating the relationship between the effects of various radiation qualities and cancer development processes using novel flow-based assays
15) Histone Acetyltransferases and the Cellular Response to DNA Damage
16) The Relation Between Mutagenesis and Genomic Instability After Particle Exposure In Vivo
17) The mechanism of excess relative risk on carcinogenesis induced by high-LET radiation
18) A role for homologous recombination in complex DSB repair after HZE particles
19) NSCOR: Lung Cancer Pathogenesis and HZE Particle Exposure
20) NSCOR: The contribution of non-targeted effects in HZE cancer risk (LBNL)
21) NSCOR: The contribution of non-targeted effects in HZE cancer risk (NYU)
22) Epigenetic effects of radiation on epithelial cell self-renewal
23) Radiation quality and the relationship between induced telomere dysfunction and mutagenesis
24) High energy proton dose-rate and mixed field effects on neoplastic transformation in vitro
25) DNA damage clusters in human cell transformation induced by single or multiple space radiation exposures
26) Radiation and gliomagenesis: a sensitive model system to evaluate the tumorigenic potential of HZE particles
27) Impact of Radiation Quality on Cancer Processes in 2D and 3D Esophageal Cell Models
28) Integrated experimental and computational study of radiation induced matrix remodeling in a human skin equivalent

- The SRP understands that biological endpoints leading to risk are sensitive to microscopic patterns of energy deposition and their mapping onto tissues by cellular signaling. For this reason, the SRP reaffirms earlier recommendations for NASA to prescribe the proper types of particles and energies to be used by experimenters, in order to ensure that experiments reveal their sensitivity to radiation quality. The SRP also suggests that NASA consider whether the radiation quality of protons has been sufficiently well determined to declare this gap closed for SPE. However, the SRP recognizes that protons may constitute a proper reference radiation. In that case, NASA should develop an appropriate protocol to ensure reproducibility.

**Cancer 4: How can models of cancer risk be applied to reduce the uncertainties in dose-rate dependence of risks from SPE's and GCR?**

Current Tasks:

1) Space Radiation Risk Assessment
2) Effects of prolonged exposure to space radiation on carcinogenesis and neuroendocrine differentiation in human prostate models
3) NSCOR: Radiation Carcinogenesis
4) NSCOR: Space Radiation and Intestinal Tumorigenesis
5) NSCOR: Lung Cancer Pathogenesis and HZE Particle Exposure
6) NSCOR: The contribution of non-targeted effects in HZE cancer risk (LBNL)
7) NSCOR: The contribution of non-targeted effects in HZE cancer risk (NYU)
8) Dose rate effects on the mechanisms of space radiation induced delayed genomic instability
9) Dose-rate effects of protons on the induction of genomic instability in vivo
10) Radiation and gliomagenesis: a sensitive model system to evaluate the tumorigenic potential of HZE particles
11) Dose-Rate Effects and Components of Systems Governing Variations in Susceptibility for Carcinogenic and Acute Radiation Risks following Gamma-Ray, Proton, or HZE Irradiation
12) Tissue-Specific Acute And Late Molecular Surveillance Of Particle Radiation Effects

- The SRP has no specific comments about any one task.
- Current uncertainty is high, and only a few projects are looking at dose rates. The SRP recommends that this risk be emphasized more in the near future to show whether there are reductions in effect or not, and then be able to move on. NASA should try to complete this aim as soon as possible so that NASA is not constantly doing expensive and time consuming does rate (DR) studies.
- High linear energy transfer (LET) does not deliver dose at a low DR in a conventional context. New non-targeted effects of radiation exposure may be sensitive to the time it takes for a total dose to be accumulated. NASA must use DRs that are relevant to the space radiation exposure. The new Electron Beam Ion Source (EBIS) system can be used to get several beams at once, and it will be important to use EBIS as soon a possible as a source of chronic exposure irradiation.
- The SRP recommends that the use of dose and dose-rate effectiveness factors be reviewed soon to determine the likely relative effect it may have if any, on overall risk considerations.

**Cancer 5 Gap: How can models of cancer risk be applied to reduce the uncertainties in individual radiation sensitivity including genetic and epigenetic factors from SPE and GCR?**

Current Tasks:

1) Mitochondrial-Derived Oxidants and Cellular Responses to Low Dose/Low LET Ionizing Radiation
2) NSCOR: Radiation Carcinogenesis
3) NSCOR: Space Radiation and Intestinal Tumorigenesis
4) NSCOR: Lung Cancer Pathogenesis and HZE Particle Exposure
5) Epigenetic effects of radiation on epithelial cell self-renewal
6) NSCOR: Solid Tumor Risk Estimation: Incorporating Intercellular Interaction Effects
7) Radiation and gliomagenesis: a sensitive model system to evaluate the tumorigenic

potential of HZE particles
8) Dose-Rate Effects and Components of Systems Governing Variations in Susceptibility for Carcinogenic and Acute Radiation Risks following Gamma-Ray, Proton, or HZE Irradiation
9) Tissue-Specific Acute And Late Molecular Surveillance Of Particle Radiation Effects
10) Structural Chromosome Aberrations Formed in Response to Changes in Proton Energy and Dose Rate
11) Patterns Of Energy Deposition By Hze Particles In Cellular Targets (03-OBPR-07)
12) Systems Biology Model of Interactions Between Tissue Growth Factors and DNA Damage Pathways: Low Dose Response and Cross-Talk in TGFbeta and ATM Signaling

- The SRP has no specific comments about any one task.
- The Cancer 5 knowledge gap is an important, highly relevant, area of current and future research. The advent of genome sequencing followed by increasingly efficient new techniques is allowing directed research into both genetic and epigenetic factors relevant to individual susceptibility to space radiation exposure. The SRPE is now supporting analysis of current data to update modeling for health standards by mid FY2010 (now completed). Importantly, the SRPE plans to support ground studies specifically addressing genomic and epigenomic susceptibility to high LET radiation beginning in FY2015. This judicious five-year delay will allow NASA to benefit from maturation of ongoing National Institutes of Health (NIH) (sequencing the epigenome) and Department of Energy (DOE) (low LET radiation) research in this field.
- The SRP considers this an important area with great promise as deep sequencing becomes easily possible and complete sequencing of the human genome at a very low price coming within reach. This allows studies on individuals at a level of detail unthinkable only a couple of years ago.
- The SRP recommends enhancing epigenetic work, as several aspects of individual susceptibility to ionizing radiation may be addressed in this way.
- The development of break through technologies will require the program to be highly alert in an effort to adopt and utilize to the full the generated opportunities.

**Cancer 6: How can models of cancer risk be applied to reduce the uncertainties in the age and gender dependence of cancer risks from SPE's and GCR?**

Current Tasks:
1) Patterns Of Energy Deposition By HZE Particles In Cellular Targets (03-OBPR-07)

- The SRP has no specific comments about the above task.
- Most studies have been done with young animals. Most astronauts are mature adults between 30-59. The SRP recommends moving to adult animals for these studies wherever possible to have molecular hallmarks of aging. At the very least validation using adult animals should be done where young animals must be used or are routinely used. The SRP is aware that adult animals may be less sensitive than young animals to the induction of certain cancers. This is actually important as it may reduce the overall risk in the risk assessment modeling. This may lead to a reduction in the incidence of cancer and the information obtained will be valuable, particularly when attempting to estimate cancer risk for astronauts

of different ages.

- The SRP recommends comparative studies between female and male animals for tumors that are important in both genders. Also, make sure gender specific diseases such as prostate and breast are given appropriate priority.

**Cancer 7: How can systems biology approaches be used to integrate research on the molecular, cellular, and tissue mechanisms of radiation damage to improve the prediction of the risk of cancer and to evaluate the effectiveness of CM's? How can epidemiology data and scaling factors support this approach?**

Current Tasks:

1) Space Radiation Risk Assessment
2) NSCOR: Radiation Carcinogenesis
3) NSCOR: Space Radiation and Intestinal Tumorigenesis
4) NSCOR: The contribution of non-targeted effects in HZE cancer risk (LBNL)
5) NSCOR: The contribution of non-targeted effects in HZE cancer risk (NYU)
6) NSCOR: Solid Tumor Risk Estimation: Incorporating Intercellular Interaction Effects
7) Low Dose IR Activation of TGF-Beta 1-IGF-1-sCLU In Vivo: Mechanisms, Functions of a Changing Microenvironment
8) Impact of Radiation Quality on Cancer Processes in 2D and 3D Esophageal Cell Models
9) Integrated experimental and computational study of radiation induced matrix remodeling in a human skin equivalent
10) Systems Biology Model of Interactions Between Tissue Growth Factors and DNA Damage Pathways: Low Dose Response and Cross-Talk in TGFbeta and ATM Signaling
11) Computational Modeling Of Chromosome Aberrations Produced By Hze Particles (03-OBPR-07)

- The SRP has no specific comments about any one task.
- The Cancer 7 knowledge gap is a high priority, highly relevant, area of current and future research. In particular, it is timely and appropriate to be developing mathematical network models using a systems biology approach. The SRPE rightly communicates that it will need a long term high priority effort, in supporting systems-level research from molecular/cellular/organismal biology to population-level epidemiology, in order to provide modeling input. The HRP Integrated Research Plan (IRP) shows this effort is ongoing and is planned to continue until through FY2021 if necessary. The SRP strongly recommends that greater effort be given to the sharing of tissues across studies, so that multiple measurements can be made on a single animal cohort. As the systems biology model matures it will be used to improve risk prediction as well as countermeasure efficacy.
- The development of new technologies along these lines will offer unique opportunities to the program to generate tools for a better risk estimate, possibly at the level of each individual astronaut.

**Cancer 8: What biological countermeasures should be used to reduce SPE and GCR cancer risks? What side effects should be tolerated vs. Mission risks?**

Current Tasks:

1) Mitochondrial-Derived Oxidants and Cellular Responses to Low Dose/Low LET Ionizing Radiation
2) NSCOR: Radiation Carcinogenesis
3) NSCOR: Space Radiation and Intestinal Tumorigenesis
4) NSCOR: The contribution of non-targeted effects in HZE cancer risk (LBNL)
5) NSCOR: The contribution of non-targeted effects in HZE cancer risk (NYU)
6) Risk assessment of space radiation enhanced colon tumorigenesis II
7) Mitigating High Z Radiation Induced Genomic Instability by Non-Protein Thiols

- The SRP has no specific comments about any one task.
- The SRP feels it may be necessary to assign a lower priority to this gap as it is not clear at the moment what can be mitigated. There is ongoing work funded by other agencies looking at anti-cancer agents which work at low doses. NASA should keep abreast of future developments at other agencies and consider possible leveraging that might be available by co- funding. Biological countermeasures are currently being developed for use in Homeland Defense programs. The goal of an effective agent would be the reduction of carcinogenic risk without side effects that could limit performance. Close cooperation with ongoing programs in NIAID Centers of Radiological Excellence, NIH funded programs; DOE and Department of Defense (DOD) funded programs should be initiated to leverage funding in this area.
- Radiation-induced adaptive response studies should be considered in light of potential for minimizing radiation risks in space. Close coordination with existing funded programs in DOE and NIH should be encouraged.
- Countermeasures for acute, degenerative risks should be kept separate from the possible cancer endpoints as mechanisms are different.

**Cancer 9: Are there significant synergistic effects from other spaceflight factors (microgravity, stress, altered circadian rhythms, changes in immune responses, depressed nutrition, bone loss, etc.) that modify the carcinogenic risk from space radiation?**

Current Tasks:

1) NSCOR: Radiation Carcinogenesis
2) NSCOR: Space Radiation and Intestinal Tumorigenesis
3) NSCOR: The contribution of non-targeted effects in HZE cancer risk (LBNL)
4) NSCOR: The contribution of non-targeted effects in HZE cancer risk (NYU)

- The SRP has no specific comments about any one task.
- The SRP feels this gap is an extension of the systems biology approach discussed in the Cancer 7 knowledge gap – the "system" is extended to encompass more of the effects of the surrounding environment on an individual; there are close tie-ins with epigenetic mechanism. As read here, this gap lists a number of specifics that are also important for Central Nervous System (CNS) risk, Acute Radiation risks, and Degenerative risks; thus they might be best combined into a single Environmental Effects knowledge gap. The National Council on Radiation Protection and Measurements (NCRP) is developing a commentary on synergistic risk for the SRPE, and the Element then plans to begin ground-based research in FY2015. It may be that a common mechanism or mode of action (such as cellular reactive oxygen

species or whole-organism circulatory problems) will emerge to link the various spaceflight factors.

- Factors that enhance and/or prolong general reactive oxygen species (ROS) production in living systems such as general stress, immune dysfunction, loss of sleep, and/or nutrition deficits have the potential of exacerbating ROS induced damage by ionizing radiation by virtue of their ability to lower endogenous cellular and tissue anti-oxidant defense mechanisms such as those mediated by superoxide dismutase, glutathione peroxidase, catalase, glutathione, etc.. The role of elevated ROS in carcinogenesis has been extensively studied. Research into dietary, medical, or environmental factors to reduce the effects of such ROS inducing agents is of merit.
- It will be helpful to generate a list indicating which of the possible synergisms are studied as subsets of work carried out for other space factors and which will need to center around the radiation program.
- The SRP suggests taking advantage of tissue sharing to study endpoints relevant to all gap areas (carcinogenesis, CNS, and degeneration) and use of common cohorts of animals may help improve risk predictions under actual mission constraints.

**Cancer 10: Are space validation experiments needed for verifying knowledge of carcinogenic or other risks prior to long-term deep space missions, and if so what experiments should be undertaken?**

Current Tasks:

1) NSCOR: Radiation Carcinogenesis
2) NSCOR: The contribution of non-targeted effects in HZE cancer risk (LBNL)
3) NSCOR: The contribution of non-targeted effects in HZE cancer risk (NYU)

- Following significant discussion the SRP felt that this gap had been closed with the NCRP report that was prepared last year.

**Cancer 11: What are the most effective shielding approaches to mitigate cancer risks?**

Current Tasks:

1) Space Radiation Risk Assessment
2) NSCOR: Radiation Carcinogenesis
3) NSCOR: Space Radiation and Intestinal Tumorigenesis
4) Integrated Radiation Analysis and Design Tools

- This is not properly a gap in the HRP IRP but an engineering problem. The HRP IRP provides the scientific basis on which shielding evaluations can be based, but additional experiments to develop shielding are not needed. In the future, a carefully defined measurement of a restricted set of critical parameters may be useful to validate such calculations. The SRP identified this task as being of lower priority and using resources that would be better applied to the biological investigations.

**Cancer 12: What level of accuracy do NASA's space environment, transport code and cross sections describe radiation environments in space (ISS, Lunar, or Mars)?**

Current Tasks:

1) Measurements and Transport Phase 2 Physics Project
2) Quantum Multiple Scattering Model of Heavy Ion Fragmentation (QMSFRG)
3) Update of the Nuclear Fragmentation Cross Section Code NUCFRG2

- The SRP believes that, at this time, the accuracy of predicting particle fluxes in space (of the order of ±15%) is sufficient for risk prediction and could not be significantly improved without a major investment in resources better utilized in addressing other gaps.

**Cancer 13: What are the most effective approaches to integrate radiation shielding analysis codes with collaborative engineering design environments used by spacecraft and planetary habitat design efforts?**

Current Task:

1) Integrated Radiation Analysis and Design Tools

- This is a technology transfer problem and not a research problem. It should be addressed by the appropriate engineering programs and the resources devoted to it would be better utilized by expanding support of the higher priority gaps.

**Cancer 14: What are the optimal biodosimetry methods for Lunar and Mars missions, and are biomarker approaches needed?**

Current Tasks:

1) A Novel Biodosimetry Method
2) MiRNA profiling of radiation response: A systems biology approach to understanding regulation of proton and heavy ion dose effects

- The Cancer 14 gap should be kept on the list, although the SRP agrees it is not currently of the highest priority for research. To date, the biodosimetry methods currently available to NASA are already sufficient to indicate moderate and higher exposure levels; useful for making treatment decisions in the case of highly unlikely space exposure scenarios. The biodosimetry is not yet able to provide biomarkers of individual risk, due to the lack of knowledge on human interindividual variability.

## III. Critique of Gaps and Tasks in the *RISK OF ACUTE RADIATION SYNDROMES DUE TO SOLAR PARTICLE EVENTS*

*The Space Radiation SRP suggests rewording the risk to:*
*Risk of Acute Radiation Effects Due to Solar Particle Events*

**Acute – 1: What are the probabilities for various acute effects from SPE's including RBE's and dose-rate modifiers?**

*The Space Radiation SRP suggests rewording the gap to:*

*What are the probabilities for prodromal and skin effects from SPE's including RBE's and dose-rate modifiers?*

Current Task:

1) Center of Acute Radiation Research: Acute Radiation Biological Effects Resulting from Exposure to Galactic Cosmic Rays and Protons from Solar Particle Events

- This task is only looking at prodromal syndrome and possibly skin (2Gy dose), and astronauts will never get a dose leading to bone marrow (BM), gastrointestinal (GI) or CNS effect. This being said, the focus is on prodromal effects, and the SRP believes this is appropriate. Relative Biological Effectiveness (RBE) and DR effects are reasonable. However, it is not clear to the SRP why the National Space Biomedical Research Institute (NSBRI) Center of Acute Radiation Research (CARR) is looking at acute radiation syndrome (ARS). It appears unlikely any astronaut would suffer ARS under present radiation exposure constraints. Therefore, this part of the gap should be a low priority.

**Acute – 2: What quantitative procedures or theoretical models are needed to extrapolate molecular, cellular, or animal results to predict acute radiation risks in astronauts? How can human epidemiology data best support these procedures or models?**

Current Task:

1) Space Radiation Risk Assessment

- The SRPE should continue to focus on this systems biology-type modeling as the data become available. It is important to bring epidemiology into the modeling effort; low dose-rate epidemiology studies of either animal subjects or human workers are particularly relevant to space radiation exposures. In addition, consideration should be given to combining the Acute 2 and Acute 3 gaps, since Acute 3 can be thought of as a critical extension of the systems biology way of modeling — the "system" is extended to encompass more of the effects of the surrounding environment on an individual (please see comments for Cancer 9 gap).

**Acute – 3: Are there synergistic effects arising from other spaceflight factors (microgravity, stress, immune status, bone loss, etc.) that modify acute risks from space radiation including modifying thresholds for such effects? (post PPBE)**

Current Task:

1) Center of Acute Radiation Research: Acute Radiation Biological Effects Resulting from Exposure to Galactic Cosmic Rays and Protons from Solar Particle Events

- The SRP feels this is important particularly for nausea and vomiting can be induced by microgravity, and recommends a more focused approach to each of these issues that might be reflected in the details of the calls for proposals in the coming years.

**Acute – 4: What are the probabilities of hereditary, fertility, and sterility effects from space radiation?**

No Current Tasks

- Current technologies exist to address concerns related to hereditary, fertility, and sterility effects from space radiation and include the storing of sperm and the collection and storing of eggs for *in vitro* fertilization as is currently done for cancer patients who are about to undergo potent radiation and chemotherapies that are known to adversely affect these endpoints. A retrospective study of past astronaut experiences regarding these endpoints should be sufficient to determine the potential of these deleterious effects. If such data are available or if it is clear that no significant problem exists, the SRP recommends that this gap be eliminated.

**Acute – 5: What are the optimal SPE alert and dosimetry technologies for EVAs?**

Current Tasks:

1) Design of a Radiation Dosimeter for Astronauts During Lunar EVAs
2) Spectroscopic Dosimeter
3) NSBRI - MIcrosDosimeter iNstrument (MIDN) System Suitable For Spaceflight
4) Tissue-Equivalent Radiation Dosimeter-On-A-Chip
5) ARC - Measurement Tech WBS

- This is a technology issue/engineering problem. If this gap remains, the SRP recommends assigning it a lower priority.

**Acute – 6: What are the most effective shielding approaches to mitigate acute radiation risks, how do we know, and implement?**

Current Tasks:

1) Integrated Radiation Analysis and Design Tools
2) Space Radiation Risk Assessment

- This is a technology transfer problem and not a research problem. It should be addressed by the appropriate engineering programs and the resources devoted to it would be better utilized by expanding support of the higher priority gaps.

**Acute – 7: What are the most effective biomedical or dietary countermeasures to mitigate acute radiation risks?**

Current Task:

1) Center of Acute Radiation Research: Acute Radiation Biological Effects Resulting from Exposure to Galactic Cosmic Rays and Protons from Solar Particle Events

- This gap should consider both acutely and chronically administered classes of mitigator agents. Development of acutely administered and robust acting biological and chemical agents capable of mitigating radiation risks should be pursued within NASA as well as with leveraged studies being conducted by National Institute of Allergy and Infectious Diseases (NIAID) Centers of Radiological Excellence, NIH RO1 grant awardees, DOE funded studies,

and DOD funded studies. Chronic administration of agents capable of enhancing endogenous anti-oxidant systems and repair systems should be investigated within NASA and in partnership with ongoing activities of the chemoprevention branch of the NIH. Focus should be on leveraged multi-agency research activities to translate existing clinical findings to space research applications.

**Acute – 8: How can Probabilistic risk assessment be applied to SPE risk evaluations for EVA, and combined EVA+IVA exposures?**

No Current Tasks

- This is an important gap. The "Space Radiation Risk Assessment" task should generate data in this area.

## IV. Critique of Gaps and Tasks in the *RISK OF ACUTE OR LATE CENTRAL NERVOUS SYSTEM EFFECTS FROM RADIATION EXPOSURE*

**CNS – 1: Is there a significant probability that space radiation would lead to immediate or acute functional changes in the CNS during a long-term space mission and if so what are the mechanisms of change? Are there threshold doses for these effects?**

Current Tasks:

1) Proteomic aided investigation of the mechanistic basis for HZE-induced cognitive impairment and the development of diagnostic biomarkers
2) Cognitive/behavioral, sensory, and motor changes induced by SPE and GCR Irradiations
3) Neurogenesis and cognition in human apoE transgenic mice following 56Fe radiation
4) Impact of HZE Particles on Adult Neural Stem Cells and Neurogenesis
5) Local CNS and systemic inflammatory effects following proton and mixed particle exposure
6) Individual Differences in the Neurochemical and Behavioral Response to Exposure to Protons
7) Charged Particle Radiation and Resultant Oxidative Stress Elicit Deleterious Functional Changes in the Central Nervous System
8) Use of a molecular marker of learning and memory to assess effects of 56Fe irradiation on hippocampus-dependent cognition and neurogenesis

- This is an important gap that requires particular attention. Ongoing research on the topic needs to be continued. The SRP recommends this gap be given a high priority.

**CNS – 2: Is there a significant probability that space radiation exposures would lead to long-term or late degenerative CNS risks if so what are the mechanisms of change?**

Current Tasks:

1) Mechanisms of Low Dose HZE Alteration of Neuronal-Astrocytic Coupling: The Role of Purinergic Receptors and Calcium Signaling

2) Inflammation in the brain after particulate irradiation predisposes the hippocampus to a heightened vulnerability after a secondary insult
3) Development and use of human 3-Dimensional tissue culture models for the study of space radiation effects on the central nervous system
4) Epigenetic Control of Radiogenic Damage Processing in *C. elegans*
5) NSCOR: Progressive Alterations of Central Nervous System Structure and Function Are Caused by Charged Particle Radiation
6) Molecular basis of DNA repair and protection from apoptosis in neuronal progenitors exposed to space radiation
7) Oxidative stress as a mechanism for altering acute and chronic functional changes in the CNS exposed to low dose, low dose rates, and mixed fields of protons and HZE nuclei
8) Dose-rate and mixed field effects of protons and HZE nuclei on oxidative injury and stem cell plasticity in the CNS
9) Long term effects of space radiation in nonhuman primates
10) Neurodegeneration and Adaptation in Response to Low-Dose Photon Irradiation
11) High LET-radiation induced DNA repair mechanisms in Oligodendrocyte progenitor cells (OPC) in vitro and in vivo
12) Non-Invasive Early Detection and Molecular Analysis of Low X-ray Dose Effects in the Lens
13) Impact of HZE Particles on Adult Neural Stem Cells and Neurogenesis
14) Local CNS and systemic inflammatory effects following proton and mixed particle exposure
15) Individual Differences in the Neurochemical and Behavioral Response to Exposure to Protons

- This is an important gap that requires particular attention. Ongoing research on the topic needs to be continued. The SRP recommends this gap be given a high priority.

**CNS – 3: How does individual susceptibility including hereditary pre-disposition (Alzheimer's, Parkinson's, apoE) and prior CNS injury (concussion or other) alter significant CNS risks? Does individual susceptibility modify possible threshold doses for these risks in a significant way?**

*The Space Radiation SRP suggests rewording the gap to:*
*How does individual susceptibility including hereditary pre-disposition (Alzheimer's, Parkinson's, apoE) and prior CNS injury (concussion or other) alter significant CNS risks? Does individual susceptibility modify possible threshold doses and latency for these risks in a significant way?*

Current Tasks:
1) Charged Particle Radiation and Resultant Oxidative Stress Elicit Deleterious Functional Changes in the Central Nervous System
2) Use of a molecular marker of learning and memory to assess effects of 56Fe irradiation on hippocampus-dependent cognition and neurogenesis
3) Inflammation in the brain after particulate irradiation predisposes the hippocampus to a heightened vulnerability after a secondary insult

4) Development and use of human 3-Dimensional tissue culture models for the study of space radiation effects on the central nervous system
5) Epigenetic Control of Radiogenic Damage Processing in *C. elegans*
6) NSCOR: Progressive Alterations of Central Nervous System Structure and Function Are Caused by Charged Particle Radiation
7) Molecular basis of DNA repair and protection from apoptosis in neuronal progenitors exposed to space radiation

- This is an important gap to address. Current interest and research within the medical community and organizations such as the National Football League (NFL) to investigate the consequences of brain damage due to concussions and head injuries of athletes and motor cycle enthusiasts could offer a source of information for use in addressing this gap. Focus should be on leveraging existing research and information obtained by groups such as these to address related issues in the NASA program.

**CNS – 4: What are the most effective biomedical or dietary countermeasures to mitigate CNS risks? By what mechanisms are the countermeasures likely to work?**

Current Tasks:

1) Individual Differences in the Neurochemical and Behavioral Response to Exposure to Protons
2) Oxidative stress as a mechanism for altering acute and chronic functional changes in the CNS exposed to low dose, low dose rates, and mixed fields of protons and HZE nuclei
3) Dose-rate and mixed field effects of protons and HZE nuclei on oxidative injury and stem cell plasticity in the CNS

- Countermeasure development to mitigate against CNS risks may be distinct from the biological countermeasure research focused on carcinogenesis and acute damage responses. Effective biological and drug agents presumably require the capability of crossing the blood-brain barrier (BBB). Systems biology approaches are needed to assess systemic effectiveness of biomedical or dietary agents that can safely elevate endogenous protective mechanisms in CNS tissues. Such agents might focus on reduction of ROS buildup and associated damage, enhancement mitochondrial function and maintenance of brain and nerve cell function and survival.
- It is unlikely that CNS risks can be mitigated during the mission, and delayed CNS effects will be treated the same as those occurring *de novo*.
- Risks associated with this knowledge gap are uncertain, and it may be premature to assign a higher priority to this gap.

**CNS – 5: How can new knowledge and data from molecular, cellular, tissue and animal models of acute CNS risks or clinical human data, including altered motor and cognitive function and behavioral changes be used to estimate acute CNS risks to astronauts from GCR and SPE?**

Current Tasks:

1) Charged Particle Radiation and Resultant Oxidative Stress Elicit Deleterious Functional

Changes in the Central Nervous System
2) Space Radiation Risk Assessment

- This is an important gap that requires particular attention. Ongoing research on the topic needs to be continued. The SRP recommends this gap be given a high priority.

**CNS – 6: How can new knowledge and data from molecular, cellular, tissue and animal models of late CNS risks or clinical human date be used to estimate late CNS risks to astronauts from GCR and SPE?**

Current Tasks:

1) Charged Particle Radiation and Resultant Oxidative Stress Elicit Deleterious Functional Changes in the Central Nervous System
2) Mechanisms of Low Dose HZE Alteration of Neuronal-Astrocytic Coupling: The Role of Purinergic Receptors and Calcium Signaling
3) Long term effects of space radiation in nonhuman primates
4) Neurodegeneration and Adaptation in Response to Low-Dose Photon Irradiation
5) High LET-radiation induced DNA repair mechanisms in Oligodendrocyte progenitor cells (OPC) in vitro and in vivo
6) Space Radiation Risk Assessment

- Together with CNS-1 and CNS-5, this was considered by the SRP to be a central task deserving higher priority than the numbering scheme would seem to indicate, because it is indispensable in establishing the existence and nature of CNS risks altogether.

**CNS – 7: What are the best shielding approaches to protect against CNS risks, and are shielding approaches for CNS and cancer risks synergistic?**

*The Space Radiation SRP suggests rewording the gap to:*
*What are the best shielding approaches to protect against CNS risks, and are shielding approaches for CNS and cancer risks correlated?*

No Current Tasks

- The SRP believes that this question is premature, at least until gaps CNS-1, CNS-5 and CNS-6 can be closed. Even in that case, it may well be that shielding sufficient for cancer risk may be adequate also to mitigate CNS risk. In any case, until the existence and nature of CNS risks, if any, are established, this should remain a low priority endeavor.

**CNS – 8: Are there significant CNS risks from combined space radiation and other physiological or space flight factors (e.g., sleep deprivation, psychological, microgravity, immune-endocrine systems or other)?**

Current Task:

1) Use of a molecular marker of learning and memory to assess effects of 56Fe irradiation on hippocampus-dependent cognition and neurogenesis

- This is a gap that cannot be addressed properly until the existence and nature of CNS risk, if any, are established.

## V. Critique of Gaps and Tasks in the *RISK OF DEGENERATIVE TISSUE OR OTHER HEALTH EFFECTS FROM RADIATION EXPOSURE*

**Degen – 1: How can tissue specific risk models be developed for the major degenerative tissue risks, including heart, circulatory, endocrine, digestive, lens and other tissue systems in order to estimate GCR and SPE risks for degenerative diseases?**

Current Tasks:

1) A Metabolomics and Mouse Models Approach to Study Inflammatory and Immune Responses to Radiation
2) Oxidative Stress and Skeletal Health with Low Dose, Low LET Ionizing Radiation
3) Mechanisms, early events, and dose dependence of radiation-induced atherosclerosis
4) Integrated experimental and computational study of radiation induced matrix remodeling in a human skin equivalent
5) Effects of Estrogen on Cataract Induction After Exposure to High LET Radiation

- The gap and approach are appropriate for the radiation program.

**Degen – 2: What are the mechanisms of degenerative tissues risks in the heart, circulatory, endocrine, digestive, lens and other tissue systems? What surrogate endpoints do they suggest?**

Current Tasks:

1) A Metabolomics and Mouse Models Approach to Study Inflammatory and Immune Responses to Radiation
2) Oxidative Stress and Skeletal Health with Low Dose, Low LET Ionizing Radiation
3) Mechanisms, early events, and dose dependence of radiation-induced atherosclerosis
4) Integrated experimental and computational study of radiation induced matrix remodeling in a human skin equivalent
5) SMO: Precise Assessment of Prevalence and Progression of Lens Opacities in Astronauts as a Function of Radiation Exposure During Space Flight and Development of Improved Routine Clinical Assessment of Ocular Lens Status
6) Mechanisms of Ocular Cataracts
7) Human endothelial cells in 2-D and 3-D systems; non-cancer effects and space-related radiations
8) Non-Invasive Early Detection and Molecular Analysis of Low X-ray Dose Effects in the Lens

- The gap is exploratory at this time attempting to define the actual risks in question; this gap and approaches are appropriate.

**Degen – 3: What are the progression rates and latency periods for degenerative risks, and**

**how do progression rates depend on age, gender, radiation type, or other physiological or environmental factors?**

Current Tasks:

1) Mechanisms, early events, and dose dependence of radiation-induced atherosclerosis
2) Integrated experimental and computational study of radiation induced matrix remodeling in a human skin equivalent
3) Early Markers of Space-Radiation Induced Human Cataractogenesis

- The SRP agreed that this gap and approach were reasonable and appropriate.

**Degen – 4: How does individual susceptibility including hereditary pre-disposition alter degenerative tissue risks? Does individual susceptibility modify possible threshold doses for these risks in a significant way?**

Current Task:

1) Effect of Space Radiation on degenerative tissue disease, genetic Instability and Oxidative DNA Damage in Ataxia Telangiectasis Deficient Mice

- Since there is little knowledge of what degenerative events will occur after high LET at very low doses, and thus what risk if any these pose, the determination of individual risk is perhaps premature and NASA should keep this as a later component after the first three risks are done. The SRP agrees with the delayed timetable proposed in the HRP IRP Update: ground-based research to begin FY 2013. Additionally, the SRP suggests that, at that time, research should also address environmentally-driven instantaneous individual susceptibility to the extent it is not covered in gap Degen 3, and that biological models reflect the whole organism risk from all sources of risk (cancer, CNS, degeneration) to the extent possible.

**Degen – 5: What quantitative procedures or theoretical models are needed to extrapolate molecular, cellular, or animal results to predict degenerative tissue risks in astronauts? How can human epidemiology data best support these procedures or models?**

Current Tasks:

1) Early Markers of Space-Radiation Induced Human Cataractogenesis
2) Space Radiation Risk Assessment

- The SRP considered this gap to be important and the corresponding tasks appropriate.

**Degen – 6: What are the most effective biomedical or dietary countermeasures to degenerative tissue risks? By what mechanisms are the countermeasures likely to work? Are these CMs additive, synergistic, or antagonistic to other Risks?**

Current Task:

1) Human endothelial cells in 2-D and 3-D systems; non-cancer effects and space-related radiations

- It may be premature to address this gap, and could be done later when more information about the size of degenerative risks and the length of time for them to occur is better understood. However finding mitigation strategies could still be important.
- This gap will become important if and when these risks are properly characterized. A large body of information currently identifies ROS damage due to redox imbalance and inflammatory processes as two potential components of the underlying mechanisms of degenerative tissue responses. Countermeasure development to address risks of carcinogenic development and acute responses may have significant overlap in effectiveness if the underlying factors include ROS imbalance, mitochondrial damage, tissue hypoxia development and inflammatory processes. The potential of angiogenesis inducing factors to counter degenerative tissue risks may also be a target for study.
- Efforts to address this gap might be enhanced through a research partnership with the DOD. Specifically, data based on degenerative tissue risks and countermeasures might have been or are currently being generated for military pilots, e.g., carrier Navy pilots, etc. If such projects exist, inter agency cooperation to leverage research resources would be useful.

**Degen – 7: Are their significant synergistic effects from other spaceflight factors (microgravity, stress, altered circadian rhythms, changes in immune responses, etc.) that modify the degenerative risk from space radiation?**

Current Task:

1) Simulated microgravity and radiation-induced bone degeneration; Oxidative Stress- and p53-Dependent Mechanisms

- There is still uncertainty in this area so investigations in the field are appropriate.

## VI. Discussion on the strengths and weaknesses of the IRP

***Please provide the Panel's assessment of the Integrated Research Plan in the areas of Space Radiation. Are important gaps in knowledge or tasks missing, are identified gaps or tasks irrelevant?***

**Strengths:**

- Overall, the Space Radiation SRP was pleased with the gaps that are being filled and the approaches designed for filling the gaps. The entire approach is thorough and unique within NASA and should facilitate the expected risk predictions for individuals. The approach of using evidence-based risk as a means of predicting risk was considered important by the group.
- Noting that the type of research required by this program is highly specialized, the SRP praised NASA's approach for investing in investigators by building up a cadre of scientists with the appropriate background, skills and capabilities for conducting the experiments needed. This is a remarkably important contribution that this program has made to the entire field in recent years. The building of a scientific community ensures that the core competencies essential for NASA's mission are available when most needed. The NASA Space Radiation Biology Summer School has also provided a means of introducing young and training investigators to the field; this has been remarkably successful. Only through proactive maintenance of expertise in the field of radiation sciences will it be possible to achieve the goals of the program and to make space travel

reality in a safe way.

- Another component of a solid program for studying the effects of space radiation is access to appropriate facilities. Through the National Space Radiation Laboratory (NSRL), NASA has provided investigators with the unique facilities required for evaluating the effects of radiation on cells and animals. This has been critical to the NASA program and to the radiation community.

**Areas not well-emphasized in the Program:**

- In general, research projects should be urged to note the beneficial as well as harmful effects on biological systems in response to aspects of the space environment being studied. For example, the radioadaptive response is defined experimentally as when a small priming dose of ionizing radiation can lessen the biological effects of subsequent exposure to a higher radiation challenge dose, or to another type of DNA-damaging insult. In the context of NASA's Space Radiation Program Element, there is great merit in knowing the extent of beneficial effects because of the extreme importance they would play in modeling human risks and extrapolating to lower doses and longer passages of time.
- A possible new gap may exist since radiation exposure effects are know to be oxygen dependent. Although this is assumed to be less for high LET, oxygen effects may still be important. Since astronaut suits use pure $O_2$, ISS is close to earth $O_2$ partial pressure and missions to moon/Mars will have $O_2$ partial pressure somewhere in between, there is a need to examine the effects of oxygenation and hypoxia on the radiation response.
- An area that should be expanded is research into stem cell development and application as a countermeasure for radiation risk reduction. Currently well recognized problems exist regarding the isolation, use, and maintenance of pluri-potential stem cells. Problems also exist and are well recognized regarding the administration of such cells to astronauts in a space environment. However, given the current general interest and resources focused by the medical research community in the development of stem cell research and applications and the long range exploration plans of NASA to travel to the lunar surface in 2020 and Mars in 2030, it would seem prudent to begin studies into the usefulness of stem cells harvested from individual astronauts as ultimate agents for individualized countermeasure effectiveness. The development of this technology could address two important needs for the NASA mission to Mars. First, shielding to protect stem cell cultures would take up less space than that required to completely shield to the same level individuals within the spacecraft and, second, such a repository would be invaluable for use in missions that are not easily aborted such as long duration deep space flights to Mars. Since earlier investigations into possible use of autologous bone marrow on space flights were considered too difficult to be useful there has been a great deal of progress in stem cell research. It is now possible to isolate specific stem cells and thus use a lot less in terms of volume and for specific biological problems. General human stem cell research as it might be applied to the health and maintenance of health of astronauts may be a gap in the risk analysis that needs a new review and possible some new research initiatives.

## VII. Other issues or concerns the panel chooses to address.

- Increased interaction with NIH, NIAID, Biomedical Advanced Research and Development Authority (BARDA), DTRA, DOD, and other agencies is strongly encouraged. The SRP recognizes the strengths of the DOE-NASA partnership and recommends other agency partnerships.
- The SRPE objectives required to enable space exploration cannot be accomplished without the research and development possible only with the use of NSRL. NASA is aware of the fact that accelerator facilities have a limited lifetime and that use of NSRL cannot be postponed indefinitely without risking it becoming unavailable. Based on historical data, it seems reasonable to use 15 years as the projected time that NSRL will be available under conditions similar to the present. Current use of the facility depends on support of the Brookhaven accelerators by DOE high energy physics and nuclear physics research. Once that research ceases to require the use of NSRL, the facility may only become available at a cost comparable to the cost of the entire accelerator complex, if at all. For this reason, it is essential for NASA to utilize NSRL to the maximum extent possible while it is available.
- Interactions with NSBRI will need to be better defined in order to evaluate complementarities of actions and potential overlaps. In order for future reviews to be fully effective it may be useful for NASA and NSBRI to give a clearer picture of the gaps and tasks being done by NSBRI and how the research is apportioned at NSBRI from the point of view of internally funded studies and externally peer reviewed funding. In the current review it was difficult from the information given to the SRP to discern if any overlaps in research tasks were occurring and if so whether these were useful or not.
- The SRP welcomed the interest of NASA staff members and their availability as a valuable resource during the SRP deliberations. The support of NASA management for the program is also considered to be a major asset. However, the presence of NASA personnel during Executive Sessions creates a perception that the SRP is not truly independent, thus reducing the effectiveness of its report. In this particular review the NASA personnel present acted with the greatest discretion and made no attempt to influence our deliberations. However, this is an issue of appearance, and the SRP recommends that provision be made in the future for one or more Executive Sessions restricted only to SRP members. Appropriate NASA personnel should be on call to respond to any questions that come up in the course of these sessions, but should not attend.

## VIII. Space Radiation 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 Space Radiation Program Element 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.

## IX. Space Radiation SRP Roster

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**Gayle Woloschak, Ph.D.**
Northwestern University

**Panel Members:**

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National Institutes of Health

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