SUMMARY REPORT

COMMERCIAL SPACEFLIGHT FEDERATION

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SOLVING PROBLEMS FOR A SAFER WORLD®

CSF/MITRE WORKSHOP TO CREATE A HUMAN RESEARCH PROGRAM FOR SPACEFLIGHT PARTICIPANTS IN THE COMMERCIALIZATION OF SPACE

Michael Marge, Ed.D.
Co-chair of the Workshop and Editor

Acknowledgements

I wish to express my deep appreciation and thanks to the many colleagues whose participation and contributions led to a successful Workshop outcome and to this Summary Report. With trepidation that I may leave out someone who contributed, I would like to begin with my sincere thanks to Tommy Sanford for his steadfast support, sagacious advice, and guidance and friendship. Without his commitment to this initiative on behalf of the members of CSF, we would not have traveled together this far. Also, my gratitude to CEO and President of CSF, Karina Drees, who also provided steadfast support and assistance. Thanks to Katherine Wilson at CSF who effectively and efficiently helped in the implementation of the Workshop.

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Michael Marge, Ed.D., Co-chair of the Workshop and Editor of the Summary Report

June 21, 2021

Executive Summary

In preparation for U.S. leadership in the commercialization of space, a proposal to create a human research program for civilians in space was submitted to the National Space Council, which was favorably considered and directed to the Commercial Spaceflight Federation for hosting. With the cooperation and sponsorship of the Commercial Spaceflight Federation, together with The MITRE Corporation, a Workshop was conducted on May 11–12, 2021. Many leading experts from the space industry, relevant federal agencies, private sector organizations, and academia joined together for one and a half days to develop a practical, prudent, and sustainable framework for a human research program.

The Workshop conferees addressed key factors that should be considered in preparing spaceflight participants for suborbital flight and orbital and beyond low Earth spaceflight and habitation. These factors include the need to seek the most effective ways to allow civilians to travel and live in space in good health, safety and comfort. In addition, the Workshop acknowledged that a near-term reality of hundreds of civilians in space, growing ultimately to thousands and possibly millions, constitutes a public health challenge.

Based on a review of the relevant literature, the recommendations of the Workshop Planning Committee, and the comments and recommendations of Workshop participants, the following represents a framework for a human research program for a diverse population of spaceflight participants:

Priority Human Research Projects for Spaceflight Participants (SFPs) in Suborbital Space

- Space Motion Sickness: Two year research project
- SFP Anxiety and Stress: Two–three year research project
- SFPs with Physical Disabilities: One–three year research projects
- SFPs Response To Acceleration Forces, G Transitions, Cardiovascular Health, Fluid Shifts, Launch/Landing Loads, Vibration and Noise: One–two year research projects
- The Impact of Nominal and Off-Nominal Launch and Landing Loads: Two year research project
- Key Phenomenon of Career Astronaut Health to be Studied in Novel Suborbital Test Subjects: One year research project

- Measuring the Effectiveness of New Microgravity Medical Sensors, Tools, and Procedures, such as Novel Biometric Sensors, Ultrasound for Jugular Venous Stasis, and Microgravity Wound Management: Three year research project

Priority Human Research Projects for SFPs in Orbital and Beyond Low Earth Spaceflight and Habitation

- Microgravity Impact on Health Status of a Large, Diverse Population of SFPs, including People with Disabilities: Five year research project
- Space-encountered Radiation Impact on the Physiology of SFPs: Five year research project
- Distance from Earth and Isolation Effects on the Psychology and Function of SFPs: Three year research project
- Effectiveness of Pre-flight training and Experience in Preparing SFPs for Orbital and Beyond Low Earth Spaceflight and Habitation: Two year research project
- Special Accommodations for SFPs with Disabilities: Two year research projects
- Effects of Acceleration Forces, Vibration, Noise and G Transition Factors on SFPs During Launch and Landing: Two year research projects

The Creation of a Database on the Health and Function of SFPs in Spaceflight and Habitation

- Create an SFP Health Working Group for the Development of a Database on the Health and Function of SFPs. The Working Group will agree on how the project will be administered, the data collection standards, procedures for the protection and safety of information, and the protocols for data collection: November 2021–April 2022
- Begin Collecting and Collating Specified and Standardized Opt-in Data from all Provider Sources into a Repository that Meets the Requirements of Safety and Privacy of Individual and Proprietary Information: May 2022

It is proposed that a public/private partnership of relevant federal agencies and private sector organizations be established to implement the human research program outlined above. The agencies should include the Federal Aviation Administration, National Aeronautics and Space Administration, National Institutes of Health, Office of the Assistant Secretary for Health/Health and Human Services, Centers for Disease Control and Prevention, Food and Drug Administration, and Department of Defense, with the guidance and partnership of the Commercial Spaceflight Federation.

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History and Introduction

During the National Space Council's (NSC) 2020 discussion about the commercialization of space, Council members referred to the prospect of civilians (spaceflight participants, or SFPs) traveling, living, and working in space in the coming decades. Significant early focus has been on the technology of space travel, with limited public discussion around the health and safety of SFPs who may become involved in space commerce as tourists, researchers, educators, industrial workers, miners, and transport agents.

Although some hazards to human health, safety, and comfort have been identified—microgravity, radiation, acceleration, and distance from Earth anxiety—physiological risks and uncertainties for spaceflight participants remain. In addition, commercialization of space will increase space access for a broad population of civilians with varying degrees of physical and mental fitness, with underlying health problems, and with no standardized medical criteria for selection. Therefore, significant opportunities exist to study the SFP in space during pre-flight, in-flight, and post-flight operations and activities to better understand or mitigate adverse outcomes and make space more accessible to the average civilian.

In September 2020, the need to address the potential biomedical risks that SFPs will face in this decade and beyond as space is commercialized was discussed with NSC staff. This led to an invitation by the NSC to Dr. Michael Marge, Health and Human Services (HHS) Space Research Consultant, to submit a proposal for a workshop to create a human research program for SFPs in the commercialization of space. The following events occurred:

September 2020	The draft Workshop proposal written by Dr. Michael Marge was reviewed and critiqued by a number of experts in space medicine. A final Workshop proposal was completed by October 1.
October 1, 2020	The proposal to conduct a "Workshop for Creating a Human Research Program for Spaceflight Participants in the Commercialization of Space" was submitted to the NSC.
October 9, 2020	The NSC responded favorably and referred the Workshop proposal to the Commercial Spaceflight Federation (CSF) for hosting. Dr. Marge contacted Tommy Sanford, Executive Director, CSF, to discuss CSF's sponsorship of the proposal.
November 9, 2020	CSF approved and agreed to host the Workshop in spring 2021.
December 14, 2020	First meeting of the CSF Workshop Planning Committee was

	held; members included Dr. John Allen (NASA), Dr. Michael Altenhofen (SpaceX), Dr. Melchor Antuñano (FAA), Sirisha Bandla (Virgin Galactic), Dr. Jonathan Clark (Baylor College of Medicine), Dr. Steven Collicott (Purdue University), Dr. Marsh Cuttino (Orbital Medicine), Dr. Kenneth Davidian (FAA), Karina Drees (CSF), Dr. Valerie Gawron (MITRE), Dr. Anil Menon (SpaceX), Philip McAlister (NASA), Dr. Paul Reed (HHS), Tommy Sanford (CSF), Dr. Michael Schmidt (Sovaris Aerospace), Dr. Victor Schneider (NASA), Dr. Mark Shelhamer (Johns Hopkins School of Medicine), Dr. Erika Wagner (Blue Origin), Dennis Stone (NASA), Taber MacCallum (Space Perspective), Dr. Jeffrey Jones (Baylor College of Medicine), and Dr. Michael Marge, Chair (HHS).
December 15, 2020 – June 2021	The Workshop Planning Committee continued as the “Governing Board” for the Workshop and the initiative to create a human research program for spaceflight participants in the commercialization of space, providing guidance and direction as needed (The Workshop Planning Committee has been expanded. Consult the appendices for the current list of members).
May 11 & 12, 2021	Conducted the CSF/MITRE Workshop.

The aim of the Workshop was to bring together leading experts in space medicine to assist in establishing a practical, prudent, and sustainable framework for a human research program for SFPs in space. This report opens with a review of previous literature, then explores the results of the May 2021 CSF/MITRE workshop with recommendations for a human research program for SFPs.

Rationale for a Human Research Program for SFPs

The federal government and the space industry have been interested in the commercialization of space for many years, beginning as early as the 1960s. In 1962, one of the first commercial uses of outer space occurred when the Telstar 1 satellite was launched to transmit television signals over the Atlantic Ocean.[1] The possibilities for commercialization of space advanced with the advent of the International Space Station (ISS) in 1969. Since then, with increased space exploration activity and as the science and technology of space have grown almost exponentially, numerous new recommendations about the advantages of the commercialization of space have been proposed. The literature now abounds with reports of scientific meetings and opinion articles about the commercialization of space.

However, the growth of the commercial human spaceflight industry has led to a number of medical and ethical questions about the health, safety, and comfort of civilian spaceflight participants. With more than 50 years of studying humans in space, we have learned a great deal about the hazards and coping strategies for humans traveling and living in space. Despite this experience and knowledge, however, many technological, ethical, and medical questions and uncertainties about spaceflight still exist.

Listed below are the types of potential commercial enterprises and activities that are feasible and will result in an economic advantage to investors; these have been gleaned from discussions with commercial space experts in the federal government, the space industry, and academia, and from an extensive review of the relevant literature.[2]

- Research: basic and applied where the study conditions of space are considered advantageous.
- Medical research for the benefit of terrestrials: study of diseases and effective interventions to prevent and/or combat those diseases, including new medications.
- Manufacturing: production of goods and materials that prove to be profitably manufactured in space, such as semiconductors, drug manufacturing (with new developments such as protein crystals to support new strategies for drug discovery), aerospace medicine methods, technology, assessment tools, therapeutics, prophylactics with translational application to Earth-based medicine, advanced fiber optics, tools, and food.

[1] Romano, A F. (2005). "SPACE A Report on the Industry". Defense Technical Information Center.

[2] https://blog.satsearch.co/2019-04-25-8-types-of-product-that-could-one-day-be-made-in-space; https://spacepolicyonline.com/topics/commercial-space-activities/

- Residential outposts and habitats in space: housing for orbital and lunar tourists and workers.
- Transportation systems for access to space facilities: orbital and lunar transportation.
- Mining: rare metals and other minerals from asteroids and helium-3 from the surface of the Moon.
- Space-based communication systems.
- Space-based solar power as a clean energy source for Earth.
- Education: space-centric approaches to teaching.

This list is partial and does not include other commercial activities that are currently envisioned and may be developed in the future.

As one reviews the potential commercial and research activities, it is important to analyze the type of entrepreneur and workforce who will pursue a commercial enterprise in space. Even for low orbit commercial activity, a review of past and current activities involving humans shows that the health needs of those who will become involved in the commercialization of space have not been adequately addressed.

In her 2020 report on Space Tourism to the United States Congress, Alyssa King writes, "Though federal law requires commercial spaceflight companies to inform passengers and crew of mission-related risks, certain medical conditions associated with spaceflight are still unknown or poorly understood."[3]

To successfully operate the planned range of potential commercial enterprises in space, the health and fitness of the workforce need to be considered. We are assuming that this workforce will include people of diverse races, cultures, and backgrounds. Based on the limited list above of possible commercial activities, the following types of personnel will be needed: researchers, scientists, corporate CEOs, factory workers, construction workers, physicians and allied medical workers, educators, engineers, miners, tourism workers, and security personnel. It is anticipated that many of these potential spaceflight participants will have underlying health conditions and disabilities. By providing expert and scientific guidance on who can safely engage in the commercialization of space, we can help facilitate this new era of expansion.

Collection of physiologic, behavioral, molecular, and phenotype data will help us generate proper assessment, screening, and countermeasures for SFPs. In support of this initiative, Dr. Michael Schmidt stated, "The vascular health of the average space

[3] https://crsreports.congress.gov/product/pdf/R/R46500

tourist/worker is likely to be more akin to the average person on Earth (as opposed to [the] average astronaut). The vascular system is one of those vulnerable systems that we should pay close attention to."[4] In addition, the research to protect and mitigate adverse effects of traveling and working in space needs to examine the activity in which the SFP will be engaged. For example, it has been reported that lunar dust clings to everything and could result in health issues for lunar SFPs who have even slight asthma. A miner working to extract helium-3 or lithium on the surface of the Moon will have to contend with this hazard. Research to prevent an adverse outcome from this hazard is essential before humans are sent to the Moon or an asteroid to mine substances.[5]

Stepanek et al. (2019) state, "Threats in the space environment vary according to the duration of the flight and range from physiological and adaptive alterations of the human body to the psychological challenges of isolation and distance from Earth."[6] In addition to the space hazards of acceleration forces on launch and landing, and long duration exposures to microgravity and radiation, other hazards include aerosols, barometric pressure, microbes, noise, spatial disorientation, temperature extremes, and vibration.

If we were to apply the selection criteria and training of a NASA astronaut to civilian workers in the commercialization of space, the cost would be prohibitive and most civilians would be excluded. NASA's astronauts are selected for their exceptional health status, are continually monitored, and undergo four to six years of training in preparation for space travel and exploration. For civilians who will engage in business and industry in space, it is essential that we review what is known about the biomedical risks to these civilians in suborbital, low Earth orbit (LEO), and deep space travel so that everyone is informed about the degree of risk and the countermeasures to address the risks. Part of the review could include what we know about the experience of career astronauts, their response to various durations in space, and their subsequent health outcomes. To a limited extent, these data could be extrapolated to predict the health outcomes of civilians. Because of the notable differences between the health and fitness of NASA's astronauts and the SFPs who will become involved in space commercialization, it is recommended that a robust human research program for spaceflight participants be considered. Our knowledge about the differential impact of space travel and habitation on age, sex, and race is notably limited and needs to be studied.

[4] Personal note, September 27, 2020.

[5] https://www.nasa.gov/exploration/humanresearch/areas_study/environment/enviro_lunar_dust.html

[6] Stepanek J., Blue, R.S., Parazynski S. Space Medicine in the Era of Civilian Spaceflight. The New England Journal of Medicine. 2019; 380(11):1053-1060. doi:10.1056/NEJMra1609012

Studies to Identify Biomedical Risks to SFPs Who Will Participate in the Commercialization of Space

In the Institute of Medicine's 2001 report by the Committee on Creating a Vision for Space Medicine During Travel Beyond Earth Orbit, an informative and significant discussion about risk is presented: "Risk is of high priority to NASA, and determination of what risks to humans exist and what countermeasures should be taken are addressed through NASA's Critical Path Roadmap project ["countermeasure" is NASA's designation for preventive and therapeutic interventions before or during space missions]."[7] These risks also can be studied for developing countermeasures during and after the mission through clinical and laboratory research. The Institute of Medicine report indicates that "there is a profound professional and ethical responsibility to evaluate honestly the risk to human life that accompanies long-duration space travel." These recommendations are still valid and should apply to civilians who may be involved in the commercialization of space.

Space medical experts know that orbital and cis-lunar and long duration space travel have significant adverse effects on the human body. These effects include physiological changes at the tissue and molecular levels. Although NASA's Twin Study represented only an N of 2, it has provided us with an insight into the omics of spaceflight and points to the possibility of unanticipated changes in human health.[8]

Antuñano et al. discuss the challenges of suborbital and orbital commercial human spaceflights, the recommended medical standards and management of medical risks, and the informed consent process applicable to the launch, flight, and landing. They state, "Space flights are associated with a number of physiological and psychological changes that may cause and/or aggravate certain medical conditions during flight, and could adversely impact an individual's health and safety."[9]

They continue that the spaceflight environment is far more hazardous than the operational risks encountered during commercial aviation flights. "Such increased risk factors include: acceleration, barometric pressure, microgravity, ionizing radiation, non-ionizing radiation, noise, vibration, temperature and humidity, breathable air and ventilation, as well as behavioral issues." They suggest that the space medical specialist "identify and mitigate significant pre-existing diseases, illnesses, injuries, infections, treatments (pharmacological, surgical, prosthetic, or other), or other physiological or pathological or psychiatric conditions among commercial space vehicle

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[7] https://www.nap.edu/initiative/committee-on-creating-a-vision-for-space-medicine-during-travel-beyond-earth-orbit

[8] The NASA Twins Study: A multidimensional analysis of a year-long human spaceflight | Science (sciencemag.org); April 2019

[9] Antuñano, Blue, Jennings, and Vanderploeg (Sept. 30, 2020). "The Commercial Spaceflight Industry: Medical Challenges and Risk Mitigation," *Handbook of Bioastronautics*.

occupants (flight crews and passengers). These medical conditions have the potential of resulting in inflight medical emergencies, resulting in inflight deaths, compromising the health and safety of commercial space vehicle occupants, interfering with the proper use (don and doff) and operation of personal protective equipment, interfering with emergency procedures (including evacuation), and/or compromising the safety of the flight." They conclude with the recommendation that commercial spaceflight participants, crew and passengers, will have to be carefully evaluated before allowing them to participate in suborbital and orbital spaceflights.

Similar recommendations were made by G. Starr Schroeder et al.[10] Their article is "the work of the Association of Spaceflight Professionals' Life Sciences Working Group, representing a review of US medical guidelines for commercial spaceflight participants. The review examines available data and publications, and makes recommendations going forward with respect to pre and in-flight mitigation of medical risk, covering medical screening and evaluation, in-flight medical capabilities, training recommendations and opportunities for refining the guidelines as more data becomes available." They conducted a search of Google and PubMed databases, using relevant search terms to identify publications of interest. Their conclusions included:

- Medical guidelines for SFPs must be guided by risk mitigation, further study of blind spots in our current knowledge, the development of more accurate models with larger sample sizes, and inclusion of data regarding physiological responses in participants with comorbidities during the transition from high-G to microgravity and back.
- A plan to medically monitor all SFPs and create a universal database to log in-flight events will inform future medical recommendations for suborbital flight. Standardizing a medical evaluation process to stratify risk as well as an immediate pre-flight screening will increase safety and delineate a role for aerospace medicine specialists.
- The suborbital environment should make an effort to eventually become more accessible to SFPs with significant medical equipment, mobility limitations, and deformities or disabilities. Future space travel needs to include a diverse population.
- As the frontiers of commercial suborbital spaceflight expand, there is a need for a simultaneous push to evolve medical recommendations/guidelines to maximize safety, while protecting flight providers from the risk of litigation.

[10] G. Starr Schroeder, J.C. Clark, Dr. M. Gallagher, Dr. S. Pandya (2021). "Medical guidelines for suborbital commercial human spaceflight: A review." *Acta Astronautica*. https://doi.org/10.1016/j.actaastro.2021.02.027

- The challenge in issuing medical recommendations for suborbital spaceflight lies in adequately protecting SFPs while protecting their autonomy, and not smothering a fledgling industry with over-regulation.
- High-risk spaceflight participants should be trained and prepared as much as possible before flight, and all SFPs should be informed of the evidence and uncertainty that exists around medical guidelines during the informed consent process.

Areas of Uncertainty

Despite years of experience and research with human spaceflight, there remain significant areas in need of essential research to meet the goal of protecting the health and safety of civilians in space. These include:

- The need for research on the impact of space travel on a representative large population of civilians, including women, people of color, people with a variety of chronic health conditions, and those with disabilities. To date, almost all data refer to fit professional astronauts and several studies of civilians subjected to the stresses of centrifuge tests simulating the acceleration profiles (+Gx and +Gz) that are expected to occur on suborbital spaceflights.[11,12,13]

- Currently, there is no research evidence in support of a type of training for suborbital or orbital flight for SFPs that will prepare them effectively for the experience, especially to ensure an appropriate response in case of an emergency. Stepanek et al. state, "Participants in suborbital spaceflight will need some degree of team training and practice of emergency procedures; they also will possibly need training in an analogue environment, such as centrifuge exposures, parabolic flights, and altitude-chamber training, to become familiar with environmental stressors and life-support systems. Participants in longer-duration missions, especially persons with pre-existing health conditions who are critically reliant on a healthy immune system, may also be subject to the known effects of the spaceflight environment (thought to be mediated by radiation and stress responses) on immune function. Alterations in T-cell function, the skin microbiome, and bacterial virulence, as well as asymptomatic viral reactivation, have been described. On the basis of current data, it is difficult to definitively discern which factors in humans appear to be the root cause for some of the alterations that have been reported (e.g., an increase in the neutrophil count after landing as a result of the stresses of reentry and readaptation). Deliberate attention to these aspects in preparation for the spaceflight, medical assessment, and preventive strategies may be warranted."

- The need to understand how factors in the space environment impact the health and capacity of civilians to fly successfully with differences in age, gender, race

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[11] Blue R.S., Pattarini J.M., Reyes D.P., et al. Tolerance of centrifuge-simulated suborbital spaceflight by medical condition. Aviat Space Environ Med 2014; 85: 721-9.

[12] Blue R.S., Bonato F., Seaton K., et al. The effects of training on anxiety and task performance in simulated suborbital spaceflight. Aerosp Med Hum Performance 2017; 88: 641-5.

[13] Blue R.S., Riccitello J.M., Tizard J., Hamilton R.J., Vanderploeg J.M. Commercial spaceflight participant G-force tolerance during centrifuge-simulated suborbital flight. Aviat Space Environ Med 2012; 83: 929-34.

and ethnicity, physical and mental health status, underlying health conditions, immunity, and resilience.

- The need to identify effective measures to prevent adverse outcomes of spaceflight and habitation in civilians, regardless of distinguishing differences in the physiology and mental characteristics of the individual, and to identify effective measures to treat adverse outcomes if they occur during and after spaceflight and habitation.
- The need to create a publicly accessible database that contains information from peer-reviewed scientifically based studies about adverse outcomes of space travel and habitation, effective measures to prevent and mitigate these outcomes, and promising new areas of research.

Schmidt et al. (2019) state the following: "The cohort of professional astronauts has been uniquely fit and exceptionally well trained. The advent of commercial spaceflight will see a wider range of individuals enter space, who lie on a variegated continuum of physical fitness, metabolic fitness, disease complexity, drug therapeutics, and genetics. Yet, there are currently little data on individuals of lesser fitness entering space."[14] Schmidt and his co-researchers acknowledge that spaceflight medicine "has grown in sophistication," but we are still confronted with serious knowledge gaps. They propose comprehensive molecular profiling for all humans facing space travel so that we can develop personalized countermeasures for the risks each individual may face. As an example, pharmacogenomics can assist in assuring the greatest degree of safety and effectiveness of drugs for all space travelers.

Current research efforts about the biomedical risks to astronauts facing deep space travel and reflected in NASA's Human Research Program are reported by NASA to be on target for addressing these hazards in preparation for Artemis and the journey to Mars. On the other hand, research efforts to address the biomedical hazards faced by SFPs who will be involved in space travel and habitation are disparate, uncoordinated, limited, and not part of a national plan of action to meet research goals according to a timetable. Stepanek et al. (2019) describe studies that have been performed to examine the degree to which civilians can tolerate the stresses of simulated suborbital spaceflights: "The participants in these studies were subjected to centrifuge tests simulating the acceleration profiles (+G_x and +G_z) that are expected to occur on suborbital spaceflights. The study participants ranged from 19 to 89 years of age and had a large variety of stable medical conditions that are prevalent in the general

[14] Schmidt, M.A., Schmidt, C.A., Hubbard, R.A. and Mason, C.E. (2019). Why personalized medicine is the frontier of medicine and performance for humans in space. New Space, Vol. 8, No. 2, 1-14.

population, including hypertension, pulmonary disease, stable coronary artery disease, and diabetes; some of the participants were taking medications to treat their disorders." The general finding was that participants with "well-controlled medical conditions" tolerated the centrifuge experience without difficulty. Additional research is needed to explore other factors that may be experienced by SFPs in suborbital flight to assure a healthy, safe and comfortable flight.

Stepanek et al. summarized the need for a robust human health research agenda for SFPs:

- The field of space medicine is poised for a substantial transition from primarily government-focused spaceflights carrying a few career astronauts to a large and diverse group of participants, mainly private citizens, who will be traveling to space, in most cases for short suborbital missions but in some cases to locations in low Earth orbit or farther.

- Data and experience accumulated from mission training and actual spaceflights will help determine the need for additional medical guidance for persons with certain medical conditions.

- A strong collaboration among practicing clinicians, space medicine specialists, and the aerospace community will ensure the safety of the participants in the expanding spaceflight industry.

The original proposal to the National Space Council recommended a Workshop dedicated to the creation of a collaborative research agenda to address the biomedical risks to spaceflight participants who will be involved in the commercialization of space. The goal of the Workshop was to begin the process of developing a Human Research Program for Spaceflight Participants comparable to the Human Research Program NASA developed for its professional astronauts, with a focus on the need for research on the biomedical risks SFPs face on suborbital and orbital flights.

Overview of the CFS/MITRE Workshop, May 11–12, 2021

There were 98 Workshop participants, with 29 presenters and moderators and 69 invited registrants, including individuals from industry, academia, and government representing the spaceflight, medical, and research communities. During the one and a half day meeting, the number of active online participants varied according to the topic. The Workshop provided a question and answer period after each presentation so invited registrants could provide input and recommendations. To respect the wishes of a number of participants, many of the recommendations made during the Workshop are not attributed to their sources here.

Day One, May 11

The meeting opened with welcoming remarks from Dr. Michael Marge and Tommy Sanford, Co-Chairs of the Workshop, followed by remarks by the leadership of the Workshop sponsors: Karina Drees, President of Commercial Spaceflight Federation, and Dr. Kerry Buckley, Vice President for MITRE.

The first plenary speaker was Dr. Michael Barratt of NASA, who provided many insights and recommendations about the challenges to the health of space travelers based on his expertise as a physician and as an astronaut. Dr. Marge served as moderator.

Next was a panel of representatives from the space industry who discussed their company's capabilities and plans for the future. The panelists were Dr. Erika Wagner of Blue Origin, Sirisha Bandla of Virgin Galactic, Dr. Jaime Mateus of SpaceX, and Christian Maender of Axiom Space. Each supported the purpose of the Workshop and commented on the importance of studying the health of SFPs in space in anticipation of a rapid growth of space travel and habitation by civilians in the coming decades. Katina Drees served as moderator.

Another panel discussion followed with representatives from three key federal agencies that have supported human space research: Dr. Kenneth Davidian of the FAA, Dr. Lucie Low of the National Institutes of Health/U.S. Department of Health and Human Services, and Dr. John Allen of NASA. Each described the roles of their agencies in support of human health research for space travelers. FAA noted their interest in the health of both astronauts and spaceflight participants.[15] NIH has had a long history of collaborative research with NASA on the biomedical risks astronauts face, with an eye towards insights for health of the general American population. NASA has conducted a program of robust human research for many years to protect their corps of astronauts. Each

[15] https://spacemedicineassociation.org/download/commercial_space_flight_medical_care_documents/COE-Commercial-Space-Flight-2012.pdf

speaker expressed their interest in the concept of a human research program for SFPs in the commercialization of space. Dr. Melchor Antuñano served as moderator.

The panel discussions were followed by two key presentations that focused specifically on the Workshop's purpose—recommendations for the creation of an HRP for SFPs in suborbital travel, and in orbital and beyond low Earth orbit spaceflight and habitation. Dr. Mark Shelhamer presented on the human research priorities for SFPs in suborbital flight. In addition, he discussed many factors related to the development and implementation of an HRP for SFPs in suborbital space. His priority research recommendations are reflected in the HRP for SFPs in this report. Dr. Marsh Cuttino served as moderator.

Dr. Michael Schmidt then presented on the human research priorities for SFPs in orbital and beyond low Earth orbit spaceflight and habitation. He emphasized the need to study "the range of genotypes and phenotypes (physiology, morphology, behavior; cognitive and physical performance) that will enter the dynamics of commercial orbital space, and converge with the varying degrees of infirmity, polypharmacy, deconditioning, and other influences." The HRP for SFPs in orbital space incorporated many of his priority recommendations. Dr. Jeffrey Jones served as moderator.

Because of the significant need to protect the safety and privacy of personal and proprietary data in human research and in the development of a database on the health and function of SFPs in space, the Workshop included a panel discussion on this topic with three experts: Dr. Valerie Gawron of MITRE, Dr. Kathy Jenkins of Boston Children's Hospital, and Dr. Sybil Klaus of MITRE. Their recommendations are included in the creation of a database on the health and function of SFPs in space found later in this report. Dr. Kenneth Davidian served as moderator.

Subgroup Discussions

To allow all Workshop participants to provide their specific recommendations for the creation of an HRP for SFPs in space, the participants were invited to attend one of two subgroup discussions conducted simultaneously—suborbital flight, chaired by Dr. Erika Wagner of Blue Origin, and orbital and beyond flight and habitation, chaired by Dr. Victor Schneider of NASA. Each subgroup opened with two invited speakers and then the participants were asked to answer the following question for day one:

> W*hat ground and flight studies would be most useful in safely opening orbital and beyond space travel for an ever wider audience? Consider underlying physical and mental health conditions, physical abilities, implanted devices, and chronic medications.*

For Question 1, the two invited speakers for suborbital were Dr. Marsh Cuttino of Orbital Medicine and Dr. Tarah Castleberry of Virgin Galactic; for orbital they were Dr. Jeffrey Jones of the Baylor College of Medicine and Dr. Christopher Scheibler of DOD.

The questions prompted a number of recommendations that are reflected in this report and in the recommendations for an HRP for SFPs presented later in this report.

Day Two, May 12

Day 2 was a continuation of the subgroup meetings to answer the next set of questions:

> A. *What is the minimum set of "standard measures" and adverse event reporting needed for research on commercial spaceflight participant safety? Do standard measures include environmental ones such as g loading?*
>
> *B. Do these differ for suborbital, short-orbital, and extended-orbital missions?*
>
> *C. If you could add one non-invasive metric beyond this minimum set, what would it be and who would be the primary stakeholder for the data?*

The invited speakers for suborbital who addressed these questions were Dr. Rebecca Blue, University of Texas Medical Branch, Galveston, and Dr. Erik Antonsen, Baylor College of Medicine. For orbital, the speakers were Dr. Emmanuel Urquieta, Translational Research Institute for Space Health, and Dr. Jonathan Clark, Baylor College of Medicine.

The question and answer periods that followed each subgroup meeting provided new and promising recommendations that were incorporated into the recommendations for the priority human research projects found later in this report.

After the subgroup meetings, Dr. Wagner and Dr. Schneider reviewed the critical comments and recommendations presented during their sessions. Karina Drees served as moderator of the session; Linda Fischetti of MITRE served as moderator for the Q&A session.

Finally, Dr. Marge chaired a session on Recommendations for Next Steps, which included Dr. Kenneth Davidian, FAA; Karina Drees, CSF; Dr. Benjamin Neumann, NASA; Dr. Valerie Gawron, MITRE; and Dr. Leith States, HHS. These panelists expressed their support and interest in the goal of the Workshop and urged continued cooperation and support in developing an HRP for SFPs in space travel and habitation.

The Workshop closed with expressions of appreciation by Tommy Sanford and Dr. Marge to presenters, moderators, and conferees for their participation, and to CSF and MITRE for their sponsorship of the Workshop.

Human Research Program for Spaceflight Participants in the Commercialization of Space

The human research projects of highest priority were identified based on review of the relevant literature, the recommendations of the Workshop Planning Committee, the subcommittee reports by Drs. Shelhamer and Schmidt, and the Workshop participants' comments and recommendations.

The identified human research priorities are presented in two sections: Suborbital Space, and Orbital and Beyond Low Earth Orbit Spaceflight and Habitation.

Priority Human Research Projects for SFPs in Suborbital Space

Recommendation #1: Space Motion Sickness (SMS)

a) Two year human research project to understand the frequency and severity of SMS in SFPs in suborbital flight, including co-factors such as sleep deprivation, anxiety, and stress. One of the research strategies is to monitor SFPs in parabolic and/or suborbital flight (applied research).

b) Two year human research project to identify the ideal and most effective methods for preventing or reducing the symptoms of SMS in SFPs in suborbital flight, including effectiveness of preflight training and medications (applied research).

c) Two year project to identify the best predictors of SMS in SFPs, examining all factors that have been substantiated as effective determiners of SMS in spaceflight crew and participants. This project may be incorporated as part of item a) described above (applied research).

Discussion

There are two main hypotheses for the mechanisms of SMS: fluid-shift theory and sensory-conflict theory. The fluid-shift theory proposes that the progressive displacement of fluid and blood from the lower to upper part of the body in microgravity leads to changes in the fluid of the vestibular system and hydrops or pressure on the vestibular apparatus. This leads to an impact on the vestibular receptors and SMS.

The sensory conflict theory is the prevailing explanation for SMS. Human spatial orientation on the 1g of Earth depends on the proper integration of information from various sensors, including the visual, vestibular, and proprioceptive systems. In an altered gravity environment such as freefall or Earth orbit, the normal pattern of sensory information is altered. This results in sensory conflict: the various senses do not agree with each other or with the pattern developed over experience in 1g. This can result in disorientation, nausea, and SMS. Head movements in the pitch and roll planes are major contributing factors, since “head tilt with respect to gravity” no longer has meaning when the net gravitational vector is removed.

Other theories include asymmetry between the otolith organs on the two sides of the head, and otolith tilt-translation reinterpretation (which is more of a theory for the adaptive process than for SMS itself). Factors that may contribute to SMS include sleep deprivation, stress, and anxiety.

Many questions remain unanswered about motion sickness in space, including the lack of correlation in susceptibility to various forms of motion sickness (terrestrial and space), the inability to explain those situations in which sensory conflict exists without sickness (and vice versa), and the mechanisms behind the high prevalence of some symptoms of SMS, such as vomiting. The lack of a predictive test for SMS susceptibility is particularly troublesome.

SMS has been treated with medications and with other preventive measures that seem to counteract the condition in parabolic flights and orbital spaceflight, but the efficacy is variable and side effects are common. There are few effective measures besides repeated exposure to the nauseogenic environment (e.g., adaptation to parabolic flight might provide some mitigation for SMS in suborbital flight). Research is needed to prevent or reduce the symptoms of SMS. This should include research into the prediction of SMS susceptibility, which could guide intervention strategies on an individual basis (medication, pre-exposure conditioning, etc.). Such a study could be started immediately, with systematic acquisition of a range of biomedical parameters to ascertain their relationship to SMS.

For SMS, the first recommended strategy is to use operational monitoring of SFPs in parabolic and/or suborbital flight to examine in greater detail the occurrence of SMS and effective ways to prevent it.

References of interest

- Shelhamer SARG ambassadors SLS.ppt (swri.edu)
- Parabolic flight as a spaceflight analog | Journal of Applied Physiology
- [Letter to Mark Shelhamer, Ph.D.] – Review of NASA’s Evidence Reports on Human Health Risks - NCBI Bookshelf (nih.gov)
- Commercial Suborbital Space Tourism – Proposal on Passenger Medical Selection | Request PDF (researchgate.net)
- The Commercial Spaceflight Industry: Medical Challenges and Risk Mitigation | SpringerLink; Howard_abstract.pdf (swri.edu)
- https://www.frontiersin.org/articles/10.3389/fphys.2021.675426/full#B55

Recommendation #2: SFP Anxiety and Stress

a) Two year research project to identify and measure degree of fear, anxiety, and stress in individuals who contemplate parabolic and/or suborbital flight (applied research).

b) Three year research project to identify the ideal and most effective methods for preventing or reducing the degree of anxiety and stress of flying in general and flying in parabolic and suborbital vehicles, including use of medications to counteract anxiety and stress (applied research).

Discussion

Anxiety disorders impact about 40 million adults and cause feelings of fear and uncertainty. These feelings can be exacerbated by stress. Symptoms of anxiety may include restlessness, fatigue, difficulty concentrating, irritability, muscle tension/aches/soreness, difficulty waking up or sleeping, trembling, twitching, shakiness, cold and clammy hands, dry mouth, heavy perspiration, nausea, diarrhea, frequent urination, difficulty swallowing, ease of being startled, increased heart rate, and heavy breathing.

In response to perceived physical or mental threats, the body's physiological reaction is to experience a fight-or-flight response. The response is generally normal and lasts only a short time, but in some individuals with anxiety disorders such intense emotions may continue for prolonged periods of time. The types of anxiety disorders are classified into generalized anxiety disorders, panic disorders, and phobia-related disorders. The generalized anxiety disorder (GAD) is the most common and is the one encountered by individuals with flight anxiety and presumably those who will face suborbital spaceflight. GAD could be activated by the following high-stress activities and fears: small spaces (claustrophobia) brought on by tight aircraft cabin environments; heights (acrophobia) provoked by being high above the ground during flight; falling associated with height (distinct from fear of heights itself); forced proximity of other people (agoraphobia).

Symptoms of anxiety disorders are thought to be a disruption of the emotional processing center in the brain's limbic system, which includes the hippocampus, amygdala, hypothalamus, and thalamus. It is postulated that individuals with an anxiety disorder may have heightened neural activity in these areas. The decision-making area of the brain determines that the individual is facing a threat. This creates a reaction in the amygdala that informs the hypothalamus to trigger the fight-or-flight response.

A number of prevention and mitigation methods have been proposed to reduce anxiety and stress when the individual faces a situation that prompts the fight-or-flight response. These include meditation (cognitive behavioral therapy), avoiding processed foods and alcohol, regular physical activity, and use of certain medications such as selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, and benzodiazepines.

It is noteworthy that anxiety is a prime (yet rare) cause of subjects withdrawing from centrifuge trials related to suborbital medical research.

Recommendation #3: SFPs with Physical Disabilities

a) Two year research project to develop a Functional Abilities Test for SFPs with Physical Disabilities that is reliable and proven valid in preparation for suborbital spaceflight (applied research).

b) Three year research project to study the post-flight and long-term impact of suborbital flight on the health status of persons with physical disabilities, especially in relation to the acquisition of additional health complications (secondary conditions) (basic and applied research).

c) One year study to determine the impact of suborbital space travel on pre-existing health conditions not considered disabling, to include medically stabilized diabetes, stabilized mild-moderate heart conditions, asthma, stabilized kidney and liver disease, treated migraine headaches, obesity, controlled high blood pressure, controlled seizures, and medically stabilized mental health conditions (psychoneuroses). What impact does spaceflight have on implanted devices and chronic medications? Should certain individuals be excluded from flight, such as those with compromised immune systems, cancer under treatment, psychoses, high risk for heart disease emergencies, dementias, high risk for stroke, or progressive neurological diseases (amyotrophic lateral sclerosis, Parkinson’s, multiple sclerosis, myasthenia gravis, Huntington’s chorea, etc.) (applied research).

d) One year study of special measures or accommodations to allow individuals with physical disabilities to engage in suborbital flight with safety and comfort, including preparation and training before the flight, proper accommodations during flight, and attention to any special needs after the flight (applied research).

Discussion

A number of experts in space medicine have proposed that space should be democratized: accessible to all those who wish to engage in space travel and habitation. Given the potential biomedical risks of space and based on the status of technology and science, it was historically believed that only the most physically and mentally fit individuals should attempt spaceflight. But with advancements in the design of spacecraft and knowledge about ways to mitigate risks, some believe it is time to make space suborbital travel accessible to people with disabilities. The protection, health, and quality of life of people with disabilities have been extensively studied, with the following conclusions:

1) individuals with disabilities wish to be treated without discrimination and offered the same opportunities given to all others in society,
2) many individuals can function as effectively as those without disabling conditions with special accommodations as needed,
3) many individuals' levels of adaptation and resilience are extraordinary because of their life experiences in living with a disability, and
4) to render spaceflight truly accessible, we need to accommodate the SFP who relies on a personal assistant or service animal for activities of daily living by including accommodations for their assistant. If the protocols of spaceflight and the design of the space vehicle are unable to accommodate individuals with these needs, one option is to limit spaceflight to individuals with disabilities who do not rely on attendant services.

It is essential, therefore, that we study all the needs and requirements for safely and comfortably transporting people with disabilities into suborbital space.

It was suggested during the Workshop deliberations that we should begin by involving people with physical disabilities as potential spaceflight participants for suborbital flights. A physical disability is defined as a substantial and chronic health condition that affects a part of a person's body that limits their physical functioning, mobility, stamina or dexterity. It results in loss or reduction of physical function in performing body movements, such as walking, movement of arms and hands, sitting and standing, and general control of muscles. Consideration of mental illness was not encouraged at this time, but it is a topic to be revisited at a later time. A Workshop presenter stated,

> *"Individuals with neurocognitive and neurobehavioral disorders who cannot control themselves can be a risk to others and disrupt flight operations. While there is no reason why the flight would exacerbate the illness, the stress of participating and being restrained can trigger behavioral events that would lead to disruption of services."*

There was some disagreement with the speculation that the flight may or may not exacerbate the mental illness.

The origin of a physical disability may be congenital (discovered at birth with the health condition) or adventitious (acquired after normal physical development and due to an injury or illness). Examples of physical disability include cerebral palsy, muscular dystrophy, auditory and visual disorders, multiple sclerosis, spina bifida, epilepsy, amputations of hands, arms, legs, and spinal cord injuries. The severity of the disability and functional limitations of an individual with physical disability are measured by tests of physical mobility, tests of functional limitations, and medical examination.

In a CDC-supported study, the following findings were reported:[16]

- Approximately 1 in 8 working-age adults in the United States have some type of disability. Of these adults, over half (51.0%) had a mobility disability and 38.3% had a cognitive disability.
- Among working-age adults with only 1 disability, the most common type was disability in mobility (33.5%), followed by hearing (24.4%) and cognition (23.1%).
- Among working-age adults with 2 or more disability types, disability in mobility, independent living, and cognition were the most common types.
- Compared with working-age adults with no disability, adults with any disability were more likely to be age 45-64 and more likely to be black, non-Hispanic.

Unfortunately, tests of functional ability in individuals with physical disabilities may not meet the levels of validity and reliability recommended for current use by the space industry. The following questionnaires contain items of significance that do provide some useful information about the functional status of individuals with physical disabilities: Functional Activity Questionnaire, Upper Extremity Functional Scale, Lower Limb Outcomes Questionnaire, and Ostwestry Lower Back Pain Disability Questionnaire. A new test of physical function that is highly valid and reliable for potential SFPs with physical disabilities should be pursued.

Recommendation #4: Additional Topics for Human Research Proposed by Workshop Participants

a) A two year research project to study g-transitions to determine effects on physiology and performance. G-transitions are a combination of acceleration forces and microgravity. In addition, address the questions of “What acceleration forces can SFPs endure without adverse outcomes” and “How to contend with acceleration forces upon launches, during flight, and landing?”

b) A three year research project to study cardiovascular (CV) responses, including vestibular-autonomic (sympathetic) stimulation inducing cardiac dysrhythmias during suborbital spaceflight. In addition, study the impact of spaceflight on blood pressure, pulse, regularity of heart beat, and heightened risk for thrombosis.

c) A three year research project pursued either separately or in concert with item b) above to study the mechanisms underlying increased risk for cardiovascular changes, such as fluid shifts, during spaceflight, and duration of experience in

[16] Adults with One or More Functional Disabilities – United States, 2011 – 2014

microgravity. Fluid shifts are expected to be relatively inconsequential on suborbital flights, but may be more pronounced in flyers with certain medical conditions (heart failure, cardiac insufficiency) and should be studied.

d) A two year research project that addresses the impact of nominal and off-nominal launch/landing loads: potential for intervertebral disc damage (IVD); explore preventive interventions.

e) A one year study to identify key phenomena of career astronaut health that could be studied in novel suborbital test subjects (e.g., Spaceflight Associated Neuro-ocular Syndrome (SANS) in flyers with in-dwelling cerebrospinal reservoirs, sensorineural adaptation in vestibular nulls).

f) A three year research project for demonstrating new microgravity medical sensors, tools, and procedures (e.g., novel biometric sensors, ultrasound for jugular venous stasis, microgravity wound management, etc.).

Priority Human Research Projects for SFPs in Orbital and Beyond Low Earth Orbit Spaceflight and Habitation

As commercial spaceflight advances into orbital and low Earth orbit and eventually beyond low Earth orbit (BLEO), there is a growing need to develop methods that allow humans to travel in safety, comfort, and good health, and to thrive in this environment. Orbital and BLEO spaceflight and habitation are areas in which NASA and other space agencies have developed a considerable body of knowledge. However, there is no such literature on the range of genotypes and phenotypes (physiology, morphology, behavior; cognitive and physical performance) that will enter the dynamics of commercial orbital space and converge with the varying degrees of infirmity, polypharmacy, deconditioning, and other influences. We need to address each of these issues in preparation for the expansion of civilian space travel in the coming decades.

To do so requires a structured approach to human research that is focused on better understanding the intersection of age, sex, illness, resiliency, prior exposures, countermeasures in place, and other features on the spaceflight response, with a dedicated effort to developing countermeasures that optimize function, performance, health, and thriving in orbital and BLEO space travel. Such an understanding could also be used for pre-mission optimization with a health/wellness focus (physical conditioning, psychological resiliency, diet, sleep, etc.), and analog training for team building and team cohesion.

Based on NASA data, the anticipated health and function problems encountered in orbital and BLEO space and habitation are:

- Anthropometry changes

- Neutral body posture
- Abdominal girth decrease
- Circular changes to the chest
- Cephalad fluid shift
- Neurosensory system unloading
- Musculoskeletal unloading
- Spinal lengthening
- Thoracic straightening
- Space adaptation
- Back pain
- Increased cardiac output and stroke volume
- Decreased vascular resistance
- Facial edema
- Nasal congestion
- Space motion sickness, spatial disorientation, motion control impairment
- Atrophy of postural bone and muscle
- Sensed volume overload; increased vascular transmural pressure
- Plasma volume and red blood cell mass decrease to new set point
- Resolution of SMS, revision of neurosensory inputs
- 3-D spatial awareness, 0G motion control, mass handling
- Stable rate of loss or maintenance based on countermeasures, nutrition/energy intake
- Inflight anthropometry norm; increased seated height, decreased leg volume from fluid and muscle loss
- Neuro-ophthalmic changes
- Impaired cerebral venous drainage
- Increased cerebral blood flow

Scientific Research vs. Clinical Medicine

A human research program for SFPs will have to maintain a balance between scientific research, the clinical practice of aerospace medicine, and commercial engagement, in the way derived data from each are treated. For instance, SFPs will typically submit to medical examinations, which will be used for individual clinical needs, including flight preparation and qualification. This is distinct from research conducted on cohorts of

SFPs for the purpose of gathering pre-flight, in-flight, and post-flight data. As these distinct areas are bridged, rules for access to such data and removal of personal health information (PHI) should be central.

Optimally, the research effort would have both flight surgeons and research scientists, with spaceflight providers, all actively engaged in the selection of research priorities, definition of critical endpoints, design of experiments, data analysis, and translation to clinical measures or countermeasures.

Personalization

While the general attributes of the SFPs will be similar, the specific phenotypic features within the physiology, morphology, and behavior will be unique to each SFP. Moreover, beneath these phenotypic features lie the genotype and a discrete molecular phenotype, which will present even more unique patterns of variance. Given that a central goal is that of optimization for SFPs entering orbital and BLEO space, attention to research of individual differences and unique needs has merit. One approach that warrants consideration in the effort to optimize and also minimize risk will be to expand research into a program that addresses personalized (precision) medicine and personalized countermeasures.

Specific Human Research Recommendations For Orbital And Beyond Low Earth Spaceflight And Habitation

Recommendation #1: Five Year Study of the Impact of Microgravity on the Health Status of a Large Diverse Population of SFPs, Including SFPs with Disabilities

This is a five year study of the impact of microgravity on the physiology and psychology of SFPs, using analog environments and simulation tests. Physiological factors include major bodily systems: cardiovascular, digestive, endocrine, eyes and ears sensory, immune and hematology, lymphatic, musculoskeletal, nervous, reproductive, respiratory, skin and urinary systems. This will require extensive testing of each SFP, including comprehensive molecular profiling of all SFPs so that personalized countermeasures may be developed to address the heightened risks each individual may face. It is essential to obtain pre-flight baselines, measures during analog experiences or flights, and post-experience or post-flight measures. This may include various durations of visits to ISS for a cohort of SFPs. Also, this study may include a collaborative research effort to address SMS as discussed under Suborbital Space Flight Recommendations (basic and applied research).

Recommendation #2: Five Year Study of the Impact of Space-Encountered Radiation on the Physiology of SFPs, Using Analog Environments and Simulation Tests

This includes the impact of radiation on the 12 bodily systems. It will require extensive testing of SFPs before, during, and after the analog experience and/or spaceflight. It may also include various durations of visits to ISS for a cohort of SFPs (basic and applied research).

Recommendation #3: Three Year Project on How "Distance From Earth" and Isolation Affect the Psychology and Function of SFPs, Using Analog Environments and Simulation Tests

This may be a collaborative research effort to examine ways to reduce anxiety and stress for SFPs as discussed under the Suborbital Space Flight Recommendations (applied research).

Recommendation #4: Two Year Research Project to Identify Pre-Flight Training and Experiences That Best Prepare SFPs With Underlying Health Conditions Who May Be Involved in Orbital Flight and Beyond

The preparation is to (1) reduce SMS, (2) reduce anxiety and stress, (3) function successfully in case of emergencies, and (4) become a team member of the spaceflight passengers and crew (applied research).

Recommendation #5: Special Accommodations for SFPs with Disabilities

These recommended studies may be harmonized with those focused on SFPs with disabilities under the Suborbital Space Flight Recommendations.

a) Two year research project to identify which special accommodations, if any, are required for SFPs with disabilities so that spaceflight is accessible, safe and comfortable. This project will entail spacecraft design, operations, emergency procedures, and other technical factors that may be modified so the needs of the SFPs are addressed (applied research).

b) Two year research project to identify pre-flight training and experiences that best prepare the SFP with disabilities for spaceflight for specific durations (e.g., days, weeks, and months in orbital space) (applied research).

Recommendation #6: Effects of Acceleration Forces, Vibration, Noise and G Transition Factors on SFPs During Launch and Landing:

a) Two year research project to measure the impact of these factors on SFPs in analog environments and experiences. The experience could include travel to ISS by a representative group of SFPs who are carefully monitored and measured before, during, and after the spaceflight to ISS. This could be accomplished in conjunction with the above recommendations that plan to transport SFPs to assess impact of orbital flight for other factors (applied research).

b) Two year research project to measure the impact of these factors on SFPs with disabilities in analog environments and experiences. This project could be collaborative with other projects stated above that involve travel to ISS (applied research).

The Creation of a Database on the Impact of Suborbital and Orbital and Low Earth Orbit Spaceflight and Beyond on the Health Status and Function of SFPs

Discussion

The Workshop presenters and participants repeatedly recommended the need to create a database on the impact of space travel on the health and function of SFPs. The presentation by Drs. Valerie Gawron, Kathy Jenkins, and Sybil Klaus on the "Protection and Safety of Private and Proprietary Information: Challenges and Solutions" discussed the following recommendations in reference to developing a database on the responses of SFPs in space travel and habitation.

- How do you develop standards for data collection without stifling innovation?
- There are good analogs for developing the type of database that we seek, such as data on skydiving (the Safety Information Database).
- We know a great deal about the effects of space on highly selected, medically monitored, healthy individuals, but we know very little about the effects of space on civilians with pre-existing conditions.
- Benefits of sharing information through a database include:
  - Mitigating human error
  - Protecting vulnerabilities
  - Predicting rare adverse events
  - Identifying unsafe equipment
  - Working together, which will give us new insights into the population
- The value of sharing data about airline safety by the commercial aviation industry is reflected in the development of the following databases: Air Traffic Safety Action Program (ATSAP), Aviation Safety Information Analysis and Sharing (ASIAS), and Aviation Safety Reporting System (ASRS).

- To create a collaborative coalition of providers to establish a shared data repository for SFPs in commercial space, the following actions and suggestions are recommended:
  - All key stakeholders engaged
  - Collaborative governance and joint industry and government decision-making
  - Aggregated information
  - Data security and privacy safeguards in place
  - Safety focused
  - Trusted third party

As an example of how a HIPAA-sensitive database was created to assist cardiologists in preventing mortality during cardiac catheterization, Dr. Jenkins discussed the Risk Mitigation in Congenital Cardiac Catheterization database, whose aim was to combine predictive analytics and machine learning to identify patient, procedural, and system-level risk for adverse events and harm in patients undergoing congenital cardiac catheterization. The Predictive Analytics Model predicts adverse events using patient and procedure risk factors collected from hospital electronic data sources in multicenter registries.

The creation of a database that collects biomedical information will be challenging. In addition to the identification of common data elements, data standardization recommendations for an SFP health database should include consideration of data equivalency and quality. An example of a data equivalency concern is human body temperature, which can be measured at the mouth (oral), ear (tympanic), armpit (axillary), or forehead (temporal). The site of measurement affects the value (e.g., axillary is approximately 1°F lower than oral) and the locations have different accuracy (e.g., environmental temperatures significantly affect temporal measurements). Inclusion of nonequivalent metrics into the same data field in a database will increase variability and negatively affect the ability to detect meaningful changes in physiology and health.

Many health data sensing technologies exist, but their use in space may not be feasible due to factors like incompatibility with equipment (e.g., space garments), mission ruggedness requirements (e.g., accelerative loading), the need for specialized clinical training for use, and size, weight, and power restrictions. Prior to selecting a sensing technology, researchers and clinical staff should consider these factors and data quality requirements for the intended use in the space environment.

Recommendation 1: Create a Public/Private Partnership for the Development of a Database on the Health and Function of Spaceflight Participants. The Partnership

Will Address Governance Issues, Data Collection Standards, Procedures for Protection and Safety of Information, and Protocols for Data Collection: November 2021 – April 2022

The public/private partnership comprises the following partners: (a) Commercial Space Federation, (b) federal agencies—FAA, NIH, Assistant Secretary for Health/HHS, CDC, FDA, and NASA; (c) private nonprofit entities, including The MITRE Corporation; and (d) academic centers conducting space medicine research (e.g., Baylor College of Medicine, Johns Hopkins University School of Medicine, Mayo Clinic, University of Texas-Medical Branch, University of Colorado, and others).

This effort will include review of existing medical databases, including their purpose, protocols, and operations procedures. It will also need to identify and recommend standards for harmonization of data from diverse sources, accessibility, and effectiveness. It should include databases recommended by Workshop participants: the Provider Surveys of the National Center for Health Statistics,[17] CDC, HHS: National Medical Care Survey, National Hospital Ambulatory Medical Care Survey, National Health Electronic Records Survey, National Hospital Care Survey, National Study of Long Term Care Providers; and the FAA's ASRS, ATSAP, and ASIAS.

Items to consider:

- Identify data elements that are essential for the database, including medical and health information of SFPs, their response to space travel and habitation, and reports of adverse outcomes.
- Include consideration of adding biobank data or creating a separate biobank database: collection of saliva, blood, urine, etc.
- Develop a shared governance model built on trust and consensus on (1) standards for collecting health data, (2) key performance indicators and definitions, (3) tailoring existing agreements, (4) deciding on IT solutions and processes, and (5) collecting spaceflight participants' medical data prior to, during, and after the spaceflight.
- All partners agree to the collection of data using the same questionnaires, testing techniques, and measurements.
- The goal is to attain data integration that combines data from different sources into one unified data repository. This is accomplished when data elements are identified with the protocols to collect the data and are transmitted in a uniform manner to a central repository.

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[17] https://www.cdc.gov/nchs/surveys.htm

- Once the protocols for collecting and analyzing data about the responses of SFPs in suborbital and orbital flight are decided, standardized, and approved by the partners, begin collecting data in a secure and safe repository managed by a trusted, objective third party.
- The partners will agree on the details of the data collection project, especially regarding protection of their participants and safeguarding private and proprietary information.
- Review issues related to real time data collection versus collection of data that is collated and reviewed for accuracy and appropriate format and then sent to the repository.

Recommendation 2: Begin Collecting and Collating Specified and Standardized Data From All Partners Into a Repository That Meets the Requirements of Safety and Privacy of Individual and Proprietary Information: May 2022

Summary

In summary, the proposed human research program for SFPs focuses on research to make space travel accessible to all. We also identify opportunities to leverage this large, diverse population of flyers to conduct hypothesis-driven research in the general flying public or specialized research subjects. While spaceflight accessibility is a specialty topic of primary relevance to public health, opportunistic research within this population represents a mixture of aeromedicine, public health, and technology maturation. We encourage funding agencies to consider both domains as fruitful areas of inquiry.

Appendices

1. List of Members of the CSF/MITRE Workshop Planning Committee

Workshop Planning Committee Members (2021)

Name	Affiliation
John Allen, PhD	Program Executive for Crew Health and Safety And the Human Research Program/HEO/NASA)
Michael Altenhofen	Senior Mission Mgr., Dragon Mission, SpaceX
Melchor Antuñano, MD	Director, FAA Civil Aerospace Medical Institute
Sirisha Bandla	Vice President for Governmental Affairs, Virgin Galactic
Jonathan B. Clark, MD	Baylor College of Medicine
Steven Collicott, PhD	Purdue University
Marsh Cuttino, MD	Orbital Medicine, Inc.
Kenneth Davidian, PhD	FAA Office of Commercial Space Transportation, Director of Research
Karina Drees	President, Commercial Spaceflight Federation
Christopher Ferguson Amanda Ireland	Boeing Company
Valerie Gawron, PhD	MITRE
Jeffrey Jones, MD	Professor, Baylor College of MedicineCenter for Space Medicine
Michael Marge, EdD	CSF & MITRE, Co-Chair, Planning Committee
Jaime Mateus, PhD	Medical Researcher, SpaceX
Anil Menon, MD	Medical Director, SpaceX
Phil McAlister	Commercial Space Flight/NASA
Taber MacCallum	Co-CEO, Space Perspective
Tommy Sanford	CSF & Co-Chair, Planning Committee
Christopher Scheibler, MD	Director, Flight and Operational Medicine; Chief, Occupational Medicine; Joint Base Elmendorf Richardson, Department of Defense
Michael Schmidt, PhD	CEO/CSO, Sovaris Aerospace; President, Life Sciences & Biomedical Engineering Branch, Aerospace Medical Association
Victor Schneider, MD	Program Scientist, NASA Headquarters

Name	Affiliation
Mark Shelhamer, PhD	Johns Hopkins University School of Medicine
Leith J. States, MD	Chief Medical Officer, HHS Office of the Assistant Secretary for Health
Emmanuel Urquieta, MD	Deputy Chief Scientist, Translational Research Institute for Space Health (TRISH)
Erika Wagner, PhD	Blue Origin

2. Workshop Agenda, May 11–12, 2021

Commercial Spaceflight Federation/MITRE Corporation's Virtual Workshop on Creating a Human Research Program for Civilians in the Commercialization of Space

Purpose: In preparation for the commercialization of space by civilians, to bring together relevant scientists and researchers in space medicine to develop a list of high priority human research topics that will address the safety, comfort and good health of civilians in suborbital and orbital and beyond space travel and habitation. This Human Research Program for Civilians in Space is of keen interest to the space industry, FAA, NASA, HHS, DOC, and a number of medical schools with a focus on space medicine.

A Final Report with recommendations will be written for public dissemination and for public knowledge about the hazards and opportunities in space travel, habitation and employment. Dr. Michael Marge will serve as Editor of the Final Report.

Outcome: We will develop a draft Human Research Program for Civilians in Space which provides a list of needed research about protecting their health and safety. The recommended studies will be rank ordered in terms of urgency and significance. The draft human research program will be reviewed and vetted by all the leading experts on this topic before a final Human Research Program is publicly disseminated. Ideally, a coalition of interested and supportive agencies (public/private sector) will be formed to assist in the implementation of the human research program.

Why Study Civilians in Space: It is important: 1) To assist the Space Industry to protect its customer base to travel in safety, comfort and good health in preparation for the commercialization of space; 2) To develop coordinated long-term research endeavors with agencies in partnership with industry; and (3) To increase the focus on protecting the health of the civilian in space travel. If we expect the average civilian to travel, live and work in space, our knowledge is currently more limited and in need of a major national human health research program.

Civilians in space are a different population of space travelers with possible underlying health conditions when compared to the

	human health status of NASA astronauts. Therefore, although NASA's Human Research Program can inform us about some human health issues and ways to mitigate them, we need to study the relevant issues of civilians in space because of new and different needs. They also offer a broad base of research subjects for developing a deeper understanding of the effects of space travel on human physiology and psychology and will provide valuable information for improving the health of people on Earth. Some of the studies planned or underway include new cures for cancer, effective treatment of glaucoma and retinal detachments, diagnosis and treatment of brain edema, and detecting a propensity to blood clots and their prevention.
Pre-Workshop Materials Sent:	Subcommittee Reports, link to meeting, the agenda and instructions how participants may provide input and ask questions.
Participants:	Scientists and researchers in space medicine and health-related areas: Members of the CSF/MITRE Workshop Planning Committee (35), recommendations by CSF (35), SpaceX, Virgin Galactic, Blue Origin, Axiom Space, Redwire Space, Boeing, Sierra Nevada, Voyager Space, NASA (8), HHS (NIH/FDA/CDC/ASPR (12)), FAA (6), Department of Commerce (2), Johns Hopkins School of Medicine (4), Baylor College of Medicine (15), Mayo Clinic Space Medicine Program (2), Purdue University (2), Harvard University Space Program (2), OMB (1), DOD/Space Force (4).

Agenda

Day 1: Tuesday, May 11, 2021

10:00	Welcome by Dr. Michael Marge and Tommy Sanford, Co-chairs of the Workshop Tommy Sanford introduces Karina Drees and Dr. Kerry Buckley
10:05	Remarks by CEO and President Karina Drees, Commercial Spaceflight Federation, and Dr. Kerry Buckley, Vice President of MITRE's Air Force Center
10:20	Plenary Speaker: Dr. Michael Marge introduces Dr. Michael Barratt, Physician and Astronaut (discusses the health challenges faced by astronauts as compared with health challenges faced by civilians in commercial space
10:50	Q&A about Dr. Barratt's presentation. Moderated by Dr. Michael Marge
11:00	Break
11:15	Commercial capabilities and plans (Suborbital/Orbital and Beyond Low Earth Orbit Spaceflight and Habitation). Moderated by Karina Drees Panel discussion by Dr. Erika Wagner (Blue Origin), Sirisha Bandla (Virgin Galactic), Dr. Jaime Mateus (SpaceX), and Christian Maender (Axiom Space)
11:45	Q&A about commercial capabilities and plans: Moderated by Karina Drees
12:00	Luncheon break
12:30	Current government efforts (Suborbital/Orbital and Beyond Low Earth Spaceflight and Habitation): Moderated by Dr. Melchor Antuñano Panel discussion by Dr. Kenneth Davidian (FAA); Dr. Lucie Low (NIH); Dr. John Allen (NASA)
1:00	Q&A about current government efforts re: the commercialization of space: Moderated by Dr. Melchor Antuñano
1:15	Challenges and opportunities to develop a Human Research Program for Spaceflight Participants in Suborbital Flight: Dr. Mark Shelhamer (issues to address: research priorities, minimum set of measures, instrumentation, developing an effective database, recommended pre-

	flight preparation training procedures, unique opportunities for high-N or unique subject science, and research to expand population that can qualify to fly.)
1:45	Q&A about Dr. Shelhamer's presentation: Moderated by Dr. Marsh Cuttino
2:00	Challenges and opportunities to develop a Human Research Program for Spaceflight Participants in Orbital and Beyond Low Earth Orbit Spaceflight and Habitation: Dr. Michael Schmidt (issues to address: research priorities, minimum set of measures, instrumentation, developing an effective database, recommended pre-flight preparation and training procedures, and unique opportunities for high-N or unique subject science, research to expand population that can qualify to fly.)
2:30	Q&A about Dr. Schmidt's presentation: Moderated by Dr. Jeffrey Jones
2:45	Break
3:00	Plenary Speakers: Protection and Safety of Private and Proprietary Information: Challenges and Solutions: Dr. Valerie Gawron, MITRE, Dr. Kathy Jenkins (Boston Children's Hospital), and Dr. Sybil A. Klaus (MITRE)
3:30	Q&A for this presentation: Moderated by Dr. Kenneth Davidian
3:45	Description of plans for two simultaneously conducted subgroup meetings: Dr. Michael Marge Discussions focused on recommendations for research on each proposed human research topic for Spaceflight Participants in suborbital flight and orbital and beyond low Earth orbit spaceflight and habitation with description of purpose, hypotheses, methodology, and issues related to protection and safety of proprietary information. Two separate virtual meetings will be conducted simultaneously to draft a near final human research agenda: Section A: Research Agenda for Suborbital for Question 1 moderated by Erika Wagner, Blue Origin, with panel; and Section B: Research Agenda for Orbital and Beyond Low Earth Orbit Spaceflight and Habitation moderated by Dr. Victor Schneider with panel. Simultaneous meetings of Suborbital and Orbital and Beyond Low Earth Orbit Spaceflight and Habitation Human Research Agenda Groups will address two sets of questions, one for the Day 1 afternoon group

	discussion session, and another for the Day 2 morning group discussion session. Suborbital Group Session A: moderator—Erika Wagner, with Panelists Dr. Marsh Cuttino and Dr. Tarah Castleberry and participation by the Workshop Participants. Question 1: *What ground and flight studies would be most useful in safely opening commercial space to an ever wider audience? Consider underlying physical and mental health conditions, physical abilities, implanted devices, and chronic medications.* Orbital and Beyond Low Earth Orbit Spaceflight and Habitation Session B: Moderator—Dr. Victor Schneider with Panelists Dr. Jeffrey Jones and Dr. Christopher Scheibler and with participation by Workshop Participants. Question 1: *What ground and flight studies would be most useful in safely opening orbital and beyond space travel for an ever wider audience? Consider underlying physical and mental health conditions, physical abilities, implanted devices, and chronic medications?*
4:30	Adjournment

Agenda

Day 2: Wednesday, May 12, 2021

10:00	Plenary Session: Goals and objectives for Day 2: Dr. Michael Marge
10:05	Continue simultaneous meetings of each Group to discuss Question 2: Suborbital Group Session A: Moderator—Dr. Erika Wagner with Panelists Dr. Rebecca Blue and Dr. Erik Antonsen and Workshop Participants Question 2: A. *What is the minimum set of "standard measures" and adverse event reporting needed for research on commercial spaceflight participant safety? Do standard measures include environmental ones such as g loading?* *B. Do these differ for suborbital, short-orbital, and extended-orbital missions?* *C. If you could add one non-invasive metric beyond this minimum set, what would it be and who would be the primary stakeholder for the data?* Orbital and Beyond Low Earth Orbit Spaceflight and Habitation Group Session B: Moderator—Dr. Victor Schneider with Panelists Dr. Emmanuel Urquieta and Dr. Jonathan B. Clark and Workshop Participants Question 2: A. *What is the minimum set of "standard measures" and adverse event reporting needed for research on commercial spaceflight participant safety? Do standard measures include environmental ones such as g loading?* *B. Do these differ for suborbital, short-orbital, and extended-orbital and beyond travel and habitation?* *C. If you could add one non-invasive metric beyond this minimum set, what would it be and who would be the primary stakeholder for the data?*
10:45	Break

11:15	Plenary Session: Receive summary reports from each of the workgroups: Moderated by Karina Drees, CEO and President/CSF Suborbital: Summary report by Dr. Erika Wagner Orbital and Beyond Low Earth Orbit Spaceflight and Habitation: Summary report by Dr. Victor Schneider
11:45	Q & A about the Summary Reports: Moderated by Linda F. Fischetti (MITRE) Corporation Questions: Defining clear objectives for each recommended research topic?
12:15	Recommendations for Next Steps: Dr. Michael Marge, Moderator: Dr. Kenneth Davidian (FAA), Karina Drees (CSF), Benjamin Neumann (NASA), Dr. Valerie Gawron (MITRE), and Dr. Leith States (HHS, representing Assistant Secretary for Health, Dr. Rachel Levine)
1:00	Adjournment

3 Workshop Participants’ Comments and Recommendations to Consider in the Development of an HRP for SFPs

The Workshop participants identified a number of issues that should be considered, and recommendations for a human research agenda. These were helpful in developing the final list of research projects for suborbital and orbital spaceflight.

Issues:

- How do you make space an accessible environment for all travelers?
- What general model might we consider? Function, Performance, Readiness, and Team Building. Utilize extensive experience of NASA and others on risk and performance.
- Advance telemedicine services in space?
- Personalized medicine for SFPs to include complex molecular analytics?
- Difference between medical research and research for operational safety is somewhat of a confused distinction, because a sick passenger can adversely impact the operations of the spaceship. There is a divergence between research for medical reasons and operational safety issues. Many chronic illnesses aren’t going to be affected in 2–4 hour suborbital flights. When there are differences in function, medical clearance is really isolated to pilots because they are mission-critical. Passengers are not held to that standard. If someone has an issue during a spaceflight, it is up to the providers to handle it.

Recommendations:

- The space industry is the key for the development of a collegial, collaborative and cooperative consortium, working together to understand, prevent and/or mitigate biomedical risks faced by SFPs.
- Who is eligible to fly suborbitally and orbitally? There is a need to assess the SFP’s capability to meet certain standards of behavior and function so their participation does not threaten their safety and comfort or the safety and comfort of other SFPs. Several Workshop conferees suggested that almost any civilian can fly suborbitally. Others argued that we need more research to include certain individuals with underlying health conditions and disabilities, including individuals with a medical history of stroke, blood clots, cardiovascular disease; disabling neurological diseases (Parkinson’s, dementia, amyotrophic lateral sclerosis, multiple sclerosis, myasthenia gravis); medical device implants, such as pacemakers, hearing aids; individuals who are physically compromised requiring a personal attendant, mentally ill, intellectually disabled, or autistic.

- This is and will become a public health issue which should be led by the U.S. Department of Health and Human Services.
- We need diversity—women, all ages, racial and ethnic distribution, people with disabilities, and people with a variety of underlying health conditions to build a diverse representative research population.
- One preparatory suggestion is to provide preflight training not on the centrifuge, but on a larger rotating environment where the SFPs can try maneuvers they would do during spaceflight.
- Lack of standardization is a common issue with databases (e.g., electronic medical records), which limits analytical power. Data standardization is needed to support analysis of SFP health risks, and the standardization guidance must be research driven.
- All studies and information for a database must receive approval of identified Institutional Review Boards (IRBs).
- Long-term goal of any research endeavor is to enhance the SFP's personal safety, comfort, performance, thriving, and enjoyment.
- Develop projects and mechanisms that allow scientists and clinicians to engage in commercial orbital spaceflight research so they have a personal experience with flight.
- (In response to the issue of collecting medical health data)—The scientific expansion of the study of SFP health leads us to occupant safety. I think that for those of us who have worked in the scientific community, the more we know the better we can make this, and the faster we can expand spaceflight to be inclusive of broader and broader populations.
- How do people with multiple different co-existing disabilities experience zero gravity? What is the impact of multiple conditions on the zero g experience?
- Teach SFPs resilience.
- We need a systematic study of labyrinthine function loss in subjects and various levels of loss to understand motion sickness.
- If we can predict who will need anti-nausea medicine or get nauseous beforehand, that would be great.
- In scenarios where it may be prudent, consider having an attendant on board with the SFPs in case of a medical emergency.
- These biologically relevant environmental factors encountered by SFPs in spaceflight (most apply to orbital and beyond flight and habitation) are in need of further research:

1. Microgravity or reduced gravity
2. Ionizing radiation
3. Altered temperature (increased heat or cold)
4. Increased CO_2
5. Isolation (long duration space missions)
6. Acceleration forces on launch and landing
7. Impact on fluid shifts, immune systems, vestibular function
8. Impact on heart leading to heart dysfunction, immune system decrease

Civilians in Space—A Public Health Challenge

With thousands or even millions of civilians anticipated to be traveling, living, and working in space in the coming decades, their health and function will require federal health agencies and commercial carriers to take steps to prevent adverse outcomes from the hazards of the space environment and to effectively treat adverse health outcomes if and when they occur. This will require the cooperation of all public and private sector agencies and organizations, under the leadership of a federal agency that would need to be determined. Cooperation will be needed to (1) support the recommended human research agenda focused on prevention and protection of the health of civilians in space, (2) support the creation of a database that can support analyses regarding the impact of the space environment on civilians traveling and/or living in space either for recreation and/or work, and (3) draw from metrics, such as those in the Healthy People Initiative, to assess population health of commercial spaceflight passengers and federal and commercial policy efforts.

4. Subcommittee Report on Suborbital by Dr. Mark Shelhamer

Proposed Elements of a Biomedical Research Agenda for SFPs in Suborbital Spaceflight

April 2021

Recommendations by the CSF Subcommittee: Mark Shelhamer (Chair), Erika Wagner, Sirisha Bandla, Christopher Scheibler, Melchor Antuñano, John Allen, Jonathan Clark, Marsh Cuttino, Steven Collicott, Michael Marge

Executive Summary

This purpose of this report by the CSF Subcommittee on Creating a Human Research Agenda for SFPs in Suborbital Travel is to begin the dialogue for creating a human research program that addresses the many issues related to the safety, comfort, and good health of SFPs. Based on recent studies and reports, the research topics of highest priority include: the potential of vestibular problems during flight; psychological responses such as fear, anxiety and stress; issues related to cardiovascular problems of the passenger and possibly exacerbated by the travel; g-transitions related to space travel; protecting the passenger during launch and landing; the application of the concept of the human system interaction design (HSID); and the feasibility of precision medicine to effectively and with validity assay the health status of each passenger.

The report discusses the key procedural issues and the goals for research that should be considered in the development of a comprehensive human research agenda for SFPs in suborbital space.

<u>Introduction</u>

With an increase in suborbital spaceflights from commercial providers, an increasing number of people will go into space, with diversity in gender, age, medical history, and other demographics. This provides an opportunity not only to study the effects of spaceflight in a large diverse group, but also to investigate what is needed to reduce barriers for future participants (who may have medical issues that might have disqualified them from flight in the past).

At the same time, there is a desire to identify the most critical immediate biomedical issues that might adversely impact suborbital spaceflight participants. Given the paucity of suborbital experience, it is important to develop a plan to monitor the participants in order to validate and update issues and concerns as flight experience is gained, and to mine existing databases for relevant analogous data.

<u>Research domains to be considered</u>

There are two main (not necessarily exhaustive or mutually exclusive) domains of research activities:

1. Research to avoid adverse effects in non-professional flyers
    a. Collect and analyze medical data on SFP before, during and post-flight
    b. Identify most likely concerns
    c. Monitor and track incidence
    d. Sponsor or promote research for mitigation of proposed high-priority research topics
2. Opportunities that take advantage of the unique characteristics of commercial spaceflight
    a. Large number of flyers with broad range of demographics and health/fitness levels
    b. Frequent flight opportunities
    c. Access for investigators to fly with their experiments

Here we outline some of the general considerations involved in suborbital research with human subjects, and outline procedures for identifying relevant research topics in the domains above.

In the Appendix, we provide a detailed example of a draft human research project involving data collection from SFPs, which could inform both of the research domains above. It is described as an initial study of SFPs in suborbital flights. The project proposes to establish a medical baseline, describe the health status of the SFP before flight, and collect additional data related to some of the potential health issues that may be encountered during and after suborbital flight. The project further proposes that the data will be collected and collated into a new database on the impact of space travel on the physiology and psychology of civilians in suborbital space.

In considering these research domains, the subcommittee identified high-priority research topics or issues. The following tables identify these research topics, prioritized by relevance, for the first domain and for two distinct categories of the second domain: operational research ("NASA research") and basic science ("NIH research").

Notes on tables:

- *Medical conditions* refer to risk associated with a pre-existing medical condition.
- Vestibular-autonomic (sympathetic) stimulation inducing cardiac dysrhythmias should be considered under *vestibular* or *CV*. (Cross-disciplinary issues are not well-captured.)
- General health and fitness, and changes such as fatigue due to flight, might be considered in a separate category as needed.
- The tables include both exposure conditions and effects caused by those conditions. (Should effects and exposures be considered separately?)

- Key to Ratings:

  Priority A: almost certainly important.
  Priority B: may be important.
  Priority C: not likely to be important.

Prioritization According to Concerns of Flight Providers

	Operational research for SFP	Medical operations/human factors	Bio-astronautics	Basic science	How to monitor
Vestibular	A/A	A/A	A/A	B/A	Inflight and pre/post tests, questionnaire
Psych	A/A	A/A	A/A	B/C	Inflight and pre/post tests
CV	A/A	A/A	A/A	A/B	Inflight and pre/post test, questionnaire
G transitions	A/A	A/B	A/A	A/B	Inflight and pre/post test
Launch/landing loads & IVD	A/A	A/A	A/A	A/B	Pre/post tests
HSID	A/A	A/A	A/B	C/B	Inflight, questionnaire
Medical cdx	A/A	B/A	B/A	A/B	Inflight and pre/post test, questionnaire

Points for discussion:

- Motion sickness and other neurovestibular effects: The *vestibular* category includes space motion sickness and spatial disorientation. Other neurologic effects (e.g., seizures, stroke, dizziness, headache) would be covered under *medical conditions*. A new category such as medical events or neurologic concerns might be needed.
- Psychological stress responses: The *psychological* category includes effects triggered by the flight conditions, resulting in fear, anxiety and stress. Pre-existing conditions are a part of this, but might better be covered under screening recommendations.
- G transitions: *G transitions* are a combination of acceleration forces and microgravity. Should these be considered separately?
- Cardiovascular (CV) responses: Impact of spaceflight on blood pressure, pulse, regularity of heart beat, and heightened risk for thrombosis.
- Launch/landing loads and potential for intervertebral disc damage (IVD).

- Human System research design (HSID): interfaces of humans with the spacecraft.
- Medical conditions: pre-existing.

Prioritization According to Concerns of NASA and Other Providers

	Operational research for SFP	Medical operations/human factors	Bio-astronautics	Basic science	How to monitor
Vestibular	A/A	A/A	A/A	B/B	Inflight and pre/post tests, questionnaire
Psych	A/A	A/A	A/A	B/C	Inflight and pre/post tests
Launch/landing loads & IVD	A/A	A/A	A/A	A/B	Pre/post tests
G transitions	A/A	A/B	A/A	A/B	Inflight and pre/post test
HSID	A/A	A/A	A/B	C/C	Inflight, questionnaire
CV	A/A	A/A	A/A	A/B	Inflight and pre/post test, questionnaire

Prioritization According to Concerns of Basic-Science Researchers (NIH)

	Operational research for SFP	Medical operations/human factors	Bio-astronautics	Basic science	How to monitor
Medical cdx	A/A	B/A	B/A	A/B	Inflight and pre/post test, questionnaire
G transitions	A/A	A/B	A/A	A/B	Inflight and pre/post test
Launch/landing loads & IVD	A/A	A/A	A/A	A/B	Pre/post tests
CV	A/A	A/A	A/A	A/B	Inflight and pre/post test, questionnaire

<u>Factors to consider in implementing a human research agenda for SFPs in suborbital space flights</u>

a. Identify concerns impacting medical issues, comfort, safety – track, mitigate.

- To the extent that research here overlaps with that in other categories, opportunities for synergies between projects would be aided by transparency

b. Identify opportunities – related to other spaceflights, exploration of collaborations.
    - Bioastronautics, medical procedures, etc.
    - NASA and other space agencies
    - Preparation and risk reduction for commercial orbital flights

c. Identify opportunities – fundamental research, outreach and education of research-user base.
    - Category with greatest long-term scientific payoff but most uncertainty
    - Will depend on “high-risk” support of early flights as pathfinders and proof of concept, before researchers seriously consider opportunities

d. Related logistical issues that need resolution:
    - Instrumentation standardization for monitoring
    - Acquisition of metadata
    - Address or recognize proprietary issues
    - Databases and accessibility issues (input and output). Data platform needs to be constructed to share the most information possible in variable levels of output details while ensuring appropriate protections (PHI, proprietary information, etc.)
    - Informed consent

<u>Points for discussion</u>

- Research should identify gaps in current understanding of the effects of suborbital spaceflight among individuals who are representative of the general population with various levels of health and physical fitness. This can inform medical-screening criteria.

- Some categories of research should be designed to decrease the likelihood of in-flight serious injury, death, disability, or loss of physical or mental function.

- Consider dedicated flights for biomedical research, and for flyers with significant medical conditions.

- Analogs such as parabolic flight should be provided and used as appropriate for research, training, and familiarization. These data should be systematically evaluated and cross-checked with the table entries above.

- Identification of pre-flight predictors of performance and adverse effects would have broad relevance for many parties.

- Environmental exposures and other metadata will be critical in interpreting any measurement from SFPs: vibration, noise, thermal, etc. (There may be proprietary barriers.)

- Concerns of frequent flyers may require different prioritization and more rigorous monitoring. Flight crew is one category of such flyers, although their monitoring might be undertaken by each flight provider. Radiation and other issues may increase in priority with frequent flights.

- In what ways can commercial research flights provide novel insights into SANS?

- How would you design a research campaign to identify predictive measures for in-flight nausea on suborbital missions?

- What ground and flight studies would be most useful in safely opening space tourism to an ever wider audience? Consider underlying physical and mental health conditions, physical abilities, implanted devices, and chronic medications.

- What is the minimum set of "standard measures" and adverse event reporting you would hope to see aggregated for all commercial spaceflight participants? Do these differ for suborbital, short-orbital, and extended-orbital missions? If you could add one non-invasive metric beyond this minimum set, what would it be and who would be the primary stakeholder for the data?

- What subsets of SFP research are best suited to each of the existing funding bodies (NASA HRP, NASA BPS, FAA AST, TRISH, and NIH NCATS)? Are there any key research agendas or opportunities that lack a home today? What is common across these orphans?

Additional research/stakeholder categories to consider

- Aviation science. Research in suborbital spaceflight could contribute to a better understanding of air-travel hazards for the general public, and vice versa. Conventional aviation affords a representative sample of the general population and yields a large sample size. This could be leveraged to provide data for suborbital research, and provides an opportunity for suborbital research to help determine travelers that may be at high risk for standard air travel.

Considerations for later research

- Possible circadian shifting if suborbital travel becomes common for global transportation.

- Fluid shifts are expected to be relatively inconsequential on suborbital flights, but may be more pronounced in flyers with certain medical conditions (heart failure, cardiac insufficiency), and could be studied to understand potential impacts on orbital flight.

- Frequent suborbital travelers may exhibit cumulative effects. Priority ratings would be different from those provided so far, and surveillance would need to be more precise and continue prospectively. (Radiation is a potential concern. Cumulative vestibular effects might be an issue for flight crew.)
- Reducing barriers for those with disabilities beyond typical medical conditions: vestibular loss, deafness, paralysis, loss of limb, etc. Should accommodation be made for them to fly? Should research into the effects of flight on these subpopulations be performed?

Appendix

Initial Draft Human Research Project For Studying The Responses of SFPs In Suborbital Space Flight

Purpose

To conduct a medical data-collection project that obtains detailed information about the physiological and psychological responses of spaceflight participants in suborbital flight. The information will be collated into a database which meets all standards for protection of personal health and proprietary information and can be mined for identifying future needed research and for epidemiological purposes.

Study Population

SFPs who are planning to engage in suborbital flights.

Methodology

In order to better understand the physiological and psychological responses of the SFP in suborbital flight, the initial research effort should focus on collecting accurate data about the SFP – Pre-flight, In-flight, and Post-flight, as follows:

A. Pre-flight Study:

1. Medical data to be collected and analyzed:
    a. Medical history from medical records, seeking information about surgeries, reports of chronic diseases (potential for thrombosis), physical and mental illnesses (e.g., PTSD), migraine headaches, cancer survivor (with neuropathy), severe injuries, current health status as reported by licensed health practitioner.
    b. Interview SFP to assess current personal assessment of state of health and psychological factors related to fear, anxiety, and stress.
    c. Test for blood pressure and heart rate.
    d. Body weight.
    e. Medical samples, including blood, saliva, and urine samples to:

(1) provide routine laboratory data for assessment of pre-flight physical status and for post-flight comparisons.

(2) detect clinical or pathological abnormalities, which might have required remedial action pre-flight.

(3) discover, as early as possible, any infectious disease process.

(4) obtain fundamental medical knowledge relative to the SFP's adjustment to and return from the spaceflight environment.

f. Test for potential vertigo, using one or more of the following diagnostic procedures: Dix-Hallpike Maneuver, Head Impulse Test, Romberg Test, Fukuda-Unterberger Test, Electronystagmography (ENG) or Videonystagmography (VNG), Rotation Tests, Posturography, and Vestibular Evoked Myogenic Potential (VEMP).

g. Test for Resiliency in Adults, using the Connor-Davidson Resilience Scale (CD-RISC).

2. Pre-flight training of SFPs will be instituted: (1) describe the details of the flight and what to anticipate in terms of physical and mental experience; (2) introduce exercise routine according to the health status of the SFP to improve physical agility and cardiopulmonary function; (3) how to avoid injury during flight; (4) how to contend with acceleration forces upon launches, during flight, and landing; (5) how to contend with potential vertigo; (6) working effectively with the spaceflight crew, and (7) the role of the SFP in the event of an emergency.

B. In-flight data collection and data analyzed during flight or after:

1. Medical samples, including blood, saliva, and urine samples (if feasible).
2. Tests for blood pressure and heart rate.
3. If and when these may occur during flight, the SFP reports pain and its location, visual distortions, hearing problems (tinnitus, loss of hearing acuity), vertigo, dizziness, nausea, diarrhea, notable stress, loss of feeling or numbness in any part of the body. If possible, the reports should be transmitted immediately to data-collection monitors and to responsible staff personnel in the vehicle.

C. Post-flight data collection:

1. Medical samples, including blood, saliva, and urine samples.
2. Tests for blood pressure and heart rate.
3. Interview with SFP about unusual physical and/or psychological experiences and, if required, referral to diagnostic testing.
4. Second post-flight data collection in two months, including blood, saliva, and urine samples; blood pressure and heart rate; reports of any unusual physical or mental health issues which may lead to further diagnostic testing.

Need to Create a Coalition of Suborbital Spaceflight Providers who will Cooperate with the Study

Once the protocols for collecting and analyzing data about the responses of SFPs in suborbital flight are decided and approved by the Principal Researcher or Researchers, we seek to form a Coalition of Suborbital Spaceflight Providers who agree to cooperate with this research program. The Coalition will agree on the details of the data collection project, especially regarding protection of their participants and safeguarding private and proprietary information.

Need to Adequately Fund the Data Collection and Analysis Project by Creating a Coalition of Federal Funders that will Support Each Phase of the Project

Create a Coalition of Federal Funders which will fund and monitor the Project (potential members include FAA, NASA, HHS, NSF).

Create a database to which information from SFPs in suborbital flight will be collected and made available to human spaceflight researchers:

1. Once the project is approved by the Coalition of Suborbital Providers, it will be processed through the IRB established for the Coalition. Or, if the Coalition itself prefers to issue a solicitation, the awardee entity (private health research company or a university) will submit the project through its IRB for approval.

2. Support the data collection and analysis project about the health of SFPs in suborbital space as described above. The support will cover the cost of the testing, data collection and analyses to identify the need for additional studies to assure safety, comfort, and good medical health during and after the flight.

5. Subcommittee Report on Orbital and Beyond Low Earth Orbit Spaceflight and Habitation by Dr. Michael Schmidt

Proposed Elements of a Biomedical Research Agenda for SFPs in Orbital and Beyond Low Earth Orbit Spaceflight and Habitation

June 3, 2021

Recommendations by the CSF Subcommittee: Michael A. Schmidt, Chair; with Subcommittee Members Valerie Gawron, Jonathan Clark, Victor Schneider, Anil Menon, Erika Wagner, Michael Altenhofen, Jeff Jones, Emmanuel Urquieta, Derek Nusbaum, Michael Marge, Mark Shelhamer, Tommy Sanford, Marsh Cuttino, Christopher Scheibler.

Executive Summary

The purpose of this report by the CSF Subcommittee on Creating a Human Research Agenda for SFPs in Orbital and BLEO Travel and Habitation[18] is to begin the dialogue for creating a human research program that addresses many issues related to the safety, comfort, and good health of SFPs. The Subcommittee proposes "a structured approach to human research that is focused on better understanding the intersection of age, gender, illness, resiliency, prior exposures, countermeasures in place, and other features on the spaceflight response, with a dedicated effort to developing countermeasures that optimize function, performance, health, and thriving in orbital and BLEO space travel." Based on recent studies and reports, the research topics of highest priority are described in detail and found in the charts below.

This report discusses the key procedural issues and the goals for research that need to be considered in the development of a comprehensive human research agenda for SFPs in orbital and BLEO spaceflight.

<u>Introduction</u>

As commercial spaceflight advances into orbital and low Earth orbit (and eventually BLEO), there is a growing need to develop methods that allow humans to travel in safety, comfort, and good health, and to thrive in this environment. Orbital and BLEO spaceflight and habitation are areas in which NASA and other space agencies have developed a considerable body of knowledge. However, there is no such literature on the range of genotypes and phenotypes (physiology, morphology, behavior; cognitive and physical performance) that will enter the dynamics of commercial orbital space, and converge with the varying degrees of infirmity, polypharmacy, deconditioning, and other influences.

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[18] BLEO refers to *beyond low Earth orbit*. Wherever the term BLEO appears, it is intended to encompass both spaceflight and habitation (including lunar surface habitation and beyond).

This represents a tremendous gap in our understanding, though it also presents an opportunity that could be met with a dedicated effort to expand research to address the needs of the specific cohort of civilian space flight participants (SFPs) about to enter orbital and BLEO space. One of the closest analogs to this type of cohort is already encountered in terrestrial active and adventure travel or wilderness expeditions, where participants of similar socio-economic status, age, degree of fitness or deconditioning, and diversity of clinical phenotype to SFPs routinely enter remote and harsh environments.

For instance, groups like National Geographic, Smithsonian, and others routinely take individuals in their 50s, 60s, and 70s, with a range of medical conditions, on trips that require moderate to high physical daily activity to sites that include alpine, marine, and even remote jungle environments. Much can be learned from the medical and guide teams who have experience supporting this cadre of individuals, which is not unlike the continuum of those who may one day fly in orbit as SFPs.

Recently, the European Space Agency announced it will be studying the inclusion of astronauts with physical disabilities. This will initially include those with lower limb deficiencies (foot, ankle, below the knee, etc.). These exemplify the types of SFPs that will eventually present themselves to commercial spaceflight providers and represent the types of unique conditions that warrant additional research.

In this context, there is a desire to better understand the major biomedical concerns that would affect this unique cohort entering space, so that their specific and unique needs could be more thoroughly addressed. This desire aligns to goals within the commercial spaceflight sector of expanding the flying population, as we become a true space-faring civilization.

To do so requires a structured approach to human research that is focused on better understanding the intersection of age, sex, illness, resiliency, prior exposures, countermeasures in place, and other features on the spaceflight response, with a dedicated effort to developing countermeasures that optimize function, performance, health, and thriving in orbital and BLEO space travel. Such an understanding could also be used for pre-mission optimization with a health/wellness focus (physical conditioning, psychological resiliency, diet, sleep, etc.), and analog training for team building and team cohesion.

Issues to Resolve in the Creation of a Human Research Program for SFPs in Orbital and BLEO Space and Habitation

General Model for Consideration

While NASA's model for addressing professional astronauts has given requisite attention to risk, there is a further opportunity in a research initiative focused on commercial spaceflight participants to give particular emphasis to:

1. Function (even in the face of potential pathology)
2. Performance

3. Readiness
4. Team building and team cohesion
5. Coping mechanisms

A research model, oriented around function and performance, would aim to study and develop means to optimize the physical and mental wellbeing of SFPs, as they enter varied types of orbital and BLEO and mission contexts. This approach derives from the premise that those whose function and performance have been optimized are likely to be more responsive to the rigors of space and to off-nominal conditions encountered in space. This may, in turn, also lower risk, benefit safety, and augment mission success. Such an approach may be especially important to help increase the number of SFPs who could safely travel to low Earth orbit for vacation or work.

The Primary Stakeholder Groups

To optimize the likelihood of a successful research effort, three primary stakeholder groups warrant consideration. These are listed below, along with a brief summary of the basic objectives and value proposition for each.

1. **Flight & Habitation Providers:**

   Specific needs of the flight providers will be important to incorporate into any research plan. These include, but are not limited to:

   a. General contribution of research to the primary needs of flight/habitation providers

   b. Limit the encumbrances to flight providers where possible

   c. Support expansion of the pool of potential people able to fly in space

   d. Support the development of a knowledge base that facilitates building greater resiliency in the flying population who become customers of flight providers

2. **Spaceflight Participants:**

   a. Increase access to spaceflight

   b. Enhance personal safety, comfort, performance, thriving, and enjoyment while in the orbital and BLEO context

   c. Develop a knowledge base that can be used for self-care and preparation for SFPs entering space. This can include “self-assessment” in order to promote research into building a knowledge base that also creates methods for future SFPs to assess their readiness while performing self-care/prep. Also, develop a knowledge base that allows for individualized pre-spaceflight participant capability and risk evaluations by trained/educated aerospace medical personnel

d. Develop a knowledge base that enables medical personnel to better serve the needs of SFP (a reliable clinical knowledge base that is contemporary and growing)
e. Develop a program in expeditionary behavior to better enable SFP to engage with teams while in the challenging orbital and BLEO environment.
f. Support occupational health programs for workers in mining, manufacturing, space hotels, and operations in space. Such efforts would expect to include crew. Although an exhaustive list is not required and is expected to grow as the industry develops, additional considerations for inclusion could be occupations of spacecraft/facility maintenance, tourism workers, researchers, couriers, and security personnel.

3. **Clinical and Research Community**:
    a. Create an organized means by which scientists and clinicians can engage in commercial orbital spaceflight research
    b. Create a mechanism by which funding can be obtained to engage in commercial orbital and BLEO spaceflight research
    c. Create a means by which scientists can engage with flight providers who are interested in conducting human research on their orbital and BLEO flights
    d. Create a means by which a centralized data repository can be developed and maintained
    e. Create a means by which clinicians in practice, who serve the needs of SFPs, can access such a data set for the purpose of providing more evidence-based care to SFP
    f. Create governance surrounding data management and an advisement that considers prioritization of research, developing and implementing mitigations, and evaluating effectiveness of those mitigations. Consider data standards such as the Fast Healthcare Interoperability Resources that create a common specification by which healthcare participants can share information.
    g. Create an ethical framework for how data will be treated and managed.

Items 3d and 3e warrant one additional consideration. It is anticipated that, as flying participant numbers grow, SFPs may seek specific counsel on how they may optimize their resiliency to best thrive in their orbital and BLEO excursion. It is likely that, beyond mission-critical training, neither flight providers nor governments would provide such a service. This represents a possible gap related to an unmet need of the flying public. A human research program for commercial spaceflight would provide an organized repository of research, which could enable health professionals who serve the flying public to make better informed clinical and preparatory recommendations.

This also represents an opportunity for a purposeful alignment of research efforts that are directed toward performance, which can balance the natural tendency of such research efforts to identify and mitigate hazards (where medicine/research routinely focus). As a final point, a need may arise for research that aids in developing pre-flight screening methods to identify SFPs who may provide enhanced spaceflight confidence or competency. Conversely, there may also be a benefit to identifying SFPs who lack spaceflight confidence or competence. The intent would be that this pre-flight rating could be used to align ideal SFP teams or to match SFPs with in-flight requirements that are consistent with their respective skill and capability level.

In general, the better we can align the needs of these three stakeholder groups, the greater the likelihood of the overall success of any research initiative, and of the mission support effort.

Scientific Research vs. Clinical Medicine

A research initiative will have to maintain a balance between scientific research and the clinical practice of aerospace medicine, in the way derived data from each is treated. For instance, SFPs will typically submit to medical examinations, which will be used for individual clinical needs, including flight preparation and qualification. This is distinct from research conducted on cohorts of SFPs for the purpose of gathering pre-flight, in-flight, and post-flight data. As these distinct areas are bridged, rules for access to such data and removal of personal health information (PHI) should be central.

It should be further emphasized that such a research initiative is focused on applied human research for its clinical and performance applications, distinct from fundamental space biology. Decisions will have to be made regarding the extent to which this effort is to include fundamental space biology. Optimally, the research effort would have both flight surgeons and research scientists, engaged with spaceflight providers, actively engaged in the selection of research priorities, definition of critical endpoints, design of experiments, data analysis, and translation to clinical measures or countermeasures. Commercial human space research data can be compared and contrasted to that derived from government/professional human space research data in the future, if all parties find that such an exercise would be of value.

Personalization

While the general attributes of the SFPs will be similar, the specific phenotypic features within the physiology, morphology, and behavior will be unique to each SFP. Moreover, beneath these phenotypic features lie the genotype and a discrete molecular phenotype, which will present even more unique patterns of variance. Given that a central goal is that of optimization for SFPs entering orbital and BLEO space, attention to research of individual differences and unique needs has merit. One approach that warrants consideration in the effort to optimize and also minimize risk will be to expand research into a program that addresses personalized (precision) medicine and personalized countermeasures. The use of pharmacogenomics to optimize for drug safety and efficacy in orbital and BLEO space would be among the first targets of a personalization research program.

Attention to Design Reference Missions (DRM) in Setting Research Priorities

While there are general principles that can be applied to humans operating in space, considerable attention must also be given to the unique conditions of a given DRM. Thus, when contemplating risk, function, performance, and countermeasure needs, each DRM must be viewed in its unique context. For instance, an SFP on a 2-week commercial mission with few safety-critical responsibilities would likely have different select-out criteria than an astronaut hired for a career’s worth of long-duration exploration missions. Posing different research questions where there are risks of loss of mission vs. loss of crew vs. SFP morbidity may be useful to contemplate.

For practical reference, there are presently several commercial missions in development, each with distinct mission characteristics that have greater or lesser risk and may require greater or lesser skills on behalf of the SFP. Research applied to humans in each of the unique DRMs warrant consideration. Some possible examples are noted below:

1. Inspiration4: Orbital flight of 2-4-days duration
2. Movie planning to be shot aboard the ISS (unknown duration)
3. Dear Moon: Circumlunar mission of 6-days duration
4. Axiom Space: Four SFPs to the ISS on a 10-day trip (2022)
5. Space Adventures: Four SFPs on a five-day “free-flyer” trip to orbit by 2022

Defining Objectives of an Orbital and BLEO Human Research Initiative

It might be considered premature to identify which biomedical issues will be of most concern to this cohort entering orbital and BLEO space. The goal at the present time should be to begin to identify a governing research philosophy, and begin to construct the landscape and a roadmap for how to satisfy the needs of the primary stakeholder groups previously noted.

Important considerations from historical practices include, but are not limited to, the following:

1. A review of the extant literature and clinical findings from NASA and other space organizations that is of direct relevance to orbital and BLEO SFPs. This will provide further insight into what is known and what warrants further study.
2. A review of the literature and field experience of humans across the continuum of analogous phenotypes who have participated in expeditions into extreme (or remote) environments on Earth (orbital space analogs). This could include civilian survival schools that involve multiple time intervals (days to weeks) in a variety of austere environments. Other representative groups might include workers (such as fishermen) who are exposed to constant stress, crew communication/teamwork requirements, need for constant readiness and risk identification, circadian rhythm disruption (e.g., continuous fishing), confined quarters, isolation, harsh conditions, vestibular impacts, and the variable time at sea for different types of such occupations that might be similar to different

DRMs. Such background or active investigation can provide insight into how cohorts with less resilient phenotypes might fare in remote and off-nominal conditions.

Additional Information:

A Draft Outline to Initiate Discussion around Orbital and BLEO Needs

The following is presented as a rough frame of reference for how one might approach a path to determining the specific objectives of an orbital and BLEO research initiative for commercial spaceflight participants. All categories are open for discussion and modification. For instance, among the categories that should also be considered are “biomedical research opportunities” and “opportunities to enhance space access.”

Procedure:

1. Create a list of major biomedical concerns, drawn from subcommittee expertise and relevant items from the NASA Human Research Roadmap. A table is included below to get started. (See also Barrett 2019).
2. For each biomedical concern, consider if it applies to each of four categories of research:[19]
    a. Specifically, for the health, comfort, and safety of SFPs (*Operational research for SFP*)
    b. Refinement and practice of procedures that are relevant for orbital and other spaceflight (e.g., surgical procedures) (*Medical operations/human factors*)
    c. Relevant to operational issues in exploration-class spaceflights (e.g., performance during g transitions) (*Bioastronautics*)
    d. Basic research relevant to terrestrial health (*Basic science*)
3. Within each of the four research categories, prioritize each biomedical concern:
    a. Priority A: almost certainly important.
    b. Priority B: may be important.
    c. Priority C: not likely to be important.
    d. Un-labelled: not for further consideration, not relevant.

[19] Categories from: Shelhamer M (2014) Life-sciences research opportunities in commercial orbital space flight. Acta Astronautica 104:432-7.

4. For each biomedical concern with an A or B priority, suggest a monitoring or assessment approach (in-flight measurements, pre/post-flight tests, questionnaires, etc.).
5. Regarding the extant literature on a given concern, levels of evidence (sometimes called hierarchy of evidence) can be assigned to studies based on the methodological quality of their design, validity, and applicability to orbital and BLEO spaceflight. These decisions can provide the “grade (or strength) of recommendation.”
6. Assign degree of concern dependent on which DRM is applicable – perhaps pre-establish three likely DRM scenario durations, e.g., 1) <3 days, 2) 3-10 days, 3) >10 days.
7. Discuss the role of in-flight countermeasures and how they may be utilized in the commercial human research plan.

Priorities According to Flight and Habitation Providers

	Operational research for SFP	**Medical operations/ human factors**	**Bio-astronautics**	**Basic science**	**How to monitor**
Launch Loads/Activities/Suit interface	**C**	**A initially**	**C**	**C**	**A initially**
Vibration	**C**	**A initially**	**C**	**C**	**C**
General physiology/ Morphology	C	**C**	**C**	**C**	**C**
Pharmacodynamics	**C**	**C**	**C**	**C**	**C**
Gene expression and genetic risk	**C**	**C**	**C**	**C**	**C**
Nutrition & Metabolism	**C**	**C**	**C**	**C**	**C**
Cardiovascular	**C**	**A initially**	**C**	**C**	**C**
Muscle strength and endurance	**C**	**C**	**C**	**C**	**C**
Bone structure and mineralization	**C**	**C**	**C**	**C**	**C**
Neurobiology	**C**	**C**	**C**	**C**	**C**
Visual changes	**C**	**C**	**C**	**C**	**C**
SANS	**C**	**C**	**C**	**C**	**C**

	Operational research for SFP	**Medical operations/ human factors**	**Bio-astronautics**	**Basic science**	**How to monitor**
Noise Load-Auditory	**C**	**C**	**C**	**C**	**C**
Vestibular	**C**	**A initially**	**C**	**C**	**C**
Human Behavior and Performance	**C**	**B**	**C**	**C**	**C**
Cognition	**C**	**C**	**C**	**C**	**C**
Sleep	**C**	**C**	**C**	**C**	**C**
Crew Cohesion-Team Dynamics	**C**	**C**	**C**	**C**	**C**
Isolation	**C**	**C**	**C**	**C**	**C**
Anxiety	**C**	**B**	**C**	**C**	**C**
Readiness	**C**	**A initially**	**C**	**C**	**C**
Environmental Hazards	**C**	**A initially**	**C**	**C**	**C**
Radiation	**C**	**C**	**C**	**C**	**C**
Microbial	**C**	**C**	**C**	**C**	**C**
Chemical, Air-Water	**C**	**A initially**	**C**	**C**	**C**
Immune System function	**C**	**C**	**C**	**C**	**C**
Genitourinary	**C**	**A**	**C**	**C**	**C**
Urinary Retention	**C**	**A initially**	**C**	**C**	**C**
Urolithiasis	**C**	**A initially**	**C**	**C**	**C**
Landing Loads/G-transition/Activities	**C**	**A initially**	**C**	**C**	**C**
Post-Flight Rehabilitation and Cautions	**C**	**A initially**	**C**	**C**	**C**

Priorities & Needs According to Spaceflight Participants

	Operational research for SFP	**Medical operations/ human factors**	**Bio-astronautics**	**Basic science**	**How to monitor**
Launch Loads/Activities/Suit interface	**C**	**A initially**	**C**	**C**	**A initially**
Vibration	**C**	**A initially**	**C**	**C**	**C**
	C	**C**	**C**	**C**	**C**
Illness & Comorbidity	**C**	**C**	**C**	**C**	**C**
Polypharmacy	**C**	**C**	**C**	**C**	**C**
General physiology/ Morphology	**C**	**C**	**C**	**C**	**C**
Pharmacodynamics	**C**	**C**	**C**	**C**	**C**
Gene expression and genetic risk	**C**	**C**	**C**	**C**	**C**
Nutrition & Metabolism	**C**	**C**	**C**	**C**	**C**
Cardiovascular	**C**	**B initially**	**C**	**C**	**C**
Muscle strength and endurance	**C**	**C**	**C**	**C**	**C**
Bone structure and mineralization	**C**	**C**	**C**	**C**	**C**
Neurobiology	**C**	**C**	**C**	**C**	**C**
Visual changes	**C**	**C**	**C**	**C**	**C**
SANS	**C**	**C**	**C**	**C**	**C**
Noise Load-Auditory	**C**	**C**	**C**	**C**	**C**
Vestibular	**C**	**C**	**C**	**C**	**C**
Human Behavior and Performance	**C**	**C**	**C**	**C**	**C**
Cognition	**C**	**C**	**C**	**C**	**C**
Sleep	**C**	**C**	**C**	**C**	**C**
Crew Cohesion-Team Dynamics	**C**	**C**	**C**	**C**	**C**

	Operational research for SFP	**Medical operations/ human factors**	**Bio-astronautics**	**Basic science**	**How to monitor**
Isolation	**C**	**C**	**C**	**C**	**C**
Anxiety	**C**	**C**	**C**	**C**	**C**
Readiness	**C**	**C**	**C**	**C**	**C**
Environmental Hazards	**C**	**C**	**C**	**C**	**C**
Radiation	**C**	**C**	**C**	**C**	**C**
Microbial	**C**	**C**	**C**	**C**	**C**
Chemical, Air-Water	**C**	**C**	**C**	**C**	**C**
Immune System function	**C**	**C**	**C**	**C**	**C**
Genitourinary	**C**	**B**	**C**	**C**	**C**
Urinary Retention	**C**	**A initially**	**C**	**C**	**C**
Urolithiasis	**C**	**B**	**C**	**C**	**C**
Landing Loads/G-transition/Activities	**C**	**B**	**C**	**C**	**C**
Post-Flight Rehabilitation and Cautions	**C**	**A initially**	**C**	**C**	**C**

Priorities According to Research Scientists and Clinicians

	Operational research for SFP	**Medical operations/ human factors**	**Bio-astronautics**	**Basic science**	**How to monitor**
Launch Loads/Activities/Suit interface	**B**	**A initially**	**A**	**C**	**C**
Vibration	C	**A initially**	**C**	**C**	**C**
General physiology/ Morphology	C	**C**	**A**	**B**	**C**
Pharmacodynamics	**C**	**C**	**B**	**C**	**C**

	Operational research for SFP	**Medical operations/ human factors**	**Bio-astronautics**	**Basic science**	**How to monitor**
Gene expression and genetic risk	**C**	**C**	**B**	**A**	**C**
Nutrition & Metabolism	**C**	**C**	**B**	**B**	**C**
Cardiovascular	**C**	**A initially**	**A**	**C**	**C**
Muscle strength and endurance	**C**	**C**	**B**	**B**	**C**
Bone structure and mineralization	**C**	**C**	**B**	**B**	**C**
Neurobiology	**C**	**C**	**B**	**B**	**C**
Visual changes	**C**	**C**	**C**	**C**	**C**
SANS	**C**	**C**	**B**	**B**	**C**
Noise Load-Auditory	**C**	**C**	**C**	**C**	**C**
Vestibular	**C**	**A initially**	**A**	**C**	**C**
Human Behavior and Performance	**C**	**B**	**C**	**C**	**C**
Cognition	**C**	**C**	**C**	**C**	**C**
Sleep	**C**	**C**	**C**	**C**	**C**
Crew Cohesion-Team Dynamics	**C**	**C**	**C**	**C**	**C**
Isolation	**C**	**C**	**C**	**C**	**C**
Anxiety	**C**	**A initially**	**C**	**C**	**C**
Readiness	**C**	**A initially**	**C**	**C**	**C**
Environmental Hazards	**C**	**A initially**	**A**	**A**	**C**
Radiation	**C**	**C**	**C**	**C**	**C**
Microbial	**C**	**C**	**A**	**A**	**C**
Chemical, Air-Water	**C**	**A initially**	**C**	**C**	**C**
Immune System function	**C**	**C**	**C**	**A**	**C**
Genitourinary	**C**	**A**	**A**	**C**	**C**
Urinary Retention	**C**	**A initially**	**A**	**C**	**C**

	Operational research for SFP	**Medical operations/ human factors**	**Bio-astronautics**	**Basic science**	**How to monitor**
Urolithiasis	**C**	**A initially**	**A**	**C**	**C**
Landing Loads/G-transition/Activities	**C**	**A initially**	**A**	**C**	**C**
Post-Flight Rehabilitation and Cautions	**C**	**A initially**	**A**	**C**	**B**