THE BIOETHICS OF COMMERCIAL SPACEFLIGHT SERIES

Roundtable I: Who Gets to Fly?

Resource & Background Materials

For the December 18, 2025 Roundtable
(12:00–1:30 p.m. ET, via Zoom)

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I. Institutional Standards and Technical Documents

NASA—Human Spaceflight Standards.....

National Aeronautics and Space Administration (NASA). *Human Spaceflight and Aviation Standards.* NASA Office of the Chief Health and Medical Officer, 2025. https://www.nasa.gov/ochmo/human-spaceflight-and-aviation-standards/

Overview: Outlines NASA's core requirements for human systems, crew health, and operational safety across government and commercial spaceflight.

II. Policy / White Papers

Langston—Legal, Ethical & Medical Implications for Commercial Spaceflight

Langston, Sara M. *Commercial Space Travel: Understanding the Legal, Ethical, and Medical Implications for Commercial Spaceflight Participants and Crew.* International Aerospace Strategies / Senmurv Consulting LLC, Arlington, VA, 2025, pp. 489–494.

Overview: Evaluates participant rights, crew responsibilities, and regulatory gaps shaping commercial human spaceflight governance.

III. Peer-Reviewed Journal Articles

Whitehouse—OSHA & Neoliberal Market Conflicts (2025)

Whitehouse, Emma. *Workers' Rights in the Space Race: OSHA and Neoliberal Market Conflicts.* Bioethics, 2025. doi:10.1111/bioe.70058

Overview: Analyzes tensions between commercial space expansion and worker protections, highlighting OSHA limitations.

Szocik & Abylkasymova—Biomodification Bioethics (2025)

Szocik, Konrad, and Rakhat Abylkasymova. *The Bioethics of Biomodification for the Future of Space Exploration.* Futures, 2025, 174:103694. doi:10.1016/j.futures.2025.103694

Overview: Assesses ethical debates around genetic and technological human enhancement through feminist and non-feminist frameworks.

Seylani et al.—Ethical Issues in Non-Government Spaceflight (2024)

Seylani, Allen, Aman Singh Galsinh, Alexia Tasoula, et al. *Ethical Considerations for the Age of Non-Governmental Space Exploration.* Nature Communications, 2024, 15:4774. doi:10.1038/s41467-023-44357-x

Overview: Highlights ethical, legal, and medical issues related to participant selection and human research in private-sector missions.

Rahimzadeh et al.—Research Ethics in Commercial Spaceflight (2023)

Rahimzadeh, Vasiliki, Jennifer Fogarty, Timothy Caulfield, et al. *Ethically Cleared to Launch? Rules Are Needed for Human Research in Commercial Spaceflight.* Science, 2023, 381(6665):1408–1411. doi:10.1126/science.adh9028

Overview: Calls for a dedicated regulatory framework for human research in commercial spaceflight.

Doarn et al.—Multinational Medical Support for ISS (2021)

Doarn, Charles R., James D. Polk, Anatoli Grigoriev, et al. *A Framework for Multinational Medical Support for the International Space Station: A Model for Exploration.* Aerospace Medicine and Human Performance, 2021, 92(2):129–134.

Overview: Describes cooperative medical support structures for ISS operations as a template for future exploration missions.

Antonsen & Reed—Precision Medicine in Spaceflight (2019)

Antonsen, Erik L., and Rebekah D. Reed. *Policy Considerations for Precision Medicine in Human Spaceflight.* Houston Journal of Health Law & Policy, 2019.

Overview: Examines ethical and legal considerations around using genomic and precision-medicine tools in astronaut care.

Doarn—Evolution of NASA Medical Policy (2011)

Doarn, Charles R. *Medical Policy Development for Human Spaceflight at NASA: An Evolution.* Aviation, Space, and Environmental Medicine, 2011, 82:1073–1077.

Overview: Reviews the development and modernization of NASA's medical policy structures over time.

Mautner—Life-Centered Ethics (2009)

Mautner, Michael N. *Life-Centered Ethics and the Human Future in Space.* Bioethics, 2009, 23(8):433–440.

Overview: Advocates for an ethical framework that supports expanding life into space as a moral imperative.

Gibson—Human Performance Enhancement Ethics (2006)

Gibson, T. M. *The Bioethics of Enhancing Human Performance for Spaceflight.* Journal of Medical Ethics, 2006, 32:129–132. doi:10.1136/jme.2005.012534

Overview: Explores ethical questions surrounding pharmaceutical and technological enhancement of astronauts.

IV. Book Chapters

Johnston et al.—Space Bill of Rights (Ch. 25, 2025)

Johnston, Smith T., Caleb M. Schmidt, Robert M. Hubbard, Marianne J. Legato, and Michael A. Schmidt. *Foundations of a Space Bill of Rights.* In *Building a Space-Faring Civilization,* Elsevier, 2025, pp. 349–359.

Overview: Proposes foundational rights and protections for humans living and working in space.

Johnston, Jones et al.—Lessons Learned Part II (Ch. 20, 2025)

Johnston, Smith L., Jeffrey A. Jones, and Smith T. Johnston. *Lessons Learned Part II: In-Flight Medical Equipment, Capabilities, and Countermeasures; and New Medical Paradigms for Future Flights.* In *Building a Space-Faring Civilization,* Elsevier, 2025, pp. 279–301.

Overview: Evaluates medical capabilities and countermeasures for in-flight healthcare and explores advanced care paradigms for deep space.

Jones et al.—Lessons Learned Part I (Ch. 19, 2025)

Jones, Jeffrey A., Smith L. Johnston, Smith T. Johnston, Aly Alrabaa, Julian C. Schmidt, and Michael A. Schmidt. *Lessons Learned—Part I: Medical Screening, Standards, and In-Flight Incidents.* In *Building a Space-Faring Civilization,* Elsevier, 2025, pp. 257–278.

Overview: Reviews medical screening practices and patterns in in-flight medical events across human spaceflight missions.

Detsis—Ethics in Space (2022)

Detsis, Emmanuel. *Ethics in Space: The Case for Future Space Exploration.* In *Ethics, Integrity and Policymaking,* Springer, 2022, pp. 111–121.

Overview: Discusses ethical foundations and responsibilities shaping future space exploration policies.

NASA—Human Spaceflight Standards

National Aeronautics and Space Administration (NASA). *Human Spaceflight and Aviation Standards.* NASA Office of the Chief Health and Medical Officer, 2025. https://www.nasa.gov/ochmo/human-spaceflight-and-aviation-standards/

Overview: Outlines NASA's core requirements for human systems, crew health, and operational safety across government and commercial spaceflight.

National Aeronautics and Space Administration

[OCHMO-STD-100.1A]

Revision A
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OFFICE OF THE CHIEF HEALTH AND MEDICAL OFFICER

NASA SPACE FLIGHT MEDICAL SELECTION, RECERTIFICATION AND MISSION EVALUATION STANDARDS

APPROVAL PAGE

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DOCUMENT HISTORY LOG

Status	Document Revision	Change Number	Approval Date	Description
Baseline			2021-05-10	Initial Release—This NASA Medical Standard establishes criteria that were initially part of the Astronaut Medical Evaluation Requirements Document (AMERD), and has been updated using evidence based medicine by the Aerospace Medical Board.
Revision	A		2024-09-09	This is a complete revision with the following clinical changes: ASCAN Exam – Added Anti-phospholipid antibodies and Factor V Leiden. Annual Recertification Exam – Added OCT imaging, updated colonoscopy age to at or over 45y from 50y, updated osteoporosis T-score to ≤ from <2.5, added MRI of shoulder. Bone – updated Osteoporosis T-score to ≤ from < 2.5, added QCT information to [6013]. Section 1-4 – Updated wording/definitions Section 5 – Clinical changes to Table 4 and 6 Disqualifying requirements moved from Table 7 to Appendix A. Section 6 – Added short duration mission table and requirement information. Added long duration mission table/removed ACI/M/OM columns. Editorial changes throughout document with the following sections/technical requirements that were materially changed either in the text of this NASA Medical Standard and/or in the rationale:[6002], [6004], [6007], [6008], [6012], [6013], [6014], [6015], [6019], [6020], [6022], [6024], [6025], [6028], [6029], [6030], [6032], [6033], [6034], [6036], [6037], [6038], [6039]. Updated all requirement schedules to “For example only” based on ISS mission information, minor editorial changes to all requirements. Section 8 – Added Private Astronaut Medical Selection Criteria including lab test tables

				for Private Astronauts with no critical duties and missions <30 days. Section 9 – Added Medical Evaluations for NASA suborbital Research Specialists Appendix A – Added Disqualifying Medical Standards. Changes to disqualifying: E.4.H, G.2, Deleted radiation table. Appendix C – Added Medical Certification Specific to Missions on the ISS for historical purposes. Deletion of the following sections/medical requirements: [6026] Isokinetic assessment, [6031] Arm Cycle ergometer. Deleted all CSA, ESA, JAXA, and Roscosmos requirements including biodosimetry and calf volume measurement. Deleted Single Flow to Launch Content. The following sections/technical requirements were added throughout this NASA Medical Standard: [6037] Vitamin D Testing and Treatment [6041] VTE Assessment [6042] Space Motion Sickness Medication [7001] Private Astronaut Medical Screening and Evaluation Ground Testing. [8001] Medical Evaluation Procedures for NASA suborbital Research Specialists.

FOREWORD

This NASA Medical Standard is published by the National Aeronautics and Space Administration (NASA) to provide uniform medical requirements for processes, procedures, practices, and methods that have been endorsed as standard for NASA programs and projects, including requirements for selection and annual recertification of NASA astronauts.

This NASA Medical Standard is approved for use by NASA Headquarters and NASA Centers and Facilities, and applicable medical requirements may be cited in contract, program, and other Agency documents.

This NASA Medical Standard provides medical requirements, clinical procedures and evaluation for the following applications:

- **NASA Astronaut Selection and Recertification:** The medical standard for NASA astronaut selection and recertification is designed to ensure the health, safety, and longevity of career NASA astronauts.
- **Mission specific medical evaluation requirements for NASA Astronauts assigned to missions:** Mission specific medical evaluation requirements are oriented toward the assurance of crew health and safety, as well as functional competence in the spaceflight environment.
- **Medical Evaluations for Private Astronauts:** Private astronauts are crewmembers who are not a U.S. Government Astronaut, or an International Partner (IP) Astronaut. They undergo a comprehensive medical evaluation as part of their mission selection.
- **Medical Evaluations for NASA Suborbital Research Specialists:** This section provides medical testing requirements for NASA Suborbital Research Specialists (NSRS). NSRS are defined as an individual who is employed by NASA or contracted by NASA to conduct research, technology testing, training, or other activities onboard a suborbital vehicle. This excludes those individuals who are the commercially employed crew of the suborbital vehicle.

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NASA SPACEFLIGHT MEDICAL STANDARDS

1. SCOPE

1.1 Purpose

This NASA Medical Standard provides medical requirements, clinical procedures, and evaluations for the following applications:

- **NASA Astronaut Selection and Recertification:** The medical standard for NASA astronaut selection and recertification is designed to ensure the health, safety, and longevity of career NASA astronauts. These medical standards reflect the medical requirements to successfully complete specific mission tasks and the multifaceted training and performance required of an astronaut including, but not limited to, flying in high performance aircraft, exposure to hypobaric and hyperbaric conditions, exposure to unique environments (e.g., microgravity), and conducting specialized operations (e.g., extra-vehicular activities (EVA), robotic arm operations).
- **Mission specific medical evaluation requirements for NASA Astronauts assigned to missions:** Mission specific medical evaluation requirements are oriented toward the assurance of crew health and safety, as well as functional competence in the spaceflight environment. The operational medical monitoring requirements for pre-flight, in-flight, and post-flight phases are used to establish flight readiness, establish baselines, effectively guide in-flight countermeasures and assessments, and guide rehabilitation of crewmembers to their baseline health status following spaceflight. Data derived from standardized testing procedures are used in a pooled, non-attributable fashion to assess the effects of spaceflight on human health.
- **Medical Evaluations for Private Astronauts**: Private astronauts are crewmembers who are not a U.S. Government Astronaut, or an IP Astronaut that interface with NASA astronauts and/or vehicles. They undergo a comprehensive medical evaluation as part of their mission selection. Private astronauts' medical evaluations are determined by duties and mission duration. Critical duties are considered but not limited to piloting the vehicle, performing robotic operations, performing an EVA or any other task that is critical to the mission safety and success. The term 'spaceflight participant' has been used in the past for this category of crew.
- **Medical Evaluations for NASA Suborbital Research Specialists:** This section provides medical testing requirements for NASA Suborbital Research Specialists (NSRS). NSRS are defined as an individual who is employed by NASA or contracted by NASA to conduct research, technology testing, training, or other activities onboard a sub-orbital vehicle. This excludes those individuals who are the commercially employed crew of the suborbital vehicle.

1.2 Applicability

This NASA Medical Standard is applicable to NASA career astronaut candidate selection and annual recertification, private astronauts, and NSRS. This Standard is also applicable to mission specific medical evaluations, which include both clinical and occupational requirements.

Health risk assessment is a complex and dynamic process, and the medical requirements and screening procedures account for the fact that the risk for a medical event is based on mission parameters such as vehicle design, duration, environment, location (LEO, BLEO, etc.), time to return to definitive medical care, and individual needs. This NASA Medical Standard retains the flexibility for incorporation of new clinical procedures as a part of the health evaluation process in a preventive, diagnostic, or treatment capacity.

Medical data, information, and records are managed in accordance with the Privacy Act of 1974, as amended, and consistent with the privacy provisions of the Health Insurance Portability and Accountability Act (HIPAA) where applicable.

This NASA Medical Standard is approved for use by NASA Headquarters and NASA Centers and Facilities, and applicable technical requirements may be cited in contract, program, and other Agency documents.

Verifiable requirement statements are numbered beginning with the section number and indicated by the word “shall.” To facilitate requirements selection, a Requirements Compliance Matrix is provided in Appendix D. Explanatory or guidance text is indicated in italics.

Although the requirements listed in this document address medical conditions and the effects of spaceflight as presently known, it is fully intended that as knowledge accumulates, this NASA Medical Standard will be revised as appropriate. Any standard invalidated by new medical information may be appended by the Aerospace Medicine Board (AMB) with Chief Health and Medical Officer (CHMO) approval.

2. APPLICABLE DOCUMENTS

2.1 General

2.1.1 The documents listed in this section contain provisions constituting requirements of this NASA Medical Standard as cited in the text.

2.1.2 The latest issuances of cited documents apply unless specific versions are designated; use of a version other than as designated must be approved by the delegated Technical Authority.

2.1.3 Applicable documents may be accessed at https://standards.nasa.gov, https://nodis3.gsfc.nasa.gov/main_lib.cfm, or obtained directly from the Standards Developing Body or other document distributors. When not available from these sources, information for obtaining the document is provided.

2.1.4 References are provided in Appendix E.

2.2 Government

Documents Federal

	Privacy Act of 1974, as amended (https://www.justice.gov/opcl/privacy-act-1974)
	Centers for Disease Control and Prevention, Third National Health and Nutrition Examination Survey (NHANES III) (https://www.cdc.gov/nchs/nhanes/nh3data.htm)
NCRP Reports No. 132	National Council on Radiation Protection and Measurements, Radiation Protection Guidance for Activities in Low-Earth Orbit (https://ncrponline.org/publications/reports/ncrp-reports-132/)

NASA

NPD 1000.3	The NASA Organization
NASA-STD-3001, Volume 1, Revision C	NASA Spaceflight Human-System Standard Volume 1, Revision C: Crew Health

2.3 Non-Government Documents

The American Psychiatric Association

Diagnostic and Statistical Manual of Mental Disorders (DSM) – Latest Version

2.4 Order of Precedence

2.4.1 The requirements and standard practices established in this NASA Medical Standard do not supersede or waive existing requirements and standard practices found in other Agency documentation, or in applicable laws and regulations unless a specific exemption has been obtained by the Office of the Chief Health and Medical Officer (OCHMO).

2.4.2 Conflicts between this NASA Medical Standard and other requirements documents will be resolved by the delegated Technical Authority.

3. ACRONYMS, ABBREVIATIONS, SYMBOLS, AND DEFINITIONS

º	Degree
%	Percent
AMB	Aerospace Medicine Board
ACI	As Clinically Indicated
AGE	Arterial Gas Embolism
AIDS	Acquired Immune Deficiency Syndrome
ALARA	As Low As Reasonably Achievable
ALP	Alkaline Phosphatase
ALS	Amyotrophic Lateral Sclerosis
ALT	Alanine Aminotransferase
AMB	Aerospace Medicine Board
AME	Annual Medical Exam
AMERD	Astronaut Medical Evaluation Requirements Document
APC	Activated Protein C
ASCAN	Astronaut Candidate
ASD	Atrial Septal Defect
AST	Aspartate Aminotransferase
AV	Atrioventricular
BCG	Bacille Calmette-Guerin
BMD	Bone Mineral Density
BMP	Basic Metabolic Panel
BRCA	Breast Cancer Gene
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CDC	Centers For Disease Control And Prevention
CHMO	Chief Health And Medical Officer
Cl	Chloride
cm	Centimeter
CMO	Crew Medical Officer
CNS	Central Nervous System
CRF	Cardiorespiratory Fitness
CROM	Cervical Range Of Motion
CS	Crew Surgeon
CT	Computed Tomography
CXR	Chest X-Ray
D	Diameter
DCI	Decompression Illness
DCS	Decompression Sickness
DOD	Department Of Defense
DSM	Diagnostics And Statistical Manual
DVT	Deep Vein Thrombosis
DXA	Dual Energy X-Ray Absorptiometry
ECG	Electrocardiogram
EEG	Electroencephalogram

ELISA	Enzyme Linked Immunosorbent Assay
ENT	Ears, Nose, And Throat
EVA	Extravehicular Activity
FAA	Federal Aviation Administration
FD	Flight Director
GABHS	Group A Beta-Hemolytic Streptococcus
GGT	Gamma-Glutamyl Transferase
GI	Gastrointestinal
G6PD	Glucose-6-Phosphate Dehydrogenase
HbA1c	Hemoglobin A1C
hCG	Human Chorionic Gonadotropin
HCW	Health Care Worker
HDL	High-Density Lipoproteins
HIPAA	Health Insurance Portability And Accountability Act
HIV	Human Immunodeficiency Virus
hs-CRP	High-Sensitivity C-Reactive Protein
HSE	Health Status Evaluation
HSV	Herpes Simplex Virus
HUS	Hemolytic Uremic Syndrome
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IGRA	Interferon Gamma Releasing Assay
IMT	Intima-Media Thickness
INF-γ	Interferon Gamma
IP	International Partner
ISS	International Space Station
ITP	Idiopathic Thrombocytopenic Purpura
JSC	Johnson Space Center
L +/-	Launch Plus Or Minus
LASIK	Laser-Assisted In-Situ Keratomileusis
LDH	Lactate Dehydrogenase
LDL	Low-Density Lipoprotein
LROM	Lumbar Range Of Motion
LSAH	Lifetime Surveillance Of Astronaut Health
MCI	Multicolor Imaging
MED	Medical Evaluation Document
MGUS	Monoclonal Gammopathy Of Undetermined Significance
min	Minute
MMD	Mass Measurement Index
mmHg	Millimeters Of Mercury
MMOP	Multilateral Medical Operations Panel
MMPB	Multilateral Medical Policy Board
MRA	Magnetic Resonance Angiogram
msec	Millisecond
MSMB	Multilateral Space Medicine Board
mSv	Millisieverts
Na	Sodium

NASA	National Aeronautics And Space Administration
NBL	Neutral Buoyancy Laboratory
NCRP	National Council On Radiation Protection And Measurements
NHANES III	Third National Health And Nutrition Examination Survey
NPD	Nasa Policy Directive
NSRS	Nasa Suborbital Research Specialist
OCT	Optical Coherence Tomography
OCHMO	Office Of The Chief Health And Medical Officer
PC	Point Of Convergence
PDA	Patent Ductus Arteriosus
PEC	Private Exercise Conference
PFO	Patent Foramen Ovale
PFT	Pulmonary Function Tests
PIP	Pseudo-Isochromatic Plates
PMC	Private Medical Conference
PRK	Photorefractive Keratectomy
PT	Prothrombin Time
PTT	Partial Thromboplastin Time
PVC	Premature Ventricular Contractions
QFT-G	Quantiferon-Tb Gold
R +/-	Return Plus Or Minus
ROS	Review Of Systems
RPR	Rapid Plasma Reagin
SANS	Spaceflight Associated Neuro-Ocular Syndrome
SS	Sickle Cell
SSP	Space Shuttle Program
STD	Standard
STS	Space Transportation System
SVP	Spontaneous Venous Pulsations
SVT	Supraventricular Tachycardia
TB	Tuberculosis
TIA	Transient Ischemic Attack
TMJ	Temporomandibular Joint
TSH	Thyroid Stimulating Hormone
TST	Tuberculin Skin Test
TTG	Tissue Transglutaminase
TTP	Thrombotic Thrombocytopenic Purpura
U.S.	United States
VDRL	Venereal Disease Research Laboratory
VSD	Ventricular Septal Defect
VxV	Void-By-Void
VZV	Varicella Zoster Virus
WHO	World Health Organization
WPW	Wolff Parkinson White

3.1 Definitions

None

4. NASA ASTRONAUTS MEDICAL EVALUATION, SELECTION, AND ANNUAL RECERTIFICATION

4.1 Medical Evaluation – General Considerations

The medical standard for NASA astronaut selection and recertification is designed to ensure the health, safety, and longevity of career NASA astronauts. These medical standards reflect the medical requirements to successfully complete specific mission tasks and the multifaceted training and performance required of an astronaut including, but not limited to, flying in high performance aircraft, exposure to hypobaric and hyperbaric conditions, exposure to unique environments (e.g., microgravity), and conducting specialized operations (e.g., extra-vehicular activities, robotic arm operations).

For past NASA programs, IP astronauts in an agreement with NASA followed equivalent selection and annual recertification requirements. These requirements would be agreed upon within program specific documents via the appropriate multilateral medical boards.

Candidate astronauts undergo a comprehensive medical evaluation as part of their selection and annual recertification.

The medical evaluation process includes an extensive medical history and physical examination by aeromedical physicians and clinical specialists, laboratory screening tests, special diagnostic tests, and psychiatric evaluation. This document defines the medical screening procedures and standards for medical certification upon selection, and annual recertification thereafter.

In compliance with NPD 1382.17, NASA Privacy Policy and in accordance with the Privacy Act of 1974, as amended, applicants are examined in accordance with approved medical procedures.

4.1.1 Selection Medical Evaluation – General Considerations

Candidates for selection as NASA astronauts are evaluated for early detection of diseases that may interfere with their ability to perform mission tasks.

The specific medical evaluation procedures used are designed to select and certify individuals who are free from medical conditions that may:

a. *Compromise the astronaut's health and safety,*
b. *Compromise the completion of mission objectives, and*
c. *Be seriously aggravated or progress as a result of the performance of duties during training (e.g., in the Neutral Buoyancy Laboratory [NBL] and U.S. Air Force T-38 aircraft) or spaceflight exposures.*

4.1.2 Annual Medical Evaluation – General Considerations

The medical evaluation that is conducted annually for recertification is based on current NASA standards for spaceflight duties, piloting of NASA aircraft, or participation in flight activities only, as applicable.

4.2 Medical Evaluation and/or Certification by NASA's AMB

[4001] The examining physician **shall** present a candidate's evaluation results to the AMB.

[4002] The AMB **shall** determine if the candidate does or does not meet medical standards or requires further evaluations before disposition can be made.

[4003] The AMB will review the medical records of all NASA astronaut applicants at selection, and of each NASA astronaut annually, and **shall** recommend qualification, disqualification, or conditional qualification (waiver for active astronauts) to the CHMO.

[4004] The Chief Health and Medical Officer (CHMO) **shall** make the final disposition on qualifications and disqualifications of NASA astronauts, based on review of the AMB recommendations.

4.3 Waiver of Medical Standards

A waiver may be requested for a NASA astronaut for recertification who does not meet a medical standard. The waiver disposition may stipulate conditions for mission assignment (e.g., mission duration, location, etc.).

[4005] The term "waiver" **shall** be used when a disqualifying condition is waived, and the NASA astronaut is conditionally medically certified.

[4006] No waiver **shall** be granted on selection of NASA astronauts.

[4007] For a NASA astronaut waiver request, the examining physician **shall** provide a detailed presentation to the AMB of all relevant medical data and address the following:

a. An evidence-based review with data derived from the medical and aeromedical literature, as well as specialist consultant opinions detailing the potential risks associated with the condition, complications, and sequelae.

b. A thorough consideration of the potential consequences of related medical events on mission safety and mission completion and on the potential incremental health risk to the individual in the space environment.

[4008] The examining physician **shall** notify the NASA astronaut that his/her medical condition is being considered for waiver or disqualification from flight status.

[4009] The Chief Health and Medical Officer (CHMO) **shall** make the final disposition based on review of the AMB recommendations. The CHMO may delegate waiver decision authority to the AMB Chair for routine medication waiver renewal.

Table 1 - NASA Medical Requirements, Disqualifying Criteria and Acceptance Process and Waiver Process for Recertification of NASA Career Astronauts

Medical Requirements	
Medical Requirements for Selection	**Laboratory Tests** Section 5.1.2, Table 3 **Special Assessments** Section 5.1.3, Table 6
Medical Requirements for Annual Recertification	**Laboratory Tests** Section 5.1.2, Table 5 **Special Assessments** Section 5.1.3 Table 6
Disqualifying Criteria	
Disqualifying Criteria	Section 5.2 [5002], Appendix A
NASA Review Process	
AMB Chair	Shall make recommendation on NASA astronaut medical status. See Section 4.2 [4003]
CHMO	Shall make the final disposition on NASA astronaut medical status. See Section 4.2 [4004]
MSMB Chair	Determines individual medical certification for missions with international collaboration
Waiver Process – Recertification Only*	
Examining Physician	Shall provide a detailed presentation to the AMB of all relevant medical data. See Section 4.3 [4007]
Examining Physician	Shall notify the NASA astronaut that his/her medical condition is being considered for waiver or disqualification from flight status. See Section 4.3 [4008]
AMB Chair	Shall make recommendation on NASA astronaut medical waiver status [4002].
CHMO	Shall make the final disposition based on review of the AMB recommendations. See Section 4.3 [4009]

** No waiver **shall** be granted on selection of NASA astronauts. See Section 4.3 [4006]*

5. NASA ASTRONAUTS MEDICAL EVALUATION, SELECTION, AND ANNUAL RECERTIFICATION – SPECIFIC CONSIDERATIONS

Note: This section also applies to private astronauts with critical duties and/or >30 days. See Section 7 Table 10.

5.1 Medical Screening of NASA Astronauts

5.1.1 Medical Evaluation Procedures for NASA Astronauts – Overview

[5001] The examining physician **shall** perform medical screening, including the procedures and consultations in Table 2, Medical Evaluation Procedures, at selection and for annual recertification as indicated.

Table 2 – Overview of Medical Evaluation Procedures for NASA Astronauts
- To be applied at selection and annually thereafter.

Overview
1. Comprehensive medical questionnaire[1]
2. Full aeromedical physical examination (per FAA guidance or equivalent regulatory body)
3. Special assessments and imaging procedures (as described in Table 6)
4. Laboratory testing (as described in Tables 3, 4, and 5)

[1] - May be completed using the NASA Medical Survey or other similar questionnaire. The following areas should be included: Past medical history and background information; psychosocial and psychiatric history including DWI and drug-related convictions; personal habits/lifestyle issues; travel history (past year); medication review, including non-prescription and herbal medications, food supplements, vitamins, and minerals; systems review; physical activities and sports.

5.1.2 Laboratory Testing

Laboratory testing for selection, shown in Table 3, Laboratory Tests on Selection; Table 4, NASA Astronaut Candidate (ASCAN) First Annual Exam; and Table 5, Laboratory Tests on Annual Recertification, are limited to those tests pertinent to the identification of the presence of, or predilection for disease states, that might compromise individual health, mission effectiveness, or safety.

Clinical laboratory studies and special diagnostic tests are performed to establish baseline values and to aid in the detection of any disease process. Results of these tests are evaluated in the context of other clinical findings.

The specific laboratory tests in Tables 3 and 4 reflect current standards of care.

Table 3 - Laboratory Tests on Selection of NASA Astronauts

Laboratory Tests on Selection of NASA Astronauts
Hematology/thrombophilia screen • Complete Blood Count – To include hemoglobin, hematocrit, red blood cell count, red blood cell indices, white blood cell count, differential count, platelet count • Reticulocyte count • Screening tests for thrombophilia: Prothrombin time (PT) and partial thromboplastin time (PTT) • Hemoglobin evaluation (A, A2, F, S, C, E)
Biochemistry • Liver function - Aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), bilirubin, alkaline phosphatase (ALP), lactate dehydrogenase (LDH) • Total serum protein, albumin • Renal function - Urea, creatinine, electrolytes (Na [sodium], Cl [chloride], K [potassium]), uric acid • Endocrine - Thyroid stimulating hormone (TSH), free T4 (thyroxine), anti-thyroid antibodies. • Fasting blood glucose, HbA1C • Cardiovascular profile - Fasting total cholesterol, high-density lipoproteins (HDL), low-density lipoprotein (LDL), triglycerides, high-sensitivity C-reactive protein (hs-CRP) • Calcium, magnesium, inorganic phosphate • Ionized calcium • Prostate specific antigen (males over age 40) • Serum ferritin, iron, total iron binding capacity, transferrin saturation
Infectious Disease Screen • Serologic screen for syphilis (VDRL or RPR or equivalent) • Hepatitis B (Hepatitis B surface antigen, Hepatitis B core antibody, Hepatitis B surface antibody) • Hepatitis C • HIV • Tuberculosis (TB) screening utilizing a tuberculin skin test (TST) or interferon gamma releasing assay (IGRA) (either QFT-G or T- SPOT). Refer to Appendix B for detailed Tuberculosis screening and management guidance.

Table 3 - Laboratory Tests on Selection of NASA Astronauts (continued)

Laboratory Tests on Selection of NASA Astronauts	
Urinalysis	• Routine (specific gravity, glucose, protein, pH, ketones, blood), microscopic • Human chorionic gonadotropin (hCG) (females; urine or serum)
Special studies	• Prolactin • Carbohydrate Deficient Transferrin • Ethyl glucuronide • Tissue transglutaminase (TTG) IgG • Tissue transglutaminase (TTG) IgA
Drug screening, urine	• Drug screen in-house for drugs of abuse • Expanded drug screen

Table 4 - NASA Astronaut Candidate (ASCAN) First Annual Exam

NASA Astronaut Candidate (ASCAN) First Annual Exam
ABO Group & Rh Type
Cytomegalovirus IgG Antibody
Epstein-Barr Virus IgG Antibody to Nuclear Antigen
Epstein-Barr Virus IgG Antibody to Viral Capsid Antigen
Herpes Simplex Virus (HSV) Type 1/2 Combined IgG Antibody
Toxoplasma gondii IgG Antibody
VZV IgG Antibody
Immunocap Mouse Epithelium Antibody
Immunocap Mouse Urine IgE Antibody
Lipoprotein (a)
Measles (Rubeola) IgG Antibody
Mumps IgG Antibody
Rubella IgG Antibody
Helicobacter pylori Breath Test
Hepatitis A antibody
Glucose-6-phosphate dehydrogenase (G6PD)
Serum Protein Electrophoresis (SPE)
Quantitative Immunoglobulins (IgG, IgA, IgM)
Calculi Risk Assessment, Urine
Venous Thromboembolism Panel: • Cardiolipin IgG Antibody • B2 glycoprotein 1 IgM/IgG Antibody • Activated Protein C (APC) Resistance • Prothrombin Nucleotide 20210 G/A Gene Mutation (Factor II) • Protein C • Protein S • Anti-Thrombin • Anti-phospholipid antibodies • Factor V Leiden

Table 5 - Laboratory Tests on Annual Recertification of NASA Astronauts

Laboratory Tests on Annual Recertification of NASA Astronauts
Hematology • Complete Blood Count – To include hemoglobin, hematocrit, red blood cell count, red blood cell indices, white blood cell count, differential count, platelet count • Reticulocyte count
Biochemistry • Liver function - Aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), bilirubin, alkaline phosphatase (ALP), lactate dehydrogenase (LDH) • Total serum protein, albumin • Renal function - Urea, creatinine, electrolytes (Na [sodium], Cl [chloride], K [potassium]), uric acid • Endocrine - Thyroid stimulating hormone (TSH), free T4 (thyroxine), • Fasting blood glucose, HbA1C • Cardiovascular profile - Fasting total cholesterol, high-density lipoproteins (HDL), low-density lipoprotein (LDL), triglycerides, high-sensitivity C-reactive protein (hs-CRP) • Calcium, magnesium, inorganic phosphate • Ionized calcium • Prostate specific antigen (males over age 40) • Serum ferritin, iron, total iron binding capacity, transferrin saturation • Vitamin D
Infectious Disease Screen • Hepatitis B (unless immunization has been confirmed with antibody titers) • HIV • Tuberculosis screening utilizing a tuberculin skin test (TST) or IGRA (either QFT-G or T-SPOT). Refer to Appendix B for detailed Tuberculosis screening and management guidance.
Urinalysis • Routine (specific gravity, glucose, protein, pH, ketones, blood), microscopic

5.1.3 Specialist Assessments for Selection and Annual Recertification of NASA Astronauts

Specialty examinations are performed to further detect and identify any potential disorders within a specific area. Throughout the selection and subsequent annual examinations, emphasis is placed on the early detection of latent pathological processes, and suitability for spaceflight and the physiological effects of reduced-gravity exposure.

Table 6 – Specialist Assessments for Selection and Annual Recertification of NASA Astronauts

Ophthalmology Specialist Assessment (Optometrist)	Selection	Annual
Visual acuity (Snellen or Landolt-C)		
• Near vision	✓	✓
• Distance vision	✓	✓
Color vision (computer-based test, Ishihara, or equivalent pseudo-isochromatic plates [PIPs] to include red-green and blue-yellow)	✓	✓
2 Cycloplegic refraction	✓	✓
Phorias	✓	✓
Tonometry	✓	✓
Perimetry	✓	✓
Fundoscopic examination	✓	✓
Retinal photographs	✓	✓
Corneal topography	✓	
OCT imaging	✓	✓
Otolaryngology/ENT	**Selection**	**Annual**
Audiometry (pure tone audiogram and speech audiogram, if indicated)	✓	✓
Tympanogram	✓	✓
Computed tomography (CT) scan or magnetic resonance imaging (MRI) of sinuses	✓	

Table 6 – Specialist Assessments for Selection and Annual Recertification of NASA Astronauts (continued)

Dental	Selection	Annual
Special Assessment by Dentist	✓	✓
Full orthopantomogram or full mouth X-ray series)	✓	
Cardiopulmonary	**Selection**	**Annual**
Resting 12-lead electrocardiogram (ECG)	✓	✓
Direct or indirect measurement of cardiorespiratory fitness (CRF) in ml/kg/min on maximum exercise stress test	✓	✓
Echocardiogram, Doppler, and color flow study	✓	
• Within the last 5 years		✓
24-Hour ECG monitoring	✓	
Pulmonary function testing	✓	
Atherosclerotic Cardiovascular Disease Risk Calculation	✓	✓
Coronary calcium scoring (>50 yrs old)	✓	
• Within the last 5 years		✓
Gastroenterology	**Selection**	**Annual**
Colonoscopy	✓	
• At or over 45: within the last 5 years		✓
• At or over 40: within the last 5 years if family history positive for colon cancer		✓

Table 6 – Specialist Assessments for Selection and Annual Recertification of NASA Astronauts (continued)

Musculoskeletal	Selection	Annual
MRI of shoulder	✓	
Neurology	**Selection**	**Annual**
MRI of brain, MRI angiogram	✓	
Carotid Ultrasound Study (to include intima-medial thickness and/or carotid plaque area)	✓	
• Age 50 and over (within the last 2 years)		✓
Behavioral Health Evaluation	**Selection**	**Annual**
Psychiatric and Psychological evaluation *Based on the most recent edition of the Diagnostic and Statistical Manual of Mental Disorders, the American Psychiatric Association*	✓	✓
Psychodiagnostic and Psychological Suitability Assessment	✓	
Gynecological	**Selection**	**Annual**
Gynecological Evaluation (Cervical Cancer Screening using Current Guidelines)	✓	✓

Table 6 – Specialist Assessments for Selection and Annual Recertification of NASA Astronauts (continued)

Radiological /Ultrasound Procedures	Selection	Annual
Chest X-ray (CXR) (PA and lateral)	✓	
• Within the last 5 years		✓
Thyroid ultrasound	✓	
• Within the last 5 years		✓
Abdominal and pelvic ultrasound	✓	
• Within the last 5 years		✓
Bone mineral density - dual energy x-ray absorptiometry (DXA) scan	✓	
• Within the last 3 years		✓
Breast Imaging for females beginning at age 40	✓	
• Within the last 2 years MRI should be used in lieu of mammography for female astronauts, if identified to be at high or intermediate risk (based on family history, breast cancer gene (BRCA) positive, heterogeneous, or dense breast tissue).		✓
Radiation	**Selection**	**Annual**
Radiation History Assessment (Includes research exposure, spaceflight and aviation exposure, and previous occupational exposure)	✓	✓

5.2 Medical Conditions to Consider for Selection and Annual Recertification of NASA Astronauts

Appendix A, Disqualifying Medical Standards, details those medical conditions that are medically disqualifying for the selection and retention of NASA astronauts, or that may require further testing and evaluation to assess medical suitability. In general, all conditions are worded as disqualifying. The term "unless" is used when specific exceptions are listed. Annual medical recertification ensures the individual has not developed any new medical conditions that would preclude safe performance of training and/or spaceflight duties or participation. This section pertains to all NASA astronauts.

[5002] The examining physician **shall** determine the suitability for selection and retention of NASA astronauts, using the conditions for disqualification specified in Appendix A.

6. MISSION MEDICAL EVALUATIONS FOR NASA ASTRONAUTS ASSIGNED TO SPACEFLIGHT MISSIONS

This section defines the mission specific medical evaluation requirements for NASA Astronauts assigned to missions greater than and less than 30 days. Mission specific medical evaluation requirements are oriented toward the assurance of crew health and safety, as well as functional competence in the spaceflight environment. The operational medical monitoring requirements for pre-flight, in-flight, and post-flight phases are used to establish flight readiness, establish baselines, effectively guide in-flight countermeasures and assessments, and guide rehabilitation of crewmembers to their baseline health status following spaceflight. Data derived from standardized testing procedures are used in a pooled, non-attributable fashion to assess the effects of spaceflight on human health.

For past NASA programs, IP astronauts in an agreement with NASA followed equivalent mission medical evaluation requirements. These requirements would be agreed upon with in program specific documents via the appropriate multilateral medical boards. These mission medical evaluations are not required for commercial astronauts.

Implementation aspects:

- The mission specific medical evaluations assume the astronaut has completed the NASA annual recertification testing/requirements described in this document.
- The pre-flight medical evaluation will be coordinated with the annual medical examination when the schedules coincide.
- The evaluation components stipulated in this section are required for each crewmember assigned to a spaceflight mission; however, the Crew Surgeon (CS) has the authority to waive tests, prescribe additional tests, or increase the frequency of testing, if clinically indicated.
- The timing of requirements is designated as pre-flight, in-flight, and/or post-flight. Requirements may also be designated ACI – As Clinically Indicated, as determined by the CS.

The information acquired from all testing shall be provided in a timely manner to the CS for inclusion in the individual crewmember's medical records.

Table 7 provides the required Medical Examinations for Assigned Crew on < 30-day Mission.
Table 8 provides the required Medical Examinations for Assigned Crew on > 30-day Missions. Details of each evaluation may be found in Section 6.

The schedules and associated hardware provided for each requirement is from a typical ISS 30- and 180-day mission, and is for example only. 30 days was chosen as a point of delineation based on physiological changes and experience but is not a stringent requirement. Schedule/need and required hardware/software should be determined based on mission parameters such as vehicle design, duration, environment, location (LEO, BLEO, etc.), time to return to definitive medical care, and individual needs. Tailoring of these requirements must be approved via the Health and Medical Technical Authority (HMTA) process.

Table 7– Mission Medical Examinations for Short Duration (< 30 days) Missions

Schedule/need provided for informational purposes only. Based on 30-day ISS mission.					
Clinical Assessment and Monitoring	**Med Eval Requirement**	**Annual *****	**PRE-FLIGHT (L-)**	**IN-FLIGHT**	**POST-FLIGHT (R+)**
CLINICAL ASSESSMENT AND MONITORING					
Pre- and Post-flight Physical Exam for Short Duration Crews	[6001]	Table 2	AME L-12/6 m, L-21/14 d, L-2/1 d		R+0 d and R+3/7 d, PEX ACI - Labs and PEX ID Swab
CMO Health Status Evaluations	[6002]			Mid Mission, ACI	
Private Medical Conference	[6003]			L+1-7 d, weekly, pre/post EVA, R-5 d, daily to R-0 d	
Neurological Assessment	[6004]		AME L-12/6 m		R+0 d and R+3/7 d ACI
Neurovestibular Platform Test	[6005]	Table 2	AME L-9/6 m, L-90/30 d		R+7/10 d
Resting ECG	[6006]	Table 6	AME L-12/6 m		ACI
24-hour Ambulatory ECG			On Record		
Hearing Assessment	[6007]	Table 6	AME L-12/6 m	ACI	R+3 d, If abnormal, R+10/14 d, R+60 d
Hearing Protection	[6008]		L-18/12 m		
Dental Examination	[6009]	Table 6	AME L-12/6 m		
Dental Orthopantomogram or Full Mouth X-Ray Series	[6010]	Table 6	AME L-12/6 m		

m= months d= days y= year L= launch R= return AME – Annual Medical Evaluation ***Annual Tests - Table 3 Overview of Medical Evaluation Procedures for NASA, Table 4 Overview of Medical Evaluation Procedures for NASA Astronauts to be applied annually, Table 5 Laboratory Tests on Annual Recertification, and Table 7 Special Assessments for Recertification

Table 7– Mission Medical Examinations for Short Duration (< 30 days) Missions Schedule/need provided for informational purposes only. Based on 30-day ISS mission.					
Clinical Assessment and Monitoring	**Med Eval Requirement**	**Annual *****	**PRE-FLIGHT (L-)**	**IN-FLIGHT**	**POST-FLIGHT (R+)**
Ophthalmology/Optometry	[6011]	Table 6	AME L-12/6 m Retinal photographs and OCT On Record		R+0/1, R+3 d and ACI R+1/10 d - Retinal photographs and OCT
Specialized Ocular Assessments	[6012]	Table 6	AME L-12/6 m	ACI	R+1/3 d, follow abnormal findings every 30 days until clinically stable or ACI
Bone Densitometry	[6013]	Table 6	ACI		ACI
Ultrasound Imaging (Sonography)	[6014]	Table 6	AME L-12/6 m		
Body Mass Measurement	[6015]	Table 2		ACI	
Photodocumentation of skin	[6016]		ACI	ACI	ACI
MRI Brain and MR angiography	[6017]	AME L-21/18 m	On Record		
MRI Cervical and Lumbar Spine (non-contrast)	[6018]	AME L-21/18 m	ACI		ACI
LABORATORY					
Laboratory Testing	[6019]	Table 5	AME L-12/6 m	ACI	ACI
Helicobacter pylori screen		Table 4	On Record		
MRSA	[6020]		L-90/30 d		ACI
GABHS	[6021]		L-90/30 d		ACI

m= months d= days y= year L= launch R= return AME – Annual Medical Evaluation ***Annual Tests - Table 3 Overview of Medical Evaluation Procedures for NASA, Table 4 Overview of Medical Evaluation Procedures for NASA Astronauts to be applied annually, Table 5 Laboratory Tests on Annual Recertification, and Table 7 Special Assessments for Recertification

Table 7– Mission Medical Examinations for Short Duration (< 30 days) Missions Schedule/need provided for informational purposes only. Based on 30-day ISS mission.					
Clinical Assessment and Monitoring	**Med Eval Requirement**	**Annual *****	**PRE-FLIGHT (L-)**	**IN-FLIGHT**	**POST-FLIGHT (R+)**
RADIATION					
Personal dosimetry	[6022]	Table 6		ongoing	
CARDIOVASCULAR					
Orthostatic tolerance Active postural stand test	[6023]	Table 6			R+0 d, then daily to stable
Screening for deep vein thrombosis and venous flow anomalies	[6041]		L-12/3 m		R+0/45d, ACI
EXERCISE AND FITNESS					
Functional Fitness Assessment	[6024]	AME L-9/6 m, L-90/30 d	L-90/30 d		R+5/7 d
On-Orbit Strength & Conditioning Monitoring	[6025]			FD3 through the day prior to undock and ACI. Resistance: 3x/wk (60 min) Aerobic: 3x/wk (30 min)	
Aerobic Functional Capacity	[6028]	AME L-12m	L-90/30	FD14, FD75, FD 165, FD 255, R-14 d	R+ 5 d, R+ 30 d, ACI
EVA					
Pre/post EVA CMO exam	[6029]			Pre- and Post-EVA	
Monitoring during EVA	[6030]			During EVA	

m= months d= days y= year L= launch R= return AME – Annual Medical Evaluation ***Annual Tests - Table 3 Overview of Medical Evaluation Procedures for NASA, Table 4 Overview of Medical Evaluation Procedures for NASA Astronauts to be applied annually, Table 5 Laboratory Tests on Annual Recertification, and Table 7 Special Assessments for Recertification

Table 7– Mission Medical Examinations for Short Duration (< 30 days) Missions Schedule/need provided for informational purposes only. Based on 30-day ISS mission.					
Clinical Assessment and Monitoring	**Med Eval Requirement**	**Annual *****	**PRE-FLIGHT (L-)**	**IN-FLIGHT**	**POST-FLIGHT (R+)**
PSYCH/BEHAVIORAL					
Pre-flight psychiatric/ psychological status check	[6032]	Table 6	L-180 d, L-90 d		
Private psychological conference	[6033]			Every 14 days or Mid Mission	
Post-flight psychiatric/ psychological status check	[6034]				R+7 d
Cognitive Assessment	[6035]		AME L-12/6 m Training (3 sessions): Baseline (3 sessions)	ACI	ACI
Behavioral Observation of Training	[6036]		Observe 1 session between assignment and flight		
NUTRITION					
Vitamin D Testing and Treatment Protocol	[6037]				
Nutritional Status Assessments	[6038]	AME L- 21/18 m, L-90/30 d	AME L- 21/18 m, L-90/30	Standard dietary assessment questionnaire-weekly, MMD-monthly or ACI, shared from [6015]	R+0, R+20/30d, DXA at R+5/7d, shared from [6013]
FATIGUE COUNTERMEASURES					
Objective Measure of Sleep	[6039]	AME L-21/18 m	L-12/6 m, L-14 d	Continuously throughout mission	End R+7 d
Sleep Medication Ground Testing	[6040]		Any time before L-30 d		
Space Motion Sickness Medication Ground Testing	[6042]		Any time before L-30 d		

m= months d= days y= year L= launch R= return AME – Annual Medical Evaluation ***Annual Tests - Table 3 Overview of Medical Evaluation Procedures for NASA, Table 4 Overview of Medical Evaluation Procedures for NASA Astronauts to be applied annually, Table 5 Laboratory Tests on Annual Recertification, and Table 7 Special Assessments for Recertification

Table 8 – Mission Medical Examinations for Assigned Crew on > 30-day Missions

Schedule/need provided for informational purposes only. Based on 180-day ISS mission.					
Clinical Assessment and Monitoring	**Med Eval Requirement**	**Annual *****	**PRE-FLIGHT (Including Annual)**	**IN-FLIGHT**	**POST-FLIGHT**
Pre- and Post-flight Physical Exam for Long Duration Crews	[6001]	Table 2	AME L-9/6 m, L-21/14 d, L-2/1 d		R+0 d, R+3 d, R+7/14 d, R+60 d
CMO Health Status Evaluations	[6002]			L+14/21, L+90, L+180, and L+270; R-21/14 d	
Private Medical Conference	[6003]			L+1-7 d, weekly, pre/post EVA, R-5 d, daily to R-0 d	
Neurological Assessment	[6004]	Table 2	AME L-9/6 m		R+0 d, R+3 d, R+7/14 d
Neurovestibular Platform Test	[6005]		AME L-9/6 m, L-90/30 d		R+7/10 d
Resting ECG	[6006]	Table 6	AME L-9/6 m to L-10 d		R+0/3 d
24-hour Ambulatory ECG			L-365/330 d		R+0, R+10/14 d
Hearing Assessment	[6007]	Table 6	L-90/30 d	On or before FD21, then every 3 months regardless of mission length	R+3 d, If abnormal, R+10/14 d, R+60 d

m= months d= days y= year L= launch R= return AME – Annual Medical Evaluation ***Annual Tests - Table 3 Overview of Medical Evaluation Procedures for NASA, Table 4 Overview of Medical Evaluation Procedures for NASA Astronauts to be applied annually, Table 5 Laboratory Tests on Annual Recertification, and Table 7 Special Assessments for Recertification

Table 8 – Mission Medical Examinations for Assigned Crew on > 30-day Missions
Schedule/need provided for informational purposes only. Based on 180-day ISS mission.

Clinical Assessment and Monitoring	Med Eval Requirement	Annual ***	PRE-FLIGHT (Including Annual)	IN-FLIGHT	POST-FLIGHT
Hearing Protection	[6008]		L-18/21 m		
Dental Examination	[6009]	Table 6	L-90/30 d		
Dental Orthopantomogram or Full Mouth X-Ray Series	[6010]	Table 6	AME L-21/18 m		
Ophthalmology/Optometry	[6011]	Table 6	L-90/30 d AME L-21/18 m - Retinal photographs and OCT		R+0/1 d, R+3 d and ACI R+1/10 d - Retinal photographs and OCT
Specialized Ocular Assessments	[6012]	Table 6	AME L-21/18 m, AME L-9/6 m	L+ 30 d, L+90 d, L+180 d, L+270 d, R- 30 d and ACI	R+1/3 d, follow abnormal findings ACI
Bone Densitometry	[6013]	Table 6	AME L-21/18 m, L-180/30 d		R+ <30, then ACI to assess BMD recovery
Ultrasound Imaging (Sonography)	[6014]	Table 6	AME L-21/18 m		
Body Mass Measurement	[6015]	Table 2		L+7d, Monthly	
Photo documentation of skin	[6016]				R+0/1 d

m= months d= days y= year L= launch R= return AME – Annual Medical Evaluation ***Annual Tests - Table 3 Overview of Medical Evaluation Procedures for NASA, Table 4 Overview of Medical Evaluation Procedures for NASA Astronauts to be applied annually, Table 5 Laboratory Tests on Annual Recertification, and Table 7 Special Assessments for Recertification

Table 8 – Mission Medical Examinations for Assigned Crew on > 30-day Missions Schedule/need provided for informational purposes only. Based on 180-day ISS mission.					
Clinical Assessment and Monitoring	**Med Eval Requirement**	**Annual *****	**PRE-FLIGHT (Including Annual)**	**IN-FLIGHT**	**POST-FLIGHT**
MRI Brain and MR angiography	[6017]	AME L-21/18 m	AME L-21/18 m		
MRI Cervical and Lumbar Spine (non-contrast)	[6018]	AME L-21/18 m	AME L-21/18 m		R+1-14 d, then ACI; consider R+180 d and R+360 d
LABORATORY					
Laboratory Testing	[6019]	Table 5	L-90/30 d	Blood and Urine L+ 180 d and ACI	R+0/1 d, (R+3/7 d), (R+14/30 d)
Helicobacter pylori Screen		Table 4			
MRSA	[6020]		L-9/6 m		ACI
GABHS	[6021]		L-90/30 d		ACI
RADIATION					
Personal dosimetry	[6022]	Table 6		Ongoing	
CARDIOVASCULAR					
Orthostatic Tolerance: Active postural stand test	[6023]				R+0 then daily to stable
Screening for deep vein thrombosis and venous flow anomalies	[6041]		L-12/3 m	L+30 days; L+60 d; R-42 d	R+0/45 d, ACI

m= months d= days y= year L= launch R= return AME – Annual Medical Evaluation ***Annual Tests - Table 3 Overview of Medical Evaluation Procedures for NASA, Table 4 Overview of Medical Evaluation Procedures for NASA Astronauts to be applied annually, Table 5 Laboratory Tests on Annual Recertification, and Table 7 Special Assessments for Recertification

Table 8 – Mission Medical Examinations for Assigned Crew on > 30-day Missions Schedule/need provided for informational purposes only. Based on 180-day ISS mission.					
Clinical Assessment and Monitoring	**Med Eval Requirement**	**Annual *****	**PRE-FLIGHT (Including Annual)**	**IN-FLIGHT**	**POST-FLIGHT**
EXERCISE & FITNESS					
Functional Fitness Assessment	[6024]	AME L-9/6 m, L-90/30 d	AME L-9/6 m, L-90/30 d		R+5/7 d, R+30 d
On-Orbit Strength & Conditioning Monitoring	[6025]			Strength and conditioning monitoring - Recurrent in-flight; L+14 days (NET 3rd session) and then at least every 30 days thereafter.	
Test for Aerobic Functional Capacity	[6028]	AME L-12 m	AME L-12 m; L-90/30 d	FD14, FD75, FD165, FD255, R-14 d	R+5 d, R+30 d
EVA					
Pre/Post EVA CMO Medical Exam	[6029]			Pre- and Post-EVA	
Monitoring during EVA	[6030]			ECG and heart rate during EVA	
PSYCH/BEHAVIORAL					

m= months d= days y= year L= launch R= return AME – Annual Medical Evaluation ***Annual Tests - Table 3 Overview of Medical Evaluation Procedures for NASA, Table 4 Overview of Medical Evaluation Procedures for NASA Astronauts to be applied annually, Table 5 Laboratory Tests on Annual Recertification, and Table 7 Special Assessments for Recertification

Table 8 – Mission Medical Examinations for Assigned Crew on > 30-day Missions Schedule/need provided for informational purposes only. Based on 180-day ISS mission.					
Clinical Assessment and Monitoring	**Med Eval Requirement**	**Annual *** **	**PRE-FLIGHT (Including Annual)**	**IN-FLIGHT**	**POST-FLIGHT**
Pre-flight psychiatric/psychological status check	[6032]	Table 6	L-12 m, L-240/180 d, L-90/30 d		
Private psychological conference	[6033]			Every 14 days	
Post-flight psychiatric/psychological status check	[6034]				R+3 d, R+10 d, R+14 d, R+30/60 d
Cognitive assessment	[6035]		Training (3 sessions): L-390 d, L-330 d, L-270 d; Baseline: L-210 d, L-150 d, L-90 d	Monthly	R+30 d
Behavioral Observation of Training	[6036]		At least 2 sessions between crew assignment and launch		
NUTRITION					
Vitamin D Testing and Treatment Protocol	[6037]				
Nutritional Status Assessments	[6038]	AME L-21/18 m, L-90/30 d	AME L- 21/18 m, L-90/30 d	Standard dietary assessment questionnaire-weekly, MMD-monthly or ACI, shared from [6015]	R+0, R+20/30 d, DXA at R+5/7 d, shared from [6013]
FATIGUE COUNTERMEASURES					
Objective Measure of Sleep	[6039]	AME L-21/18 m	Baseline (2 weeks): AME L-21/18 m, Begin L-7 d	Continuously throughout mission	End R+7 d
Sleep Medication Ground Testing	[6040]		Any time before L-30 d		
Space Motion Sickness Medication Ground Testing	[6042]		Any time before L-30 d		

m= months d= days y= year L= launch R= return AME – Annual Medical Evaluation ***Annual Tests - Table 3 Overview of Medical Evaluation Procedures for NASA, Table 4 Overview of Medical Evaluation Procedures for NASA Astronauts to be applied annually, Table 5 Laboratory Tests on Annual Recertification, and Table 7 Special Assessments for Recertification

6.1 Clinical Assessment and Monitoring

6.1.1 Pre- and Post-flight Physical Examination for > 30 days Crews

[6001] Requirement: NASA Astronauts **shall** undergo clinical examinations with the Crew Surgeon (CS), Deputy Crew Surgeon, or Partner Flight Surgeon (FS) according to the specifications and schedule described below.

***Rationale**: To assess the medical status and flight readiness of crewmembers for long-duration missions before flight, and medical status after landing.*

Description: Clinical examinations include medical interview, interval history since the previous evaluation and basic vital signs (pulse and blood pressure, body temperature, respiratory rate), and may also include some or all of the following, per the discretion of the examining surgeon:
Clinical History
Physical Examination
Vital signs: height, weight, pulse, and blood pressure recumbent, sitting, standing, body temperature, respiratory rate
Head and face (nares/nasal mucosa, sinuses, maxillary and frontal), oropharynx
Ears (external meatus, tympanic membrane, and response to Valsalva)
Eyes (general appearance, extra-ocular movements, pupil reactivity, ophthalmoscopic exam)
Neck (thyroid, vascular exam, motion)
Heart and lungs (cardiovascular exam, including cardiac auscultation, carotid and venous upstrokes, and peripheral pulses)
Abdomen (auscultation, palpation of major organs and herniations)
Rectum/anus (to include prostate exam for males, rectal vault, and occult blood testing)
Genitourinary exam (appearance, general exam, and herniations)
Breast/chest exam
Pelvic exam (for female crewmembers)
Extremities (to include range of motion and general strength assessments on a 1-5 scale)
Spine (general appearance and mobility)
Skin (includes lymphatics and identifying body marks)
Neurological (may include [6004])
***Example Schedule based on 30-day ISS mission**: AME L-12/6 m, L-21/14 d, L-2/1 d, R+0 d and R+3/7 d, PEX ACI - Labs and PEX ID Swab.*
***Example Schedule based on 180-day ISS mission**: AME L- 9/6 m, L- 21/14 d, L- 2/1 d, R+ 0 d, R+ 3 d, R+ 7 /14 d, R+ 60 d (return to duty), and ACI.*
Table 7, Table 8

6.1.2 Crew Medical Officer (CMO) Health Status Evaluations

[6002] Requirement: Crewmembers **shall** complete periodic health status evaluations in-flight.

***Rationale**: To assess the medical status of the crewmember in-flight and report the findings to the CS. For example, in the past this evaluation has included medical history and vital signs (temperature, blood pressure, pulse & respiratory rate), but trending of data has not*

indicated any abnormalities. It is recommended that testing is based on symptomology.

Description: Health Status Evaluation (HSE). May also include blood labs – See [6019].
Example Schedule based on 30-day ISS mission: *Mid Mission ACI*
Example Schedule based on 180-day ISS mission*: L+ 14/21 d, L+ 90 d, L+180 d, L+270 d, R- 21/14 d, and ACI.*
Table 7, Table 8

6.1.3 Private Medical Conference

[6003] Requirement: Crewmembers **shall** participate in private medical conferences with a mission assigned FS.

Rationale*: The primary purpose of private medical conferences is to monitor crewmember health. Private communication between the FS and crewmember enables medical consultation and provides an opportunity to discuss human support and habitability factors.*

Description: Dedicated private communications link between vehicle and console.
Example Schedule based on ISS missions*: L+1-7, weekly, pre/post EVA, R- 5 d, daily to R-0 d, and ACI.*
Table 7, Table 8

6.1.4 Neurological Assessment

[6004] Requirement: Crewmembers **shall** undergo a neurological assessment before and after flight.

Rationale*: Because of the neurovestibular problems often associated with spaceflight, a standardized neurological assessment is obtained pre-flight for comparison with post-flight status.*

Description: A brief standardized clinical neurological assessment (example below) will be completed by either the Crew Surgeon or a neurology specialist.

NEUROLOGICAL FUNCTION RATING SCALE	0	1	2	3	4
Scale 0 = no symptoms, normal performance 4 = persistent symptoms/severe performance decrement					
Headache					
Dizziness/Faintness					
Vertigo/Spinning					
Gaze/Ocular Movements (nystagmus)					
Finger to nose (close eyes touch nose, open eyes touch finger)					
Drift (close eyes, extend arms, palms up)					
Rising from chair (without use of arms)					
Standing/Romberg (feet together, arms extended, close eyes) 30 seconds					

	Leg lift – Hop (close eyes, lift leg, hop 3 times, alternate)					
	Tandem/Heel to toe walk (5 meters)					
	Dynamic equilibrium (close eyes walk 9m turn 180 and return)					
Example Schedule based on 30-day ISS mission: *AME L- 12/6 m, R+ 0 d, R+ 3 d, R+ 7d, and ACI.*						
Example Schedule based on 180-day ISS mission*: AME L- 9/6 m, R+ 0 d, R+ 3 d, R+ 7d R+14 d, and ACI.*						
Table 7, Table 8						

6.1.5 Neurovestibular Platform Test

[6005] Requirement: Crewmembers **shall** undergo an objective assessment of neuro-vestibular function before and after flight.

Rationale*: To perform functional assessments regarding neuro-vestibular re-adaptation to Earth gravity following prolonged weightlessness. Results will be used to establish a more precise return-to-normal daily activities (stairs, driving a car, showering, etc.) criteria and return-to-duty criteria.*

Description: Balance control performance and sensory integration performance are measured using Equitest Posture Platform, Optotrak Motion Analysis System, and Subject Safety Restraint System.
Example Schedule based on 30-day ISS mission*: AME L- 9/6 m; L- 90/30 d, R+ 7/10 d, and ACI until stable.*
Example Schedule based on 180-day ISS mission*: AME L-9/6m, L-90/30 d, R+7/10 d, and ACI.*
Table 7, Table 8

6.1.6 Resting ECG

[6006] Requirement: Each crewmember **shall** complete a resting ECG prior to launch to provide a baseline study.

Rationale: *A 12-lead electrocardiogram (ECG) is used to establish a baseline study for comparison with subsequent studies obtained in-flight and post-flight.*

Description: Subject lies supine for 15 minutes while ECG tracings are recorded from 10 electrode sites using chest and limb leads.
Example Schedule based on 30-day ISS mission*: AME L-12/6m, and ACI.*
Example Schedule based on 180-day ISS mission: *AME L- 9/6 m to L- 10 d, R+0/3 d, and ACI.*
Table 7, Table 8

6.1.7 Hearing Assessment

[6007] Requirement: Crewmembers will be tested with conventional audiometry before and after flight. Crewmembers **shall** also conduct pre-flight and in-flight hearing assessments utilizing in-flight hardware.

***Rationale**: To monitor crewmember hearing sensitivity before, during, and after long-duration flights, in order to identify changes caused by the onboard environment. For established vehicles with well characterized acoustic environments testing may be reduced.*

Pre/Post-flight Conventional Audiometry Description: Hearing sensitivity is determined with pure-tone, air conduction audiometry, using a calibrated audiometer in a quiet room.
***Example Schedule based on 30-day ISS mission**: AME L-12/6m, in-flight ACI, R+3d, (If abnormal, R+10/14d, R+60d), and ACI.*
***Example Schedule based on 180-day ISS mission**: L- 90/30 d, R+ 3 d, (If abnormal, R+ 10/14 d, R+ 60 d), and ACI.*
In-flight Audiometry Description: Hearing sensitivity is determined with pure-tone audiometry, using a calibrated audiometer with earphones (or equivalent device/method) that can attenuate noise levels found on the Space vehicle. The condition of the middle ear and mobility of the eardrum (tympanic membrane) is determined with tympanometry, an objective test of middle-ear function.
***Example In-flight Schedule based on ISS missions**: On or before FD 21, then every 3 months regardless of mission length, with supplemental test(s) as requested by crewmember or Crew Surgeon based on noise environment or other medical concerns. All tests will be scheduled within 24 hours following acoustic dosimetry measurements.*
Table 7, Table 8

6.1.8 Hearing Protection

[6008] Requirement: Crewmembers **shall** be provided with hearing protection earwear.

***Rationale**: Noise levels in some areas of the space vehicle may exceed accepted noise thresholds as listed in NASA-STD-3001, Volume 2. Hearing protection is required to ameliorate the risks associated with excessive noise exposure which may include temporary or permanent threshold shifts as well as possible behavioral health issues. To adequately protect crewmembers from excessive noise, crewmembers will be offered hearing protection (to include custom and/or universally fitting earwear), to provide protection while enabling speech perception and ability to listen to media at safe levels. Crewmembers may use electronic molded earplugs with personal listening devices while exercising and non-electronic flat-attenuating custom earplugs as desired.*

Description: Crewmembers are provided with hearing protection earwear. Custom earwear may need additional time for manufacturing/preparation and proper crewmember earwear fit adjustment.
***Example* S*chedule based on 30-day ISS mission**: L-18/12 m*
***Example Schedule based on 180-day ISS mission**: L-18/12 m*
Table 7, Table 8

6.1.9 Dental Examination

[6009] Requirement: The dental health of each crewmember **shall** be assessed before launch.

***Rationale**: To assess general dental health and flight readiness, identify and mitigate dental health risks, obtain baseline measurements, and address needs/changes over time.*

Description: Brief dental examination.
***Example schedule based on 30-day ISS mission**: AME L-12/6 m.*
***Example Schedule based on 180-day ISS mission**: L-90/30 d, and ACI.*
Table 7, Table 8

6.1.10 Dental Orthopantomogram or Full Mouth X-Ray Series

[6010] Requirement: A full dental orthopantomogram x-ray or full mouth x-ray series **shall** be performed within two years of launch.

***Rationale:** To fully assess the underlying dental health of the crewmember in order to correct any potential dental problems well in advance of mission launch*

Description: An orthopantomogram (e.g., Panorex) is a panoramic scanning x-ray of the maxilla and mandible. (Full mouth x-ray series can be used as an alternative for dental screening).
***Example schedule based on 30-day ISS mission**: AME L-12/6 m.*
***Example Schedule based on 180-day ISS mission**: AME L- 21/18 m.*
Table 7, Table 8

6.1.11 Ophthalmology/Optometry Examinations

[6011] Requirement: Each crewmember **shall** undergo ophthalmological exams before and after flight in addition to regular annual checkups.

***Rationale**: To establish baseline measurements for comparison to post-flight measurements, measure changes, assess future flight readiness, and assist in planning for in-flight healthcare.*

Description: Examination at L- 90/30 d and R+ 3 d will be conducted by an eye specialist. Examination at R+0/1 d will be conducted by the flight surgeon and includes an ophthalmoscopic exam. Retinal photographs and optical coherence tomography (OCT) will be taken at L-21/18 m and at R+1/10 d.
***Example schedule based on 30-day ISS mission**: AME L-12/6m Retinal photographs and OCT, R+0, R+3d and ACI, R+1/10d Retinal photographs and OCT.*
***Example Schedule based on 180-day ISS mission**: L- 90/30d, AME L-21/18m, - Retinal photographs and OCT, R+ 0/1 d, R+ 3 d and ACI, R+1/10 d - Retinal photographs and OCT.*
Table 7, Table 8

6.1.12 Specialized Ocular Assessments

[6012] Requirement: To assess the effects of exposure to the spaceflight environment on ocular health, crewmembers **shall** undergo specialized eye examinations pre-flight, in-flight, and post-flight.

Rationale*: Medical eye examinations on returning crewmembers have demonstrated the presence of significant changes in ocular structure and function. Additional specific testing is required for crewmembers to document baseline ocular status and to assess changes which may occur during the mission with early post-flight status assessment and continuing follow-up for crewmembers who demonstrate mission-related ocular changes.*

Description: The following ocular assessments will be performed on all Crewmembers. Crewmembers will require training on specific ocular tests which they will perform in-flight. These ocular assessments are in addition to the standard tests required of all crewmembers detailed in [6011].
Pre-flight
AME L-21/18 m
➢ MRI brain and orbits [Spaceflight Associated Neuro-Ocular Syndrome (SANS) protocol]
AME L-21/18 m and AME L-9/6 m
➢ Ocular questionnaire
➢ Visual acuity, distance and near
➢ Refraction – manifest and cycloplegic
➢ Threshold visual fields
➢ Amsler grid
➢ Pupil reflexes
➢ Extraocular muscle balance
➢ Biomicroscopy (slit lamp)
➢ Dilated fundoscopic examination
➢ Retinal photography
➢ Tonometry
➢ Optical coherence tomography (high resolution) including Spontaneous Venous Pulsations (SVP) videography and multicolor Imaging (MCI).
➢ Optical biometry
L-9/6 m
➢ 2-D imaging ultrasound
In-flight
L+30, L+90, L+180, L+270, R-30, ACI
➢ Ocular questionnaire
➢ Visual acuity distance and near
➢ Amsler grid
➢ Threshold visual fields
➢ Fundoscopy (ACI only)
➢ 2-D imaging ultrasound

➢ Optical coherence tomography (high resolution) and Multicolor Imaging (MCI).
Post-flight
R+1/3, follow abnormal findings ACI
➢ Ocular questionnaire
➢ Visual acuity, distance and near
➢ Refraction – manifest and cycloplegic
➢ Threshold visual fields
➢ Amsler grid
➢ Pupil reflexes
➢ Extraocular muscle balance
➢ Biomicroscopy (slit lamp)
➢ Dilated fundoscopic examination
➢ Retinal photography
➢ Tonometry
➢ Optical coherence tomography (high resolution) including SVP videography and Multicolor Imaging (MCI).
➢ Optical biometry
➢ 2-D imaging ultrasound
➢ MRI brain and orbits [special visual impairment and intracranial pressure (SANS) protocol]
Example Schedule based on 30-day ISS mission*: AME L-12/6 m, in-flight ACI, Post Flight: R+1/3 d, follow abnormal findings every 30 days until clinically stable or ACI.*
Example Schedule based on 180-day ISS mission*: Pre-flight: AME L-21/18 m, L- 9/6 m, In-flight: L+30; L+90; L+180d, L+270 d, R-30; and ACI, Post-flight: R+1/3d; follow abnormal findings ACI*
Table 7, Table 8

6.1.13 Bone Densitometry

[6013] Requirement: Pre- and post-flight measurements of bone mineral density (BMD) **shall** be performed.

Rationale*: Bone densitometry measures are needed to track individual skeletal integrity (loss and recovery). This is particularly important for long-duration flights. This information will aid in targeting rehabilitation efforts and facilitating a timely recertification for long-duration missions. These data will also be analyzed to evaluate the efficacy of in-flight exercise countermeasures and post-flight rehabilitation programs.*

Description: BMD is measured by Dual Energy X-ray Absorptiometry (DXA) or equivalent measurement method. DXA provides accurate measures of whole body lean mass and fat mass in addition to localized measurements of bone density. DXA is the standard terrestrial test of BMD and should be performed on all crewmembers. Quantitative Computed Tomography (QCT) distinguishes between cortical and trabecular bone compartments which can allow for improved assessment of fracture risk. QCT may therefore be used as a supplemental tool.
Example schedule based on ISS 30-day mission*: ACI.*

Example Schedule based on ISS 180-day mission*: AME L- 21/18 m; L- 180/30 d (as close to launch as feasible), R+ < 30 days, at R+1 year, then as clinically indicated to assess BMD recovery.*
Table 7, Table 8

6.1.14 Ultrasound Imaging (Sonography)

[6014] Requirement: Ultrasound imaging **shall** be conducted for each crewmember.

Rationale*: To evaluate health status using ultrasound.*

Description: Assessment is conducted using abdominal/retroperitoneal/pelvic ultrasound, and thyroid ultrasound. A heart ultrasound (echocardiogram) is obtained periodically as part of the annual physical examination. Carotid artery ultrasound utilizes ultrasound techniques to assess for atherosclerosis, and should include assessment of intima-medial thickness (IMT) and carotid plaque burden (volume or area)
Example Schedule based on 30-day ISS mission*: AME L-12/6 m.*
Example Schedule based on 180-day ISS mission*: Thyroid – AME L- 21/18 m, Abdominal/retroperitoneal/pelvic AME L-21/18 m, Carotid ultrasound AME 21/18 m unless completed within previous 5 years, other imaging applications may be used on an "as required" basis in-flight.*
Table 7, Table 8

6.1.15 Body Mass Measurement

[6015] Requirement: Crewmembers **shall** evaluate body mass periodically while in-flight.

Rationale*: To monitor body mass changes in-flight as part of a general crew health assessment.*

Description: Body mass may be measured utilizing a mass measurement device.
Example Schedule based on 30-day ISS mission*: ACI.*
Example Schedule based on 180-day ISS mission*: L+7, (baseline), then monthly and ACI.*
Table 7, Table 8

6.1.16 Photodocumentation of Skin

[6016] Requirement: The Crew Medical Officer or Crew Surgeon **shall** document, through photographic imaging, the condition of the crewmember's skin, including any signs of skin disease or injury.

Rationale*: To provide objective evidence of the condition of the skin, particularly injuries and/or disease, such as reactions to allergens or chemicals for diagnostic and follow-up purposes.*

Description: Assessment using a digital camera and ruler.
Example Schedule based on 30-day ISS mission*: ACI.*

***Example Schedule based on 180-day ISS mission**: ACI and R+ 0/1 d.*
Table 7, Table 8

6.1.17 MRI Brain and MR Angiography

[6017] Requirement: Each crewmember **shall** undergo an MRI study of the brain and MR angiographic study of the supra-aortic and intracranial vessels.

***Rationale**: To assess for vascular and structural abnormalities that might lead to crewmember incapacitation or performance decrements during a long-duration mission. An MRI and MR angiogram is obtained at selection. The pre-flight study will assess for interval changes that might have developed since selection.*

Description: MRI/MRA protocols and imaging sequences, selected for this testing, including the use of gadolinium-based contrast agents, may vary depending on available capability. Testing must follow best current neuroimaging practices to characterize intracranial and cerebrovascular anatomy with sufficient depth and detail to address all conditions identified in MED Volume A standards.
***Example Schedule based on ISS missions**: AME L- 21/18m if greater than 2 years since astronaut selection MRI/A.*
Table 7, Table 8

6.1.18 MRI Cervical and Lumbar Spine Imaging

[6018] Requirement: Each crewmember **shall** undergo pre- and post-flight non-contrast MRI studies of the cervical and lumbar spine.

***Rationale**: To assess for spinal or pathology that:*

a) May pre-dispose crewmembers to in-flight changes on long-duration missions that could lead to crewmember pain, dysfunction, or performance decrements during the mission.
b) Will inform decision making of management and exercise prescriptions for pre-flight and in-flight conditioning tailored to the needs of the crewmember based on their unique baseline.
c) Will assess for space related changes and inform decision making of exercise prescription for post-flight conditioning to rehabilitate crewmembers and minimize risk of post-flight injury.

Description: MRI protocols and imaging sequences should characterize normal and pathological anatomy with sufficient depth and detail to address all conditions of spinal related pathology identified in OCHMO-STD-100.1A standards. Testing must follow current spinal imaging practices, but may vary depending on available capability
***Example Schedule based on 30-day ISS mission**: AME L-12/1 8 m, and ACI.*

Example Schedule based on 180-day ISS mission*: AME L- 21/18 m; R+1-14 d, and ACI thereafter (Consider at R+180, R+360 to confirm resolution and prevent injury related to spaceflight-related changes).*
Table 7, Table 8

6.1.19 Laboratory Testing

[6019] Requirement: A clinical laboratory assessment **shall** be completed for each crewmember before and after flight.

Rationale*: To evaluate crewmember medical fitness for flight and to determine post-flight recovery by analysis of clinical specimens.*

Descriptions and example schedules (below) based on ISS mission: **L- 90/30 days:**
Blood: Hematology – Complete Blood Count (CBC) w/differential, reticulocytes; Chemistry profile – fasting glucose, BUN, creatinine, AST, ALT, GGT, alkaline phosphatase, total bilirubin, total protein, globulin (calc), electrolytes (NA, K, CL), calcium, ionized calcium, magnesium, phosphorus, LDH, uric acid, albumin; Thyroid function – free T4, TSH; Iron profile – iron, iron binding capacity, transferrin saturation, ferritin; Special chemistry – C-reactive protein (High Sensitivity assay), 25-OH Vitamin D; Urine or Serum HCG on females, Agency-specific: Immunocap Mouse Urine IgE, Immunocap Mouse Epithelium, Archive tube, TB Screen (unless covered during annual recertification).
Urine: Urinalysis (specific gravity, glucose, protein, pH, ketones, blood), microscopic.
In-flight:
Blood and urine testing in-flight L+180d and ACI.
R+ 0/1 day:
Blood: Hematology – CBC w/differential, Chemistry Profile – fasting glucose, BUN, creatinine, AST, ALT, GGT, alkaline phosphatase, total bilirubin, total protein, globulin (calc), electrolytes (NA, K, CL), calcium, magnesium, phosphorus, LDH, uric acid, albumin; Agency-specific Archive tube.
Urine: Urinalysis
R+ 3/7 days:
Blood: Hematology – CBC w/differential, reticulocytes; Chemistry profile – fasting glucose, BUN, creatinine, AST, ALT, GGT, alkaline phosphatase, total bilirubin, total protein, globulin (calc), electrolytes (Na, K, CL), calcium, magnesium, phosphorus, LDH, uric acid, albumin; Creatine kinase; Iron profile – iron, TIBC, transferrin saturation, ferritin; Special chemistry – C-reactive protein; Thyroid profile-TSH, FT4, Agency-specific: Immunocap Mouse Urine IgE, Immunocap Mouse Epithelium, Archive tube.
Urine: Urinalysis

R+14/30 days:
Blood: Hematology – CBC w/differential, reticulocytes; Chemistry profile – glucose, BUN, creatinine, AST, ALT, GGT, alkaline phosphatase, total bilirubin, total protein, globulin (calc), electrolytes (NA, K, Cl), calcium, magnesium, phosphorus, LDH, uric acid, albumin; Iron profile – iron, TIBC, transferrin saturation, ferritin; Special chemistry – C-reactive protein, High Sensitivity assay); 25-OH Vitamin D, HbAlC; serum lipids (total cholesterol, LDL, HDL, Triglycerides), Thyroid profile-TSH, FT4, Archive tube.
Urine: Urinalysis
Example Schedule based on ISS missions*: See above, and ACI.*
Table 7, Table 8

6.1.20 Methicillin Resistant Staphylococcus aureus (MRSA) Screening and Suppression

[6020] Requirement: Nasal screening for Staphylococcus aureus **shall** be conducted on all crewmembers at L-90/30 days.

Rationale*: MRSA may cause skin or other infections in crewmembers onboard which would be difficult to treat with manifested medications. Screening for individuals who are carriers will reduce the risk for active infection or transmission.*

Description: Using a single swab, both nostrils will be sampled and cultured or, using alternate techniques, for MRSA organisms. Crewmembers identified as MRSA positive will undergo topical treatment with mupirocin intranasal three times daily for 5 days. Crewmembers who are MRSA positive will also require anti-staphylococcal body washes daily for 5 days. MRSA screening and sensitivity will be repeated after the course of eradication, and if positive, appropriate antibiotics will be manifested.
Example Schedule based on 30-day ISS mission*: L-90/30 d, post-flight ACI.*
Table 7, Table 8

6.1.21 Group A Beta-Hemolytic Streptococcus (GABHS, Strep pyogenes) carrier state

[6021] Requirement: Throat swab for Group A Beta-Hemolytic Streptococcus carriage **shall** be conducted on all crewmembers at L-90/30 days.

Rationale: *Group A Streptococcus can cause both pharyngitis as well as a variety of highly aggressive soft tissue infections such as cellulitis and necrotizing fasciitis which in terrestrial settings may proceed to surgical intervention even when appropriate antibiotics are given.*

Description: Testing by pharyngeal swab, either classic throat culture or "rapid strep" testing using ELISA (Enzyme Linked Immunosorbent Assay) is performed to identify the carrier state. If identified and confirmed it will be treated with antibiotics and re-testing performed to confirm clearance of the carrier state.
Example Schedule based on ISS missions*: L-90/30 d.*
Table 7, Table 8

6.2 Radiation

6.2.1 Radiation Monitoring/Personal Physical Dosimetry-

[6022] Requirement: In-flight radiation monitoring **shall** be performed with crew personal dosimetry according to the specifications in NASA-STD-3001, Volume 2.

		LEO		BLEO		Extraterrestrial Surface	
		Area Monitoring Vehicle/ Habitat	Personal Monitoring IVA-EVA	Area Monitoring Vehicle/ Habitat	Personal Monitoring IVA-EVA	Area Monitoring Vehicle/ Habitat	Personal Monitoring IVA-EVA
Charged Particles*	**SPE – solar particle event**	**For mission exposures projected to be less than 50 mSv**** Can be assessed via analysis** Or Area and/or personal monitors with vehicle analysis can be utilized for IVA and EVA. **For exposures projected to be greater than 50 mSv**** Area and/or personal monitors with vehicle analysis can be utilized for IVA and EVA.*		Required	Required	Required	Required
	GCR - galactic cosmic rays			Required	Required	Required – environment analysis may be substituted	Required – environment analysis may be substituted
	Trapped Particles			Required	Required	N/A	N/A
	Neutrons	N/A	N/A	Required – environment analysis may be substituted	Required – environment analysis may be substituted	Required – environment analysis may be substituted	Required – environment analysis may be substituted

**May be monitored with a single device*
*** Utilizing the quality factors that are utilized to calculate the NASA effective dose space PEL (refer to Volume 1, Section 4.8)*

For exposures greater than 50 mSv the uncertainty of the analysis affects the ability to accurately communicate the risk to the crew member. Crewmembers with multiple missions that exceed 75 mSv of total dose will need additional assessment (actual monitoring vs. analytical assessment) to ensure adequate communication of risk.

Rationale: *To characterize and manage crew exposure to ionizing radiation while ensuring the PELs are not exceeded, the ionizing radiation in habitable environments must be monitored throughout the course of a mission. Appropriate dose monitoring provides data on the radiation type, linear energy transfer (LET), intensity, and angles of incidence. Timepix-based instruments have been used by past programs to characterize the ionizing radiation inside crewed vehicles and to measure the dose and dose rates.*

Description: To characterize and manage crew exposure to ionizing radiation while ensuring the PELs are not exceeded, the ionizing radiation in habitable environments will be monitored throughout the course of a mission. Appropriate dose monitoring provides data on the radiation type, linear energy transfer (LET), intensity, and angles of incidence.
Example Schedule based on ISS 180-day missions: *Ongoing*
Table 7, Table 8

6.3 Cardiovascular

6.4 6.3.1 Active postural stand tests

[6023] Requirement: Each crewmember **shall** undergo orthostatic tolerance testing by means of an active stand test.

Rationale: *Orthostatic intolerance is a common feature of re-adaptation to gravitational fields following microgravity exposure. A standardized clinical procedure helps to document the degree of intolerance, to follow return to stability, and to provide standardized data for cohort comparison.*

Description: Baseline blood pressure and pulse are obtained in the supine position, then at one-minute intervals in the seated position over a period of five minutes, and then at one-minute intervals over a period of 10 minutes on transition to the standing position.
Example Schedule based on ISS missions*: R+ 0 d, then daily until orthostatic stability.*
Table 7, Table 8

6.3.2 Screening for Deep Vein Thrombosis and Venous Flow Anomalies

[6041] Requirement: Every crewmember **shall** be screened for deep vein thrombosis (DVT) and flow anomalies of the internal jugular veins.

Rationale:

- *Primary DVT of the left internal jugular vein has been observed at elevated rates in microgravity. Flow anomalies are observed in a significant subset of crewmembers examined for both research and surveillance purposes, and likely represent a risk for DVT development.*
- *DVT is associated with significant mission impact and poses an acute risk to crewmember health.*
- *Early diagnosis of abnormality will help identify crewmembers at risk for DVT formation and may allow the provisioning of early treatment before DVT becomes symptomatic or results in a life- or mission- threatening complication such as pulmonary embolism.*

Description: Using an ultrasound device, duplex ultrasound of the bilateral extracranial internal jugular veins, with breathing and compression maneuvers, is performed with teleguidance and/or autonomously with just-in-time training. An onboard ultrasound device will be used for in-flight DVT and venous flow anomaly screening.
Example Schedule based on 180-day ISS mission*: L-12/3 m, L+30 days; L+60 days; R-42 days, R+0/45d, ACI.*
Table 7, Table 8

6.4 Exercise and Fitness

6.4.1 Functional Fitness Assessments

[6024] Requirement: Each crewmember **shall** complete a series of tests designed to establish functional fitness before and after flight.

Rationale: *Physical fitness is assessed to establish flight readiness and baseline individual norms. Assessments are done pre- and post-flight to guide individual physical training, to determine individual responses to training countermeasures, and to assess a crewmember's ability to perform strength and endurance tasks. Testing provides information regarding*

musculoskeletal and neuromotor deficits and helps identify crewmembers who may be at risk for injury, and to guide reconditioning.

Description: Functional fitness will be assessed by exercises that measure flexibility, strength, endurance, muscle power, sensorimotor integration/agility, and balance. These may include Sit & Reach, Push-Ups, Pull-Ups, Bench, Crunches, Leg-Press, Agility, Stand Test, Hand Grip, and isokinetic testing.
***Example Schedule based on ISS missions**: AME L-9/6 m; L-90/30 d, R+5/7 d, R+30 d.*
Table 7, Table 8

6.4.2 On-Orbit Strength and Conditioning Monitoring

[6025] Requirement: Each crewmember **shall** undergo strength and conditioning monitoring during flight.

***Rationale:** Based on the information derived from the assessments, recommendations will be provided regarding in-flight exercise and conditioning programs. Past programs have required real time audio/video instruction session for use of exercise hardware to prevent injury and optimize performance. Also, a private exercise conference (PEC) may be required to allow for direct, efficient, and comprehensive exchange of information between ground exercise specialists and crewmembers.*

Description: Individual exercise data and video are downlinked from activities on exercise countermeasure systems. This information is evaluated by ground exercise specialists and crewmembers are provided with individual recommendations regarding strength and conditioning exercises.
***Example Schedule based on 30-day ISS mission**: FD3 through the day prior to undock. Resistance: 3x/wk (60 min) Aerobic: 3x/wk (30 min).*
***Example Schedule based on 180-day ISS mission**: Strength and conditioning monitoring - Recurrent in-flight; L+14 days (NET 3rd session) and then at least every 30 days thereafter.*
Table 7, Table 8

6.4.4 Test for Aerobic Functional Capacity

[6028] Requirement: Each crewmember **shall** complete tests to assess aerobic functional capacity and exercise induced arrhythmias before flight, periodically in-flight, and post-flight. Prior to an EVA or at any point during the mission, this test may be requested by the Crew Surgeon.

***Rationale:** The Aerobic Functional Capacity test provides data for assessment of crewmember aerobic capacity. The interpretation of the test results is used to establish a baseline of crewmember cardiovascular health before flight, monitor it during the flight, and to assess post-flight recovery. A maximal load protocol is conducted pre-flight to define the crewmember's maximum heart rate, maximum workload, and maximum oxygen consumption (VO_2 max). If ventilatory threshold can be derived from the data, it will be provided. The assessment of aerobic capacity at specified intervals before, during, and after flight is used to*

develop individual exercise conditioning prescriptions and determine individual responses to exercise countermeasures. The assessments also provide data for analyzing the effectiveness of exercise countermeasures and rehabilitative programs.

Description: The peak aerobic functional capacity tests are performed to establish a max HR and VO_2 max. If ventilatory threshold can be derived from the data, it will be provided. All pre-, in-, and post-flight peak cycle test will be done in the upright position using the same incremental load protocol.
***Example Schedule based on ISS missions**: AME L-12 m, L-90/30 d, FD14, FD75, FD 165, FD 255, R-14 d, R+ 5 d, R+ 30 d, ACI.*
Table 7, Table 8

6.5 EVA

6.5.1 Pre- and Post-EVA Medical Examinations

[6029] Requirement: All EVAs **shall** be preceded and followed by an assessment of medical fitness by the Crew Surgeon.

***Rationale:** The primary focus of a pre-EVA medical evaluation is to identify and manage medical issues that would constrain an EVA or potentially harm a crewmember during EVA. For example, medical suitability for EVA can be impacted by Eustachian tube dysfunction, dehydration, and a variety of other considerations. A post-EVA medical evaluation is necessary to ensure continued crewmember health and identify potential EVA and suit related medical issues, including but not limited to decompression sickness (DCS) and musculoskeletal injuries.*

Description: The Pre- and Post-EVA Medical Exams are performed by the CS to assess readiness for the EVA and post-EVA health. For ISS operations - within 48 hours of suit donning and 24 hours of suit doffing the medical evaluation will consist of a review of systems (ROS) by the expedition Crew Surgeon, a brief skin and extremity examination by the crew medical officer (CMO) via private medical conference, and a urinalysis. On the day of EVA, vital signs (BP, body temp) are measured. The Crew Surgeon may direct a specific medical exam (such as additional skin, muscle-skeletal, GI, otoscopy, tympanometry, urinalysis, cardiovascular assessments) based on ROS findings. For example, for ISS EMU EVA: tympanometry shall be performed 72-96 hours prior to suit donning. Vitals may be collected prior to EVA at Crew Surgeon discretion. For Orlan EVA: Vitals shall be measured Pre and Post EVA and an ECG-DS is performed as part of the nominal suit check-out the day of the EVA.
***Example Schedule based on ISS missions:** Pre- and Post-EVA.*
Table 7, Table 8

6.5.2 Monitoring during EVA

[6030] Requirement: Crewmembers **shall** undergo EVA monitoring as per the requirements in NASA-STD-3001, Volume 2.

Rationale: *To monitor crew health during the EVA, identify any possible crew health concerns, and provide immediate feedback to the EVA Flight Director.*

Description: Past missions have included the following: ECG and derived heart rate, suit pressure, suit CO_2 partial pressure, O_2 tank pressure and derived metabolic rate, personal radiation dosimetry, and when possible, real-time personal dosimetry.
Example Schedule based on ISS missions*: During EVA.*
Table 7, Table 8

6.6 Psychiatric/Psychological Evaluation

6.6.1 Pre-flight Psychiatric/Psychological Status Check

[6032] Requirement: Crewmembers **shall** be evaluated by designated experts to confirm psychiatric/psychological readiness for flight.

Rationale: *Confirmation of behavioral readiness for flight by designated expert including psychiatric, psychological, and behavioral assessment allow assessment of crew and their support systems needs to ensure mission safety and success.*

Description: For example, ISS operations include: a. Psychiatric/Psychological Assessment of behavioral readiness for flight on ISS includes specialist review of individual and crew psychological support. b. Check of life events that would have an impact on the astronaut's fitness for launch. c. Baseline assessments needed for in-flight monitoring to be completed between L-12 months and launch: Neurocognitive baseline and Behavioral health baseline.
Example Schedule based on 30-day ISS mission*: L-180d, L-90 d.*
Example Schedule based on 180-day ISS mission*: L-12 m, L- 240/180 d, L- 90/30 d.*
Table 7, Table 8

6.6.2 Private Psychological Conference

[6033] Requirement: Crewmembers **shall** participate in a private psychological conference, performed by a specialist, according to the specifications and schedule described below.

Rationale: *These conferences will address behavioral health, mood, and performance issues, such as personal and group dynamics issues, and ground-crew interactions. Elements of the behavioral health countermeasures will be coordinated in part through these conferences. In support of the CS, the private psychological conferences will provide one of the key elements of in-flight monitoring and countermeasures to maintain crewmember behavioral health and performance.*

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the key elements of in-flight monitoring and countermeasures to maintain crewmember behavioral health and performance.
***Example Schedule based on 30-day ISS mission**: In-flight **every** 14 days or Mid Mission.*
***Example Schedule based on 180-day ISS mission**: In-flight every 14 days, and ACI.*
Table 7, Table 8

6.6.3 Post-flight Psychiatric/Psychological Status Check

[6034] Requirement: Crewmembers **shall** undergo a psychiatric/psychological clinical interview post-flight by a specialist to assess behavioral health and performance mission support and behavioral re-adaptation.

Rationale: *Expert assessment of behavioral status post-flight enables re-adaptation and enables assessment of in-flight behavior support.*

Description: Crewmembers undergo a Psychiatric/Psychological clinical interview post-flight by a specialist to assess behavioral health and performance mission support and enable behavioral re-adaptation. The following schedule was implemented for a post-180-day ISS mission: (a) Initial clinical interview by a specialist regarding behavioral re-adaptation, [30 min each crewmember at R+3] (b) Initial review of behavioral health and performance mission support, [30 min each crewmember at R+3] (c) Review of behavioral health and performance mission support, [60 min each crewmember at R+10] (d) Clinical Interview by specialist regarding behavioral re-adaptation, [60 min each crewmember at R+14] (e) Supplemental assessment ACI (f) Psychiatric/Psychological assessment regarding behavioral re-adaptation, [60 min each crewmember at R+30]
***Example Schedule based on ISS 30-day mission**: R+7.*
***Example Schedule based on ISS 180-day mission**: R+ 3 d, R+ 10 d, R+ 14 d, R+ 30/60 d, or ACI.*
Table 7, Table 8

6.6.4 Cognitive Assessment

[6035] Requirement: Crewmembers **shall** undergo a cognitive assessment before, during, and after flight.

Rationale: *The main purpose of a cognitive assessment is to evaluate the impact of specific events including, but not limited to, head injury, (DCS) with Central Nervous System (CNS) involvement, atmosphere contamination, high CO_2 levels, a change in normal behavior and any other indication of a reduced performance state. In order to maintain test proficiency and to obtain an in-flight baseline, regular in-flight assessments are required.*

Description: Performance functions to be assessed include, but are not limited to memory, attention, reasoning, and spatial processing. Assessments will consist of cognitive tests that require 30 minutes to complete (not including pre- and post-test activities).
***Example Schedule based on 30-day ISS mission**: AME L-12/6m Training (3 sessions) Baseline (3 sessions).*
***Example Schedule based on 180-day ISS mission**: L- 390 d, L- 330 d, L- 270 d, L- 210 d, L-150 d, L- 90 d, In-flight: 1/month and as indicated, Post-flight: R+ 30 d, and ACI.*
Table 7, Table 8

6.6.5 Behavioral Observation of Training

[6036] Requirement: Training events of crewmembers (preferably of whole assigned crews) **shall** be observed by behavioral specialists.

***Rationale:** Behavioral observation provides important data about individual behavior and crew interactions. These data are necessary for: (1) providing consultation and recommendations to crewmembers pre-flight in order to optimize behavior and team performance and (2) providing baseline data for support and consultation of crewmembers in-flight.*

Description: The preferred training events include, but are not limited to, field training, simulations and any other training events that provide opportunities to collect the data described in the rationale. Observations may also include self-report data and peer feedback. All data related to crew observation will be treated as psychologically confidential.
***Example Schedule based on 30-day ISS mission**: Observe 1 session between assignment and flight.*
***Example Schedule based on 180-day ISS mission**: At least two training events will be observed between time of crew assignment and launch.*
Table 7, Table 8

6.7 Nutrition

6.7.1 Vitamin D Testing and Treatment Protocol

[6037] Requirement: Crewmembers **shall** be evaluated and treated prior to a long-duration mission. The timing of the testing will be at the discretion of the Crew Surgeon. The optimal/desired range for 25-OH Vitamin D is 35-90 ng/ml. The recommended maintenance dose of Vitamin D3 is 1,000 I.U. daily or 5000 I.U. once a week.

If 25-OH Vitamin D results are:	Vitamin D3 Treatment
35 ng/ml or higher	• Prescribe 1000 I.U. daily or 5,000 I.U. weekly (Maintenance dose)
20 o 34 ng/ml	• Prescribe 50,000 I.U. once a week or 5000 I.U. once a day for 4 weeks, and then revert to maintenance dosing (1,000 I.U. daily or 5000 I.U. once a week).

	• May recheck 25-OH Vitamin D levels in 3 months.
Less than 20 ng/ml	• Prescribe 50,000 I.U. once a week or 5000 I.U. a day for 6 to 9 weeks, and then revert to maintenance dosing (1,000 I.U. daily or 5000 I.U. once a week). • Recheck 25-OH Vitamin D levels in 3 months. • Note: Rule out other causes such as celiac sprue or other malabsorption maladies.

Rationale: *Due to the lack of exposure to the sun in space vehicles, Vitamin D is supplemented to aid in bone and immune function.*

Description: Due to the lack of exposure to the sun in space vehicles, Vitamin D is supplemented to aid in bone and immune function. Crew will be evaluated before long-duration missions and treated with Vitamin D as clinically indicated per the chart above.
Example Schedule based on ISS 180-day missions: *ACI daily or once/week.*
Table 7, Table 8

6.7.2 Nutritional Status Assessments

[6038] Requirement: Crewmembers **shall** undergo nutritional assessment testing according to the specifications and schedule described below.

Rationale: *On-orbit dietary assessments may help assure adequate nutrient intake during the mission. Assessment of nutritional patterns of crewmembers may help guide adjustments to nutrient and micronutrient dietary composition for future missions.*

Description: Nutritional assessment may include determination of typical dietary intake using a standard dietary assessment questionnaire administered via a manual or electronic system. Blood samples and 24-hour void-by-void (VxV) urine pools will be collected for determination of nutritional status including: body mass and composition, protein status, calcium/bone status, antioxidant status, water-soluble vitamin status, iron status, mineral status, general blood chemistry, fat-soluble vitamin status, and renal stone risk. Body composition assessment will include height and DXA. Data will be examined, and the necessity/details of a diet prescription will be assessed. In-flight, food intake is estimated using a data collection system. If a crewmember displays signs of unexpected changes such as loss of mass, changes in energy expenditure, and/or malaise, additional follow-up may be required.
Example Schedule based on ISS missions*: AME L- 21/18 m, L-90/30 d, In-flight Activities: Standard dietary assessment questionnaire – weekly, Body mass measurement– monthly or ACI, shared from [6015] R+0 d, R+20/30 d, DXA at R+5/7 d, shared from [6013].*
Table 7, Table 8

6.8 Fatigue Countermeasures

6.8.1 Sleep Assessment

[6039] Requirement: Each crewmember **shall** provide a daily assessment of sleep quality and quantity: for a 2-week pre-flight period, 1 week pre-launch, weekly in-flight via Private Medical Conference, and 1-week post-flight to supply daily sleep data to the crewmember and Crew Surgeon.

***Rationale**: Assessment of sleep quality and quantity will be utilized by the crewmember and Crew Surgeon to assess operational sleep duration requirements prior to critical events, to adjust crewmember countermeasures (timeline work rest scheduling, photic manipulation, medications).*

Description: Sleep can be assessed by several different methods, including a simple rating scale (suggested range: 1 – very poor quality to 7 – excellent quality sleep) and the number of hours slept completed on a daily basis on awakening, Actimetry sensor, or other technologies. Actimetry sensor is an accelerometer-based device that measures motion and translates that into a graphic analysis of sleep patterns. Actimetry data, if available, can be downloaded remotely. Just-in-time downloading capability is required for the Crew Surgeon based on operational need.
***Example Schedule based on 30-day ISS mission**: L-12/6m, L-14d, in-flight continuously throughout mission, R+7.*
***Example Schedule based on 180-day ISS mission**: AME L- 21/18 m, 2-week baseline period, L-7 days continuously until R+7 days. Analog data will be discussed at the weekly PMC with the Crew Surgeon. Other data, if available, will be downloaded periodically on a just-in-time basis for operational crewmember and Crew Surgeon use.*
Table 7, Table 8

6.8.2 Sleep Medication Ground Testing

[6040] Requirement: Each crewmember **shall** undergo a baseline assessment of program approved sleep medications prior to in-flight use.

***Rationale**: Crewmembers may utilize sleep medications in-flight as a fatigue countermeasure. To assess the potential for delayed performance decrements, each crewmember undergoes a baseline assessment to rule out significant performance side effects of such medication use on emergent awakening.*

Description: Sleep medications designated for use by a specific crewmember is tested by the crewmember prior to flight to assess efficacy and adverse effects. This baseline assessment should be monitored by the crewmember's Flight Surgeon (or Flight Surgeon designate – e.g., Fatigue Management Team member) regarding the efficacy of the medication and any significant side effects.
***Example Schedule based on ISS missions**: Any time before L-30 d.*
Table 7, Table 8

6.8.2 Space Motion Sickness Medication Ground Testing

[6042] Requirement: Each crewmember **shall** undergo a baseline assessment of program approved space motion sickness medications prior to in-flight use.

Rationale*: Crewmembers may utilize motion sickness medications in-flight as a motion sickness countermeasure. To assess the potential for performance decrements, each crewmember undergoes a baseline assessment to rule out significant performance side effects of such medication use.*

Description: Space motion sickness medications designated for use by a specific crewmember is tested by the crewmember prior to flight to assess efficacy and adverse effects. This baseline assessment should be monitored by the crewmember's Flight Surgeon (or Flight Surgeon designate) regarding the efficacy of the medication and any significant side effects.
Example Schedule based on ISS missions*: Any time before L-30 d.*
Table 7, Table 8

7. MEDICAL EVALUATIONS FOR PRIVATE ASTRONAUTS

7.1 Medical Evaluation – General Considerations

Private astronauts are crewmembers that interface with NASA Astronauts or vehicles who are not a U. S. Government Astronaut, or an IP Astronaut. They undergo a comprehensive medical evaluation as part of their mission selection. Private astronauts' medical evaluations are determined by duties and mission duration as per the table below. Critical duties are considered but not limited to piloting the vehicle, performing robotic operations, performing an EVA or any other task that is critical to the mission safety and success. The term spaceflight participant has been used in the past for this category of crew.

The medical evaluation process includes an extensive medical history and physical examination by aeromedical physicians and clinical specialists, laboratory screening tests, special diagnostic tests, and psychiatric evaluation. This document defines the medical screening procedures and standards for medical certification.

In compliance with NPD 1382.17, NASA Privacy Policy, and the Privacy Act of 1974, as amended, private astronauts are examined in accordance with approved medical procedures.

[7001] Private astronauts **shall** have the medical screening, including the procedures and consultations in Table 9, Medical Evaluation Procedures, completed and evaluated prior to flight.

Table 9 – NASA Medical Requirements for Private Astronauts

	Private Astronauts with critical duties and/or >30-day missions	**Private Astronauts without critical duties and ≤ 30-day missions**
Medical Requirements for Selection	Laboratory Tests Section 5.1.2, Table 5 Special Assessments Section 5.1.2, Table 6	Section 8.2, Table 10 Medical Evaluation Table 11 Laboratory Tests Table 12 Specialist Assessments
Disqualifying Criteria	Section 5.2 [5002], Appendix A	Section 5.2 [5002], Appendix A
AMB Chair	Shall make recommendation on medical risk assessment Section 4.2 [4003]	
CHMO	Shall make the final disposition on medical risk assessment Section 4.2 [4004]	
MSMB Chair	Determines medical risk for private astronauts on missions with international partners.	

8. MEDICAL EVALUATIONS FOR PRIVATE ASTRONAUTS WITH NO CRITICAL DUTIES AND MISSIONS 30 DAYS OR LESS

8.1 Purpose

This section provides the medical evaluations for testing of private astronauts that do NOT perform safety critical tasks (e.g., piloting of a vehicle, EVAs, robotic operations etc.) and are in mission planned for 30 days or less. The testing is based on NASA experience and the risk of not completing these tests should be considered for each mission to ensure that safety, health, and mission success is not compromised.

8.2 Overview

Table 10 - Spaceflight Private Astronauts Overview

Spaceflight Private Astronauts Overview
1. Comprehensive medical questionnaire[1]
2. Full aeromedical physical examination (per FAA guidance or equivalent regulatory body)
3. Special assessments and imaging procedures (as described in Section 8.1 Table 12)
4. Laboratory testing (as described in Section 8.1 Table 11)

[1] - May be completed using the NASA Medical Survey or other similar questionnaire. The following areas should be included: Past medical history and background information; psychosocial and psychiatric history including DWI and drug-related convictions; personal habits/lifestyle issues; travel history (past year); medication review, including non-prescription and herbal medications, food supplements, vitamins, and minerals; systems review; physical activities and sports.

Table 11 - Laboratory Tests for Private Astronauts with NO Critical Duties and on Missions <30 Days

The following are required laboratory assessments for Private Astronauts with NO critical duties and on missions less than 30 days stratified by those assessments required prior to the first flight versus those required prior to subsequent flights. Validity periods for each test are with respect to the mission end date (e.g., valid within 1 year of mission end date). As clinically indicated tests are expected to address U.S-based national screening standards and guidelines, as applicable, and any applicable evaluation for off nominal findings identified during the evaluation process.

Hematology/Thrombophilia Screen	First Flight	Subsequent Flights
Complete Blood Count – To include hemoglobin, hematocrit, red blood cell count, red blood cell indices, white blood cell count, differential count, platelet count	1 year	1 year
Screening tests for thrombophilia: Prothrombin time (PT), Activated Partial Thromboplastin time (aPPT)	1 year	On record
Biochemistry	**First Flight**	**Subsequent Flights**
Liver function – Aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), bilirubin, alkaline phosphatase (ALP)	1 year	1 year
Renal function – Urea, creatinine, electrolytes (Na [sodium], Cl [chloride], K [potassium]), uric acid	1 year	1 year
Endocrine – TSH	1 year	1 year
Prostate specific antigen (PSA) (males over age 40)	1 year	1 year
HbA1C, fasting blood glucose	1 year	1 year
Cardiovascular profile – Fasting total cholesterol, high-density lipoproteins (HDL), low-density lipoprotein (LDL), triglycerides, high-sensitivity C-reactive protein (hs-CRP)	1 year	1 year
Calcium, magnesium, inorganic phosphate	1 year	1 year
Ionized calcium	1 year	On record

Table 11 - Laboratory Tests for Private Astronauts with NO critical duties and on missions < 30 days (continued)

Infectious Disease Screen	First Flight	Subsequent Flights
Hepatitis A	1 year	1 year
Hepatitis B (Hepatitis B surface antigen, Hepatitis B core antibody, Hepatitis B surface antibody)	1 year	1 year
Hepatitis C	1 year	On record
Serologic screen for syphilis (VDRL or RPR or equivalent)	1 year	On record
HIV	1 year	On record
Tuberculosis (TB) screening utilizing a tuberculin skin test (TST) or interferon gamma releasing assay (IGRA) (either QFT-G or T- SPOT). Refer to Appendix B for detailed Tuberculosis screening and management guidance	1 year	1 year
Vaccine immune status	1 year	1 year
MRSA Swab	3/1 month	3/1 month
Group A beta hemolytic strep	3/1 month	3/1 month
Helicobacter pylori breath test	1 year	On record
Urinalysis	**First Flight**	**Subsequent Flights**
Routine (specific gravity, glucose, protein, pH, ketones, blood), microscopic reflex	1 year	1 year
Human chorionic gonadotropin (hCG) (females) (urine)	1 year	1 year
Drug screen for drugs of abuse	1 year	1 year

Table 12 - Specialist Assessments for Private Astronauts with NO Critical Duties and on Missions < 30 Days

The following are required specialist assessments for Private Astronauts with NO critical duties and on missions less than 30 days stratified by those assessments required prior to the first flight versus those required prior to subsequent flights. Validity periods for each test are with respect to the mission end date (e.g., valid within 1 year of mission end date). As clinically indicated tests are expected to address U.S.-based screening standards as applicable and any applicable evaluation for off nominal findings identified during the evaluation process.

Ophthalmology Specialist Assessment (Optometrist)	First Flight	Subsequent Flights
Uncorrected and corrected near and distance visual acuity (Snellen or Landolt-C)	1 year	1 year
Color vision (computer-based test, Ishihara, or equivalent pseudo-isochromatic plates [PIPs] to include red-green and blue-yellow)	1 year	1 year
Cyclopegic refraction	1 year	1 year
Tonometry	1 year	1 year
Perimetry	1 year	1 year
Fundoscopic exam	1 year	1 year
Otolaryngology/ENT	**First Flight**	**Subsequent Flights**
Audiometry (pure tone audiogram and speech audiogram, if indicated)	1 year	1 year
Tympanogram	1 year	1 year
Dental	**First Flight**	**Subsequent Flights**
Special Assessment by Dentist	1 year	1 year
Full orthopantomogram or full mouth X-ray series)	1 year	On record

Table 12 - Specialist Assessments for Private Astronauts with NO critical duties and on missions < 30 days (continued)

Cardiopulmonary	First Flight	Subsequent Flights
Resting 12-lead electrocardiogram (ECG)	1 year	1 year
Aerobic Capacity – fDirect or indirect measurement of cardiorespiratory fitness (CRF) in ml/kg/min or METS) on maximum exercise stress test	1 year	1 year
24-Hour ECG monitoring	5 year	5 year
Coronary calcium scoring (males > 40 yrs old; females >50 yrs old)	5 year	5 year
Transthoracic echocardiogram (TTE)	On record	On record
Atherosclerotic Cardiovascular Disease Risk Calculation	1 year	1 year
GI Evaluation	**First Flight**	**Subsequent Flights**
Colonoscopy	ACI	ACI
Neurology	**First Flight**	**Subsequent Flights**
MRI of brain, MRI angiogram	On record	On record
Carotid Ultrasound Study (to include intima-medial thickness and/or carotid plaque area)	ACI	ACI
Behavioral Health Evaluation	**First Flight**	**Subsequent Flights**
Psychiatric and psychological evaluation Based on the most recent edition of the Diagnostic and Statistical Manual of Mental Disorders, the American Psychiatric Association)	1 year	1 year
Psychological Suitability and Psychodiagnostic Assessment	1 year	1 year
Radiological/Ultrasound Procedures	**First Flight**	**Subsequent Flights**
Chest X-ray (CXR) (PA and lateral)	5 year	5 year
Thyroid ultrasound	ACI	ACI
Abdominal and pelvic ultrasound	5 year	5 year
Mammogram	1 year	1 year
Bone mineral density - dual energy x-ray absorptiometry (DXA) scan	ACI	ACI

9. MEDICAL EVALUATIONS FOR NASA SUBORBITAL RESEARCH SPECIALISTS

9.1 Medical Evaluation – General Considerations

This section provides medical testing requirements for NASA Suborbital Research Specialists (NSRS). NSRS are defined as an individual who is employed by NASA or contracted by NASA to conduct research, technology testing, training, or other activities onboard a sub-orbital vehicle. This excludes those individuals who are commercially employed crewmembers of the suborbital vehicle.

9.2 Medical Evaluation Procedures for NASA Suborbital Research Specialists

[8001] NSRS **shall** have the medical screening, including the procedures as listed below, completed, and forwarded to the AMB prior to flight.

- FAA Class III Exam or equivalent
- plus: EKG, Standard Blood (CBC, BMP) & Urine Analysis,
- Valid for 1 year

APPENDIX A. DISQUALIFYING MEDICAL STANDARDS

A. GENERAL
1. Any medical condition that, in the judgment of the AMB, may compromise mission operations, performance of duties, or crew health or safety.
2. All injuries, contusions, fractures, or surgery unless healed and not associated with functional deficit that could interfere with the performance of duties.
3. History of heat stroke, temperature intolerance, or environmental injuries associated with significant sequelae that could interfere with performance of duties.
4. History of sensitivity or demonstrated allergy of sufficient severity so as to interfere with the performance of duties.
5. Habitual use of tobacco products.
6. Chronic use of any medication requires AMB review.
7. All malignancies or history of malignancies, except those permitted within the medical standards.
8. Any foreign body or implant, unless considered not to be a hazard during the performance of duties.
9. Any condition or situation that precludes completion of the NASA medical evaluation process.
10. Sarcoidosis, all forms.
11. Decompression Illness (DCI): A. Type II decompression sickness (DCS) or Arterial Gas Embolism (AGE) (involving the CNS, spinal cord, pulmonary DCS, or cardiovascular collapse) unless all signs and symptoms resolve with treatment. Such cases require specialist evaluation. B. Type I DCS involving joint pain, the peripheral nervous system, or skin is not disqualifying if adequately treated and completely resolved.
12. Presence or history of systemic exertion intolerance disease or myalgic encephalomyelitis (previously known as chronic fatigue syndrome) and fibromyalgia.
13. Autoimmune disorders, including conditions such as systemic lupus erythematosus and dermatomyositis.
14. Any standard invalidated by new medical information may be appended by the AMB with CHMO approval.

B. HEAD, FACE, AND NECK
1. Deformities (e.g., scars, depressions, or exostoses) or chronic muscular contractions or spasms (e.g., torticollis) of the skull/head, face, and neck that interfere with wearing equipment/headgear and/or performance of duties.
2. Loss or congenital absence of bony substance of the skull.
3. Maxillofacial skeletal deformities (e.g., benign tumors, large birthmarks, large hairy moles, extensive scars, or mutilations due to injuries or surgery, ulcerations, fistulae, and atrophy or paralysis of part of the face or head) that interfere with the performance of duties or wearing of equipment.
4. Temporomandibular disorders (e.g., chronic temporomandibular joint (TMJ) arthritis, complete or partial ankylosis, recurrent dislocation, or chronic myofascial pain).
5. Congenital branchial cleft or thyroglossal duct cysts, unless greater than 1-year post-surgical resection and without evidence of residual cysts or tracts.
6. Chronic draining fistulae, regardless of cause.
7. Cervical ribs with signs or symptoms of thoracic outlet compression.
C. NOSE, SINUSES, MOUTH, AND THROAT
1. Deformities, injuries, or destructive diseases of the mouth, nose, throat, pharynx, or larynx that interfere with breathing, speech, mastication, and/or the swallowing of ordinary food, unless surgically corrected with normal function restored.
2. Deviation of the nasal septum, enlarged turbinates, or other obstructions to ventilation that significantly restrict nasal breathing, unless medically or surgically corrected with normal function restored.
3. Chronic rhinitis of any cause that may interfere with the performance of duties.
4. Perforation of the nasal septum if accompanied by recurrent epistaxis, an intrusive whistling sound, or if a sign of organic disease.
5. Sino-nasal polyps or a history of sino-nasal polyps, unless at least 1 year after surgical removal and without evidence of recurrence.
6. Anosmia.
7. Chronic sinusitis (persistent sinus infection for more than 3 months), unless treated without evidence of recurrence for at least 3 years.
8. Cleft lip and/or palate unless satisfactorily repaired.
9. Loss or mutilation of a lip in whole or part, unless satisfactorily repaired and does not interfere with the performance of duties or wearing of equipment.
10. Partial loss, atrophy, hypertrophy, benign tumors, or other malformations of the tongue if these conditions interfere with mastication, speech, swallowing, or appear to be progressive.

11. Presence or history of marked stomatitis, leukoplakia, or severe recurrent ulcerations of the mouth that may interfere with the performance of duties.
12. Ranulae, which might interfere with the performance of duties.
13. Salivary fistula, unless surgically corrected.
14. Presence of enlarged tonsils, adenoids, or redundant soft tissue of the oral pharynx that interfere with speech, swallowing, breathing, or are associated with recurrent otitis media.
15. Recurrent calculi of any salivary gland or duct, unless surgically corrected.
16. Obstructive sleep apnea.
17. Any disorder or defect that affects the clarity of speech to the extent that it impairs the performance of duties (e.g., chronic, or recurrent laryngitis, vocal cord paralysis).
18. Tracheostomy or tracheal fistula, unless surgically repaired.
19. Recurrent epistaxis, unless from a benign lesion that has been corrected.
20. Any chronic disorder or defect that interferes with normal ventilation of paranasal sinuses or middle ear.
21. Zenker's diverticulum, unless surgically corrected.
D. EARS
1. Any diseases of the ear or mastoid with residual auditory or vestibular dysfunction sufficient to interfere with performance of duties.
2. Congenital deformation of the external meatus or canal that interferes with hearing or performance of duties.
3. Tumors of the external auditory canal, unless benign or surgically removed. Small exostoses are not disqualifying.
4. Chronic external otitis.
5. Chronic otitis media, suppurative or serous.
6. Persistent perforation of the tympanic membrane.
7. History of stapedectomy.
8. Chronic mastoiditis, mastoid fistula, or mastoidectomy, unless complete recovery from simple mastoidectomy.
9. History or presence of abnormal labyrinthine function (e.g., vestibular neuronitis), unless an isolated, remote episode with full recovery.
10. History or presence of Meniere's disease.
11. Chronic inability to equalize the pressure of the middle ear (Valsalva's maneuver).
12. Tinnitus that interferes with the performance of duties.

13. Hearing Standards:
    A. History of acute or sudden sensorineural hearing loss, unless due to trauma with complete recovery.
    B. Inability to meet the pure tone audiometry hearing thresholds in Table 11, Pure Tone Audiometry Hearing Thresholds.

Table 11 - Pure Tone Audiometry Hearing Thresholds

	Frequency Hz	500	1000	2000	3000	4000
Astronaut candidate selection	Both Ears	30	25	25	35	50
Annual examination or mission selection	Better Ear	30	25	25	35	50
	Poorer Ear	35	50	50	75	75

C. Inability to meet above hearing standards in pure tone audiometry on the annual examination requires a word recognition score of 92% or better in the better ear and 88% or better in the poorer ear.

E. EYES

1. Disease, defect, or deformity of either eye or supporting structure that may interfere with the performance of duties.

2. Lids and Ocular Adnexae:
    A. Any condition of the eyelids that impairs normal eyelid function.
    B. Chronic blepharitis
    C. Blepharospasm.
    D. Ptosis, unless a benign etiology that is not progressive and does not interfere with vision in any field of gaze or direction.
    E. Growths on the eyelid unless small, asymptomatic, non-progressive, and benign.
    F. Dacryocystitis or history of dacryocystitis.

3. Conjunctivae:
    A. Chronic or recurrent conjunctivitis requires specialist evaluation.
    B. History of trachoma requires specialist evaluation.
    C. Dry eye syndromes requiring treatment, including xerophthalmia, requires specialist evaluation.
    D. Pterygium that encroaches on the cornea more than 2 millimeters or recurs after two operative procedures (evaluation will be performed no earlier than 6 months post-operatively).

4. Cornea:
    A. Chronic or recurrent keratitis requires specialist evaluation.
    B. History of corneal ulcer or erosion requires specialist evaluation.
    C. Herpetic ulcer or history of herpetic ulcer.
    D. Vascularization, haze, or opacification of the cornea from any cause when it is progressive or interferes with vision.

E. Corneal dystrophy of any type, including keratoconus of any degree. *Form fruste keratoconus requires specialist evaluation.*
F. History of orthokeratology treatments within the previous 6 months.
G. History of penetrating or lamellar keratoplasty.
H. Refractive surgical procedures other than Photorefractive Keratectomy (PRK, LASEK, epi-LASIK; or other excimer laser surface procedures), or laser-assisted in-situ. keratomileusis (LASIK, Wavefront guided procedures with a femtosecond laser are preferred. The following criteria apply:
   i. All standard accepted clinical eligibility criteria for the procedure are met (e.g., corneal thickness).
   ii. Pre-operative cycloplegic refractive error is between +4.00 to -8.00 sphere, and astigmatism is 3.00 or less in minus cylinder format.
   iii. At least 6 months since last refractive/augmenting procedure, with no ongoing active ophthalmologic treatment or need for ophthalmic medications.
   iv. Post-operative refraction stable as demonstrated by two separate refractions ≥ 1 month apart differing by ≤ +/-0.50 diameter (D) (sphere) and ≤ +/-0.25 D (cylinder).
   v. Post-operative manifest refractive errors within applicant standards.
   vi. No demonstrated adverse sequelae, including contrast sensitivity, glare, or night vision problems. All other vision standards are met.

5. Uveal Tract:
   A. Acute, chronic, or recurrent inflammation of the uveal tract (iris, ciliary body, choroid).
   B. History of uncomplicated post-traumatic iritis requires specialist evaluation.

6. Retina and Vitreous:
   A. History or evidence of retinal detachment, unless traumatic with no sequelae, retinal tears, or edema.
   B. Retinal hole with presence of fluid or vitreous traction. Other retinal holes require specialist evaluation.
   C. Degeneration or dystrophies of the central or peripheral retina, including lattice degeneration, require specialist evaluation.
   D. Pigmentary degenerations require specialist evaluation.
   E. Retinitis, chorioretinitis, or other inflammatory conditions of the retina, unless single episode that has healed and does not impair central or peripheral vision.
   F. Hemorrhages, exudates, or other retinal vascular conditions that potentially impair vision require specialist evaluation.
   G. Vitreous opacities or conditions that may cause loss of central acuity or peripheral visual field require specialist evaluation.
   H. Previous retinal treatment of any type requires specialist evaluation.

7. Optic Nerve:
   A. Any history of optic nerve disease, including but not limited to, optic nerve inflammation, optic nerve swelling, or optic nerve atrophy.
   B. Any optic nerve anomaly requires specialist evaluation.

8. Lens:
   A. Aphakia.
   B. Lens opacities that interfere with vision or are considered progressive require specialist evaluation.

C. Lens dislocation, partial or complete.
D. Intraocular implants or intraocular contact lenses.

9. Malignancy, and Other Defects and Disorders:
   A. History or presence of malignant tumors of the eye or orbit.
   B. Resected basal cell cancers or benign tumors require specialist evaluation.
   C. Exophthalmos, anophthalmos, or microphthalmos.
   D. Pathologic nystagmus.
   E. Abnormal pupil(s) or loss of normal pupillary reflexes requires specialist evaluation.
   F. Coloboma.

10. Refractive standards—inability to meet the following refractive requirements:
   A. Distance or near visual acuity not correctable to 20/20 in each eye.
   B. Refractive error (distant vision):
      i. Cycloplegic refractive error of more than +5.50 or -5.50 diopters in any meridian.
      ii. Astigmatism requiring more than 3.00 diopters of cylinder correction.
      iii. Anisometropia of more than 3.50 diopters.

11. Visual Fields: Any visual field defect, whether active, inactive, or migrainous requires specialist evaluation.

12. Extraocular muscle balance:
   A. Esophoria greater than 10 prism diopters measured at 6 meters or 20 feet.
   B. Exophoria greater than 10 prism diopters measured at 6 meters or 20 feet.
   C. Hyperphoria greater than 2 prism diopters measured at 6 meters or 20 feet.
   D. Any heterotropia measured at any distance.
   E. Point of convergence (PC) greater than 100 millimeters.
   F. Paralysis of ocular motion in any of gaze.
   G. Diplopia, suppression, or a history of diplopia or suppression.

13. Depth Perception: Lack of adequate depth perception on objective testing, with a minimum of 40 arcseconds.

14. Abnormal night vision, including retinitis pigmentosa, requires specialist evaluation.

15. Color Vision Deficiency: Greater than mild deficiency on red-green or blue-yellow color vision testing.

16. Intraocular Pressure:
   A. History of glaucoma, ocular hypertension, pre-glaucoma, or glaucoma suspect.
   B. Pigmentary Dispersion Syndrome requires specialist evaluation.

17. Medically required use of a contact lens.

F. LUNGS AND CHEST WALL
1. Any condition of the lungs, pleura, mediastinum, and chest wall that could interfere with performance of duties.
2. Pneumothorax or pneumomediastinum: A. History of spontaneous pneumothorax or pneumomediastinum unless surgically corrected with apical pleurodesis or pleurectomy and free of complications, with full expansion of lungs on chest X-ray (CXR), normal pulmonary function tests (PFTs), and thin-cut CT showing no pathology predisposing to recurrence. This requires specialist evaluation. B. Presence or history of traumatic pneumothorax, unless total resolution and free of complications, with full expansion of lungs on CXR, normal PFTs, and thin-cut CT showing no pathology predisposing to recurrence. This requires specialist evaluation.
3. Chronic pulmonary processes: A. Chronic obstructive pulmonary disease (chronic bronchitis or emphysema) with evidence of pulmonary dysfunction and causing impairment or increased risk for pulmonary barotrauma. B. Chronic pulmonary processes such as interstitial pneumonias, pulmonary injury, neuropulmonary disorders, hypersensitivity, and pneumoconiosis are disqualifying. C. Abnormal pulmonary function tests require specialist evaluation.
4. Bronchiectasis. History of childhood bronchiectasis requires specialist evaluation.
5. Asthma: A. Current asthma of any degree. B. History of asthma will require provoked bronchoconstriction testing and specialist evaluation.
6. Pulmonary blebs, bullae, or cysts.
7. History of lung abscess requires specialist evaluation.
8. Granulomatous inflammation: A. Non-infectious granulomatous inflammation (such as sarcoidosis, Wegener's, allergic, or bronchocentric). B. History of infectious causes, including mycotic infection (such as coccidioidomycosis, histoplasmosis) or protozoal infection (such as dirofilariasis, pneumocystis) requires specialist evaluation.
9. History of intrathoracic surgery requires specialist evaluation: A. History of lobectomy or multiple segmental resections with normal pulmonary function requires specialist evaluation. B. Removal of more than one lobe is cause for rejection.

10. Any malignant tumor of the trachea, bronchi, lungs, pleura, or mediastinum: History of a benign tumor requires specialist evaluation.
11. History of suppurative periostitis, osteomyelitis, or necrosis of the ribs, sternum, clavicle, scapulae, or vertebrae with complete resolution and normal lung function requires specialist evaluation.
12. Chronic or recurrent mastitis.
13. Benign tumor or surgery of the breast or chest wall that interferes with the performance of duties.
14. History of unprovoked or recurrent pulmonary embolus. History of single provoked pulmonary embolus requires specialist evaluation.
15. History of empyema or sinus tracts of the chest wall require specialist evaluation.
16. History of surgically corrected tracheoesophageal fistula requires specialist evaluation.
17. History of pleural effusion of unknown etiology.
18. History of hemoptysis requires specialist evaluation.
19. History of breast cancer.
G. CARDIOVASCULAR
1. Any condition of the cardiovascular system that interferes with the performance of duties.
2. Cardiomyopathy such as hypertrophic or right ventricular cardiomyopathy (other than physiologic heart changes). History of acquired cardiomyopathy if recovered and left ventricular ejection fraction is <50% requires specialist evaluation.
3. Hypertension, as defined by sustained systolic blood pressure of 140 mmHg or greater or diastolic of 90 mmHg or greater.
4. Recurrent syncope or symptomatic orthostatic intolerance (e.g., medication-induced, autonomic dysfunction, or other causes not otherwise specified), excepting post-spaceflight orthostasis. Recurrent neurally mediated syncope with clear precipitating factors requires specialist evaluation.

5. History of pericarditis, myocarditis, and endocarditis without residual dysfunction requires specialist evaluation.

6. Congenital abnormalities:
   A. History or findings of major congenital abnormalities of the heart and vessels.
   B. History of atrial septal defect (ASD), ventricular septal defect (VSD), or patent ductus arteriosus (PDA), that has been surgically repaired requires specialist evaluation.
   C. A patent foramen ovale (PFO) requires specialist evaluation.

7. Clinical evidence (angiographic, imaging, symptoms, history of prior event) of coronary artery disease.

8. Electrocardiographic abnormalities: Any cardiac dysrhythmia, conduction defect, or other ECG abnormalities on resting ECG, ambulatory ECG monitor, or any monitoring ECG rhythm strips require specialist evaluation.
   A. Supraventricular arrhythmias:
      i. Require AMB review and may be disqualifying:
         (1) Supraventricular tachycardia (SVT) assessed at least 6 months after ablation.
         (2) Atrial fibrillation/flutter assessed at least 6 months after ablation.
         (3) Presence or history of SVT or atrial fibrillation/flutter > 5 seconds.
         (4) Atrial ectopy (premature atrial complexes) > 1% and ≤ 20% of total beats on ambulatory ECG.
         (5) Presence of sustained (> 1 hour) sinus tachycardia at rest > 130 beats/min not related to physical activity during evaluation.
         (1) Disqualifying (other than those due to identifiable, reversible causes): Presence or history of SVT or atrial fibrillation/flutter that is recurrent after intervention.
         (2) Presence of SVT with hemodynamic compromise.
         (3) Presence or history of atrial ectopy (premature atrial complexes) > 20% of total beats on ambulatory ECG.
   B. Ventricular arrhythmias:
      i. Require AMB review and may be disqualifying:
         (1) Presence or history of ventricular tachycardia of 11 beats or greater without hemodynamic compromise.
         (2) Presence or history of frequent ventricular ectopy (frequent premature ventricular contractions [PVC]) > 1% and ≤ 20% of total beats on ambulatory ECG.
         (3) Right ventricular outflow tract tachycardia at least 6 months after ablation.
      ii. Disqualifying (other than those due to identifiable, reversible causes), presence or history of:
         (1) Ventricular tachycardia > 11 beats with ventricular dysfunction.
         (2) Ventricular tachycardia > 30 seconds.
         (3) Ventricular tachycardia with hemodynamic compromise.
         (4) Ventricular flutter/fibrillation or sudden cardiac arrest requiring resuscitation.
         (5) Frequent ventricular ectopy (frequent premature ventricular complexes) > 20% of total beats on ambulatory ECG.
   C. Conduction/repolarization defects:

i. Require AMB review and may be disqualifying:
   (1) First degree atrioventricular (AV) block > 300 msec.
   (2) Right bundle branch block with axis deviation or atrial enlargement.
   (3) Left bundle branch block.
   (4) Wolff Parkinson White (WPW) ECG pattern.
   (5) WPW syndrome after successful ablation.
   (6) Prolonged QT > 470 msec for men and > 480 msec for women in the absence of drugs known to prolong QT interval.
   (7) Brugada ECG pattern.
   (8) Prolonged sinus pause > 3 seconds or heart rate < 30 beats per minute not during sleep.

ii. Disqualifying:
   (1) WPW syndrome.
   (2) Third-degree AV block and Mobitz type 2 AV block.
   (3) Prolonged QT > 500 msec.

ii. Brugada syndrome.

9. Cardiac tumors. Benign cardiac tumors successfully resected and without residual cardiac disease require specialist evaluation.

10. All valvular disorders of the heart require specialist evaluation:

A. Require AMB review and may be disqualifying:
   i. Greater than mild mitral, tricuspid, or pulmonic regurgitation.
   ii. Aortic valve regurgitation greater than trace.
   iii. Mitral valve prolapse with greater than mild mitral regurgitation.
   iv. Bicuspid aortic valve.

B. Disqualifying:
   i. Any degree of valvular stenosis other than trivial.
   ii. History of valve replacement or repair.

11. Venous and lymphatic disorders such as chronic venous insufficiency, varicose veins, and lymphedema that impair performance of duties.

12. Abnormalities of the arteries, including aneurysms, atherosclerosis, and arteritis. Includes intermittent claudication or any condition associated with inadequate blood flow to any extremity. Arterial wall thickening (including carotids), focal plaque, or calcifications detected with imaging studies require specialist evaluation.

13. Primary Raynaud's disease or other symptomatic vasospastic disorders require specialist evaluation.

H. HEMATOLOGY

1. Red cell disorders:
   A. Anemias require specialist evaluation.
   B. Hemoglobin sickle cell (SS) and sickle-hemoglobin C (SC) disease.
   C. Hemoglobin S trait with a history of complications such as renal papillary necrosis, pulmonary sequestration, or splenic infarct condition.
   D. Hemoglobinopathies other than hemoglobin SS or SC disease, or S trait (example: thalassemias) require specialist evaluation for physiologic impairment (such as magnitude of anemia, level of anaerobic impairment, splenomegaly).
   E. Hemolytic anemia with laboratory evidence of hemolysis or physiologic impairment.
   F. Polycythemia requires specialist evaluation.
   G. Miscellaneous red cell disorders (example, hereditary spherocytosis) require specialist evaluation for physiologic impairment. Glucose-6-phosphate dehydrogenase deficiency is not disqualifying.

2. White cell disorders:
   A. Absolute leukopenia and absolute leukocytosis require specialist evaluation.
   B. History of leukemia.
   C. History of Hodgkin or non-Hodgkin lymphoma.
   D. History of lymphoproliferative disorders.
   E. Plasma cell dyscrasias, including monoclonal gammopathy of undetermined significance (MGUS), require specialist evaluation.
   F. Lymphadenopathy requires specialist evaluation.

3. Platelet disorders:
   A. Thrombocytopenia requires specialist evaluation.
   B. History of idiopathic thrombocytopenic purpura (ITP), unless isolated episode in childhood with complete recovery.
   C. History of thrombotic thrombocytopenic purpura (TTP) or hemolytic uremic syndrome (HUS).
   D. Thrombocytosis requires specialist evaluation.

4. History of chronic myeloproliferative diseases or myelodysplastic syndromes.

5. Hypercoagulable disorders:
   A. Vascular thrombosis or embolism requires specialist evaluation.
   B. Two or more episodes of deep venous thrombosis are disqualifying.

6. Disorders of hemostasis:
   A. Personal history of bleeding disorder requires specialist evaluation.
   B. Hemophilias.

7. Splenic disorders:
   A. Splenomegaly requires specialist evaluation.
   B. Hyposplenism or post-splenectomy state requires specialist evaluation.

8. Other hematologic or reticuloendothelial disorders that could interfere with the performance of duties.

I. ABDOMEN AND DIGESTIVE SYSTEMS
1. Chronic diseases or disorders of the gastrointestinal tract that interfere with the performance of duties.
2. Wounds, injuries, scars, or weaknesses of the muscles of the abdominal wall sufficient to interfere with function.
3. Abdominal wall hernias other than small asymptomatic umbilical hernias unless surgically corrected. A. Relaxed inguinal ring or a diastasis recti without herniation is not disqualifying. B. Any other herniations of clinical significance require specialist evaluation.
4. Sinus or fistula of the abdominal wall that is associated with underlying disease or is not surgically corrected.
5. Diseases of the esophagus such as strictures or Barrett's esophagus. A. Diverticula, rings, orwebs unless corrected. B. History of mild reflux esophagitis requires specialist evaluation.
6. Chronic abdominal pain is disqualifying unless asymptomatic for 5 years and after specialist evaluation.
7. History of gastric or duodenal ulcers. Medication or Helicobacter pylori-induced ulcers, until appropriately treated and must be endoscopically cleared as resolved.
8. Chronic dependence on acid-reduction medication.
9. History of gastrointestinal surgery for malignant or recurrent conditions.
10. Benign gastrointestinal neoplasm that is likely to enlarge or show malignant potential, unless removed.
11. History of intestinal obstruction due to any chronic or potentially recurrent disease. Surgery to relieve childhood pyloric stenosis, intussusception, volvulus, or Meckel's diverticulum is not disqualifying if there are no sequelae.
12. Adhesive disease. Asymptomatic adhesive disease requires specialist evaluation.
13. Inflammatory bowel disease such as Crohn's disease and ulcerative colitis.
14. Functional bowel disorder that interferes with the performance of duties.
15. Malabsorption syndromes: A. Celiac Disease. B. Food sensitivities/intolerances are not considered malabsorption syndromes but require specialist evaluation.
16. Chronic diarrhea.
17. Chronic constipation requiring chronic or continuous medication or therapy.
18. History of diverticulitis. Diverticulosis requires specialist evaluation.

19. Gastrostomy, ileostomy, or colostomy unless surgically corrected and resulting in no post-operative dysfunction.

20. History of gastrointestinal bleeding from any cause except for post-traumatic bleeding, medication-induced gastritis, or minor bleeding (such as hemorrhoids or resolved infectious colitis).

21. Acute or chronic diseases of the rectum or anus. External or internal hemorrhoids that cause marked symptoms that could interfere with the performance of duties.

22. Liver:
   A. History of non-viral or self-limited hepatitis (e.g., drug-induced) within the previous year requires specialist evaluation.
   B. Benign liver tumors such as hemangiomas that are under 2 cm and demonstrated to be stable with serial scanning for 2 years require specialist evaluation.
   C. Disorders of copper and iron metabolism
      a. History of Hereditary Hemochromatosis requires further evaluation.
   D. Fibropolycystic diseases of the liver
      a. Benign non-infectious hepatic cysts require specialist evaluation.
   E. Any chronic, recurrent, or progressive liver disease.
   F. See infectious disease conditions in this table (Section 7R INFECTIOUS DISEASE), for hepatitis B and hepatitis C.

23. Pancreas:
   A. History of acute pancreatitis is disqualifying, unless due to trauma, medication, or due to surgically corrected cholecystitis with no further episodes and requires specialist evaluation.
   B. Chronic, recurrent, or progressive pancreatic disorders (e.g., pseudocyst).

24. Biliary tract:
   A. Cholecystitis, cholelithiasis, or acalculous cholecystitis, until surgically corrected and resulting in no post-operative dysfunction.
   B. Any chronic, progressive biliary tract disorder.

J. ENDOCRINE

1. Any endocrine disease or disorder that may affect the performance of duties.

2. Presence or history of diseases of the hypothalamus or pituitary gland. History of prolactin secreting pituitary adenoma 5 years after surgical resection requires specialist evaluation.

3. Diseases of the thyroid gland:
   A. Presence or history of multi-nodular goiter, autoantibodies, benign cysts, or palpable nodules of the thyroid require specialist evaluation.
   B. History of toxic adenoma 1 year after surgical resection requires specialist evaluation.

4. Diseases of the parathyroid gland. Parathyroid adenoma after surgical resection requires specialist evaluation.

5. Diseases of the adrenal medulla or cortex. Adrenal androgen excess requires specialist evaluation.

6. Metabolic disorders:
   A. Diabetes mellitus, type 1 or 2.
   B. Presence or history of gout or pseudogout.
   C. Familial hyperlipidemias.
   D. Inborn errors of metabolic pathways (except for Gilbert's disease):
      i. Acquired errors of metabolic pathways with potential pathologic sequelae require specialist evaluation.
   E. Metabolic syndrome, in accordance with established guidelines.

7. Presence or history of malignant endocrine tumor.

8. Carcinoid syndrome: History of carcinoid tumors requires specialist evaluation.

9. Pancreatic endocrine tumors (e.g., islet cell tumor or gastrinoma).

K. GENITOURINARY

1. Any disorder of the genitourinary tract that may interfere with the performance of duties.

2. Anatomical abnormalities of one or both kidneys and lower urinary tract producing functional impact to the urogenital system:
   A. A duplicated collecting system is considered a variant of normal anatomy and is not disqualifying unless associated with other pathology (e.g., hydronephrosis, nephrolithiasis, or recurrent episodes of infection).
   B. Loss or absence of one or both kidneys.

3. Polycystic kidney disease.

4. Acute nephropathy or history of chronic nephropathy (e.g., hypertensive nephrosclerosis, diabetic nephropathy, and glomerulonephritis).

5. Autoimmune parenchymal disorders.

6. Vascular renal disorders.

7. History of tubular necrosis from any cause if associated with residual renal dysfunction that may interfere with the performance of duties.

8. Presence or history of urinary calculus (crystalline concretion within the urine-collecting system).

9. History of recurrent (≥ 3 per year) infections of the urinary tract require specialist evaluation.

10. Bladder, prostate, or urethral diseases that result in urinary retention, or interfere with micturition. History of the above requires specialist evaluation.

11. Hydrocele or varicocele that is symptomatic or interferes with the performance of duties.

12. Any disorders of the testes, genitalia, or associated anatomical structures that interfere with the performance of duties. Penile prosthetic implants.

12. History of primary or secondary neoplastic disorders of the urinary tract (kidneys, ureter, and bladder) and male genitals (testes, scrotal contents, prostate, and seminal vesicles).

L. MUSCULOSKELETAL DISORDERS
1. Any disorder of the bone, joint, muscle, or supporting structure that may interfere with the performance of duties.
2. Arthritic disorders: A. Chronic osteoarthritis with functional disability that may interfere with the performance of duties. B. Presence or history of inflammatory arthropathies requires specialist evaluation.
3. Infections: A. Active infections of bone, joint, muscle, tendon, or supporting structures. B. History of recurrent osteomyelitis.
4. History of non-traumatic avascular necrosis.
5. Presence or history of musculoskeletal malignancy.
6. Benign tumors or cysts of the bone require specialist evaluation.
7. Cartilaginous/Intra-articular disorders: A. Osteochondromatosis or multiple cartilaginous exostoses that interfere with performance of duties. B. History of osteochondromatosis or multiple cartilaginous exostoses that have been successfully surgically excised require specialist evaluation. C. Intra-articular loose bodies in any joint (osteocartilaginous or foreign objects) that interfere with performance of duties. D. History of intra-articular loose bodies in any joint surgically removed with no residual dysfunction requires specialist evaluation.
8. Joint instability: A. Joint instability (recurrent subluxations or dislocations of an articulation). B. History of joint instability that has been medically or surgically corrected requires specialist evaluation.
9. Fractures: A. Non-union of fractures. B. Mal-union of fractures that interferes with performance of duties.
10. Retained orthopedic hardware requires specialist evaluation.

11. Range of Motion: Deviations from the following range of motion or unexplained asymmetry requires specialist evaluation:
    A. Shoulder:
        i. Forward elevation to 170º-180º.
        ii. Abduction to 170º-180º.
        iii. Adduction 30º-40º.
        iv. Extension to 50º-60º.
        v. Internal rotation in abduction to 60º-90º or in neutral to 45º.
        vi. External rotation in abduction to 60º-104º or in neutral to 40º-60º.
    B. Elbow:
        i. Flexion to 135º-150º.
        ii. Extension to 0º in males and ≤ -5º in females.
        iii. Forearm supination in neutral to 80º-90º.
        iv. Forearm pronation in neutral to 80º-90º.
    C. Wrist:
        i. Dorsal extension to 65º-85º.
        ii. Palmar flexion to 70º-80º.
        iii. Ulnar deviation in neutral to 30º-45º.
        iv. Radial deviation in neutral 15º-20º.
    D. Hand/fingers: Any limitation in range of motion, strength, or dexterity that impairs functional performance requires evaluation by a specialist:
        i. Limitation in full composite grip.
        ii. Limitation in full finger extension, i.e., palm flat on table.
        iii. Atrophy of intrinsic hand muscles or thenar eminence.
        iv. Inability to fully oppose thumb and fingers.
    E. Hip:
        i. Flexion to 125º-130º.
        ii. Extension to 10º-20º.
        iii. Abduction to 30º-45º.
        iv. Adduction to 20º-30º.
        v. Internal rotation at 90º hip flexion to 40º-50º.
        vi. External rotation at 90º hip flexion to 30º-45º.
    F. Knee:
        i. Extension to 0º in males and ≤ -10º in females.
        ii. Flexion to 125º-135º.
    G. Ankle:
        i. Dorsiflexion to 10º.
        ii. Plantar flexion to 45º.
        iii. Inversion 50º-60º.
        iv. Eversion 20º-30º.
    H. Spine:
        i. Cervical Range of Motion (CROM):
            (1) Forward flexion between 50º-60º.
            (2) Extension between 65º-75º.
            (3) Lateral bending between 35º-45º.
            (4) Rotation between 70º-80º.

ii. Lumbar Range of Motion (LROM):
(1) Forward flexion from the waist to 70º-80º.
(2) Extension from the waist to 30º-40º.
(3) Lateral bending from the waist to 30º-45º.
(4) Rotation from the waist to 25º-40º.

12. Spine disorders:
A. Symptomatic disorders of the spine, including but not limited to, herniated nucleus pulposus, spondylolisthesis, spina bifida, fractures and dislocations, scoliosis, kyphosis, or lordosis.
B. History of ankylosing spondylitis.
C. History of disorders of the spine that are asymptomatic, including but not limited to, osteoarthritis, herniated nucleus pulposus, spondylolisthesis, spina bifida occulta, fractures and dislocations, scoliosis, kyphosis, and lordosis require specialist evaluation.
D. Presence or history of herniated nucleus pulposus, fractures, or dislocations of the spine resulting in persistent neurologic deficit.
E. History of recurrent mechanical spinal or sacroiliac pain with disabling episodes of pain, muscle spasm, postural deformities, or chronic limitation of motion of the spine (range of motion) or pelvis requires specialist evaluation.

13. Any amputation that interferes with the performance of duties.

14. Hand disorders:
A. Hyperdactyly.
B. Syndactyly (webbed fingers) that interferes with the performance of duties or wearing of equipment.
C. Scars and deformities of the fingers or hand that impair dexterity, grip strength, circulation, are symptomatic, interfere with the performance of duties, or preclude the wearing of equipment.

15. Chronic or recurrent bursitis, tendinitis, and synovitis sufficient to interfere with the performance of duties.

16. Lower extremity disorders:
A. Disorders of the foot that compromise the wearing of equipment or are associated with chronic pain, including but not limited to, clubfoot, pes planus, pes cavus, hammer toes, hallux valgus, overriding digits, hallux rigidus, and bunions.
B. Varus or valgus deformities that interfere with the performance of duties.
C. Leg length discrepancy of more than 3.0 cm (from the anterior superior iliac spine to the distal tip of the medial malleolus).

17. Disqualifications for Abnormal Bone Mineral Density:
A. Osteoporosis, defined as the presence or history of a fragility fracture or T-score $\leq$ -2.5 at the femoral neck, total hip, or lumbar spine using the female, white, age 20 -29 years Third National Health and Nutrition Examination Survey (NHANES III) database as the reference population standard.
B. Bone mineral density below the expected range for age (Z-score < -2.0) at the femoral neck, total hip, or lumbar spine without evidence of normal bone strength.

M. SKIN DISORDERS
1. Presence or history of disorders of the skin or nails, acute or chronic, that is severe enough to interfere with the performance of duties or the wearing of flight equipment.
2. Extensive or deep scars, burns, keloids, or body piercings that interfere with muscular movements or with the wearing of equipment or that show a tendency to break down.
3. Acne, furunculosis, atopic dermatitis, eczema, or other chronic dermatitis that interferes with the wearing of equipment.
4. Cysts, nevi, or benign tumors of the skin of a size or location that interfere with the wearing of equipment, unless surgically corrected.
5. Hyperhidrosis, if chronic or severe that may interfere with the performance of duties.
6. Infections of the skin if communicable, extensive, or not amenable to treatment. Chronic tinea pedis and onychomycosis require specialist evaluation.
7. Primary malignancies of the skin or secondary cutaneous manifestations of systemic malignancies: A. Basal cell carcinoma that has been adequately excised is not disqualifying. B. Squamous cell carcinoma that has been adequately excised requires specialist evaluation.
8. Neurofibromatosis.
9. Pilonidal sinus: A. History of inflammation or discharging sinus in the preceding 2 years. B. History of pilonidal sinus with surgery without post-operative signs or symptoms indicative of residual disease for > 6 months requires specialist evaluation.
10. Presence or history of psoriasis, unless limited to < 1% total body surface area and asymptomatic.
11. Presence or history of pemphigus vulgaris, bullous pemphigoid, dermatitis herpetiformis, or other bullous disorders: History of secondary bullous disorders that are resolved require specialist evaluation.
N. NEUROLOGICAL
1. Any neurological disorders that may interfere with the performance of duties.
2. Primary or secondary malignancies of the nervous system. Benign tumors or history of benign tumors of the nervous system, including acoustic neuromas, require specialist evaluation.
3. Vascular disorders of the nervous system (e.g., arteriovenous malformation, intracranial aneurysms, Moya-Moya disease). Cavernous angiomas require specialist evaluation.
4. History of a cerebrovascular accident (stroke, transient ischemic attack [TIA], subarachnoid hemorrhage). Asymptomatic disease of the carotid or vertebral arteries requires specialist evaluation.

5. History of infection of the nervous system within 2 years, or with residual neurologic defects that may compromise performance of duties: A. Uncomplicated viral meningitis and other CNS infections without residual neurologic sequelae are evaluated on a case-by-case basis. B. History of encephalitis is disqualifying.
6. Peripheral or CNS demyelinating disease (e.g., multiple sclerosis). Acute inflammatory demyelinating polyneuropathy without neurologic sequelae after 5 years requires specialist evaluation.
7. History of metabolic, toxic, or nutritional disorders of the nervous system without residual neurologic sequela requires specialist evaluation.
8. History of elevated intracranial pressure.
9. Congenital or developmental abnormalities of the nervous system that interfere with the performance of duties.
10. Personal history of diseases of hereditary neurologic disorders or hereditary disorders with neurologic features (e.g., neurofibromatosis, Huntington's chorea, hepato-lenticular degeneration, spinocerebellar ataxia, muscular dystrophy, familial periodic paralysis, and congenital lower spastic paraparesis).
11. History of seizure disorders: A. Febrile convulsions before the age of 5 years are not disqualifying. B. History of single seizure without neurologic sequelae after 5 years requires specialist evaluation. C. Benign age-related seizures (e.g., Juvenile Myoclonic Epilepsy) require specialist evaluation.
12. History of craniotomy or skull defects that interfere with the performance of duties. Craniotomy performed more than 5 years earlier with no skull defects requires specialist evaluation.
13. History of traumatic brain injury associated with any of the following: A. Any loss of consciousness or amnesia requires specialist evaluation. B. Intracerebral and/or subdural hemorrhage. C. Penetrating injuries or laceration of the brain. D. Skull fractures require specialist evaluation. E. Imaging evidence of retained intracranial metallic or bony fragments. F. Absence of bony substance of skull. G. Parenchymal CNS injury with persistent neurologic deficits. H. Cerebral leptomeningeal cysts, aerocele, brain abscess, traumatic CNS infections, or arteriovenous fistula. I. Transient cerebrospinal fluid rhinorrhea or otorrhea requires specialist evaluation. J. Post-traumatic syndrome manifested by changes in personality, deterioration of higher intellectual functions, anxiety, headaches, or disturbances of equilibrium for more than 3

months is disqualifying, and for less than 3 months may be disqualifying and requires specialist evaluation.

14. Migraine headache with visual or motor involvement, or any continuous or incapacitating headache:
    A. History of acephalgic migraine requires specialist evaluation.
    B. History of chronic headaches without recurrence for 10 years requires specialist evaluation.

15. History of electroencephalogram (EEG) abnormalities with historical, clinical, or supporting laboratory evidence of a neurologic abnormality requires specialist evaluation.

16. Disorders or injuries of peripheral nerves that interfere with performance of duties:
    A. Uncomplicated Bell's palsy without sequelae after 6 months is considered on a case-by-case basis.
    B. Cervical or lumbar radiculopathy. History of cervical or lumbar radiculopathy requires specialist evaluation.

17. Movement disorders (e.g., Tourette's syndrome, dystonia, or chorea). Essential tremor requires specialist evaluation.

18. Disorders of neuromuscular transmission (e.g., myasthenia gravis) and myopathies.

19. Neurodegenerative disorders (e.g., Parkinson's and related disorders or amyotrophic lateral sclerosis [ALS]).

20. History of chronic pain syndromes requiring medical intervention or medical therapy within last 10 years is disqualifying; if greater than 10 years prior, requires specialist evaluation.

O. PSYCHIATRIC DISORDERS AND SUITABILITY FOR SPACEFLIGHT

1. The NASA Clinical Psychiatrist/Psychologist ensures, based on available data, that a past or present diagnosis of a psychiatric disorder meets the criteria established in the most recent edition of DSM-5, Diagnostic and Statistical Manual of Mental Disorders (DSM):
    A. Any behavior or mental condition that, in the opinion of the examiner, makes or is likely to make, the individual a hazard to flight safety, crew coordination, or mission execution.
    B. Neurodevelopmental disorders that interfere with social or occupational functioning or that require ongoing treatment.
    C. Presence or history of schizophrenia spectrum and other psychotic disorders.
    D. Presence or history of bipolar and related disorders.
    E. Presence or history of depressive disorders.
    F. Presence or history of anxiety disorders.
    G. Presence or history of obsessive-compulsive and related disorders.
    H. Presence of trauma- and stressor-related disorders, or history of trauma- and stressor-related disorders that may interfere with the performance of duties.
    I. Presence or history of dissociative disorders.

J. Presence or history of somatic symptom and related disorders.

K. Presence or history of feeding and eating disorders.

L. Presence of sleep-wake disorders or a history of sleep-wake disorders that may interfere with the performance of duties.

M. Presence of dysphoria, affective distress, or other affective states (e.g., elevated mood) of any etiology that may interfere with the performance of duties.

N. Presence or history of disruptive, impulse-control and conduct disorders, present or history of substance-related and addictive disorders.

O. Presence of neurocognitive disorders or history of neurocognitive disorders if there is a likelihood of recurrence or evidence of residual deficits of cognition, memory, judgment, insight, or behavior.

P. Presence or history of personality disorders (an inflexible, maladaptive, and enduring pattern of personal interaction that has been present since early adulthood).

Q. Presence or history of paraphilic disorders.

R. Presence or history of abuse or neglect of a child or adult.

S. Other conditions that may be a focus of clinical attention (V-Codes) that may interfere with the performance of duties.

2. The NASA Psychologist/Psychiatrist ensures, based on available evidence from comprehensive assessment of mission-relevant spaceflight psychological competencies such as performance under stress, group living, self-management, teamwork, communication, judgment, and decision-making that an individual is deemed suitable for spaceflight:

   A. An individual can be deemed unsuitable for spaceflight for characterological behaviors or personality traits that represent lower levels of signs and symptoms than those required for a diagnosed disorder, if in the opinion of the examiner, such characteristics present risks to crew cohesion, flight safety, or mission execution. A determination of unsuitability is not a medical diagnosis.

   B. Difficulties functioning as a team member or crewmate in an operational setting. A history of poor or unstable work or interpersonal relationships or personality traits that interfere with the forming and maintenance of social connections or functioning cooperatively with others as a teammate or astronaut. This may include personality traits or characteristics such as self-centeredness (egocentrism), lack of concern for others, arrogance, entitlement, lack of empathy, insensitivity, and social avoidance or withdrawal.

   C. Poor self-management or regulation. A pattern of behavior or traits that suggest poor impulse control. Examples may include a history of arrests, illicit drug use, social "acting out," or other misconduct or irresponsible behaviors that indicate poor impulse control, lack of judgment, difficulty with authority, or disregard for social norms and rules; maladaptive internalizing behaviors such as self -damaging behaviors, and substance misuse.

   D. Limited or poor stress tolerance. A history of physical or psychological problems when under stress, evidence of poor stress-coping skills or resilience, emotional instability, or other traits or behaviors that suggest an impaired capacity to adapt to stressful situations.

   E. Poor self-awareness or emotion management. Poor insight or awareness into one's impact on others such as deficiencies in self -knowledge and emotional awareness, or in

the ability to understand or manage emotions that disrupt personal relationships or team or crew cohesion and effectiveness.
P. OBSTETRICS AND GYNECOLOGY
1. Any disorder of the gynecologic system that may interfere with the performance of duties.
2. Any acute or chronic disorder of the uterus and/or adnexa that may interfere with the performance of duties (e.g., endometriosis). History of any chronic disorder of the uterus and/or adnexa that is adequately managed requires specialist evaluation.
3. Dysmenorrhea or other irregularities of the menstrual cycle such as premenstrual syndrome that may interfere with performance of duties.
4. History of recurrent abnormal uterine bleeding or menorrhagia may require specialist evaluation.
5. Chronic or recurrent infections or inflammation of the endopelvic organs. History of a single episode of pelvic inflammatory disease requires specialist evaluation.
6. History of gynecological malignancies. History of carcinoma in situ of the cervix requires specialist evaluation.
7. History of recurrent, symptomatic ovarian cysts or history of recurrent corpora hemorrhagica unless definitively resolved.
8. Any menstrual abnormality caused by polycystic ovarian conditions, anovulation, or disorders of the hypothalamic-pituitary-ovarian axis requires specialist evaluation.
9. Any chronic dermatologic condition of the vulva and/or vestibule requires specialist evaluation.
10. Obstetrical: A. All candidates are examined while not pregnant. Pregnancy itself will not be cause to deny appointment as a candidate. B. Pregnancy is disqualifying for spaceflight until complete post-partum recovery.
Q. DENTAL
1. Any dental defects that interfere with clear speech or cause changes in the contours of the face that interfere with the performance of duties.
2. Complete edentulism in either the mandible and/or maxilla or insufficient number of natural healthy teeth to masticate a normal diet or enunciate clearly.
3. Dental prostheses: A. Any removable dental prosthesis, which if lost or broken, would not leave enough natural healthy teeth to masticate a normal diet or enunciate clearly. B. Any unilateral removable dental prosthesis that could be swallowed.

4. Diseases and abnormalities of the jaws or associated structures, including periodontal disease, that are not easily remedied or may interfere with the performance of duties.
5. Severe malocclusion that interferes with the mastication of a normal diet or clear enunciation.
6. Any dental defects such as dental caries, dental dysplasia, enamel dysplasia, symptomatic cracked teeth, defective restorations, defective prosthesis, and defective implants until resolved.
7. Partially erupted or impacted third molar teeth with the potential to cause erosion of adjacent teeth, pericoronitis, or periodontal defect until corrected.
8. Infections of endodontic or periodontic origin until resolved.
9. Active orthodontic treatment requires dental consultation. Active orthodontic treatment is disqualifying for spaceflight duties.
R. INFECTIOUS DISEASE
1. Acute or chronic infectious disease until appropriately treated that might compromise mission operations, performance of duty, or crew health and safety.
2. Tuberculosis: A. Active tuberculosis. B. History of active tuberculosis, unless 2 years have elapsed following appropriate therapy (as per current Centers for Disease Control and Prevention [CDC] guidelines) and evaluations show the individual free from active disease. C. Documented conversion of the Tuberculin Skin Test or positive Interferon Gamma Releasing Assay (IGRA). Specialist evaluation required following treatment with anti-tuberculosis drugs as per current CDC guidelines.
3. History of malaria or other blood-borne parasites, unless adequately treated and cured.
4. Clinical or laboratory evidence of HIV infection or Acquired Immune Deficiency Syndrome (AIDS).
5. Lyme disease, unless adequately treated.
6. Viral hepatitis: A. History of hepatitis B unless laboratory evidence of seroconversion and at least 1 year has passed since full recovery. Chronic hepatitis B carrier state is disqualifying. B. History of hepatitis C until 1 year after completion of CDC-approved treatment with eradication of viral load.
7. Herpes simplex virus type I or type II that may interfere with performance of duties or compromise crew health.
8. History of Herpes zoster, unless resolved for greater than 1 month and without post-herpetic neuralgia.
9. Helicobacter pylori carrier state, until adequately treated. No repeat testing is required.

10. Syphilis, gonorrhea, and chlamydia, unless adequately treated without sequelae.

11. Non-immune status or lack of documented vaccination status against the following: Measles, mumps, rubella, tetanus, polio, diphtheria, pertussis, meningococcus, and pneumococcus.

S. RADIATION (for recertification)

1. Per NASA-STD-3001, Volume 1, Revision C, section 4.2.8, the short-term radiation exposure limits shown in Table 12, NASA Short-term Ionizing Radiation Exposure Limits, have not been exceeded for any NASA astronaut. The current values are based on the use of Gray-Equivalents (Gy-eq) and relative biological effectiveness values provided by the National Council on Radiation Protection and Measurements (NCRP) Reports No. 132, Radiation Protection Guidance for Activities in Low-Earth Orbit.

   Short-term exposure limits are designed to prevent deterministic effects resulting from acute exposure. Each planned exposure is managed in adherence to the as low as reasonably achievable (ALARA) principle, which directs that exposure always be maintained as low as reasonably achievable.
   NOTE: DQ for recertification due to short term limits would only be exceeded for multiple missions within one year.

2. Per NASA-STD-3001, Volume 1, Revision C, section 4.8.2, An individual crewmember's total career effective radiation dose due to spaceflight radiation exposure shall be less than 600 mSv. This limit is universal for all ages and sexes.

T. ANTHROPOMETRY CRITERIA

1. Failure to satisfy anthropometric criteria, including height and weight, which should be compatible with human factors for specified crewed space vehicles.

APPENDIX B. TUBERCULOSIS (TB) TESTING

B.1 Purpose

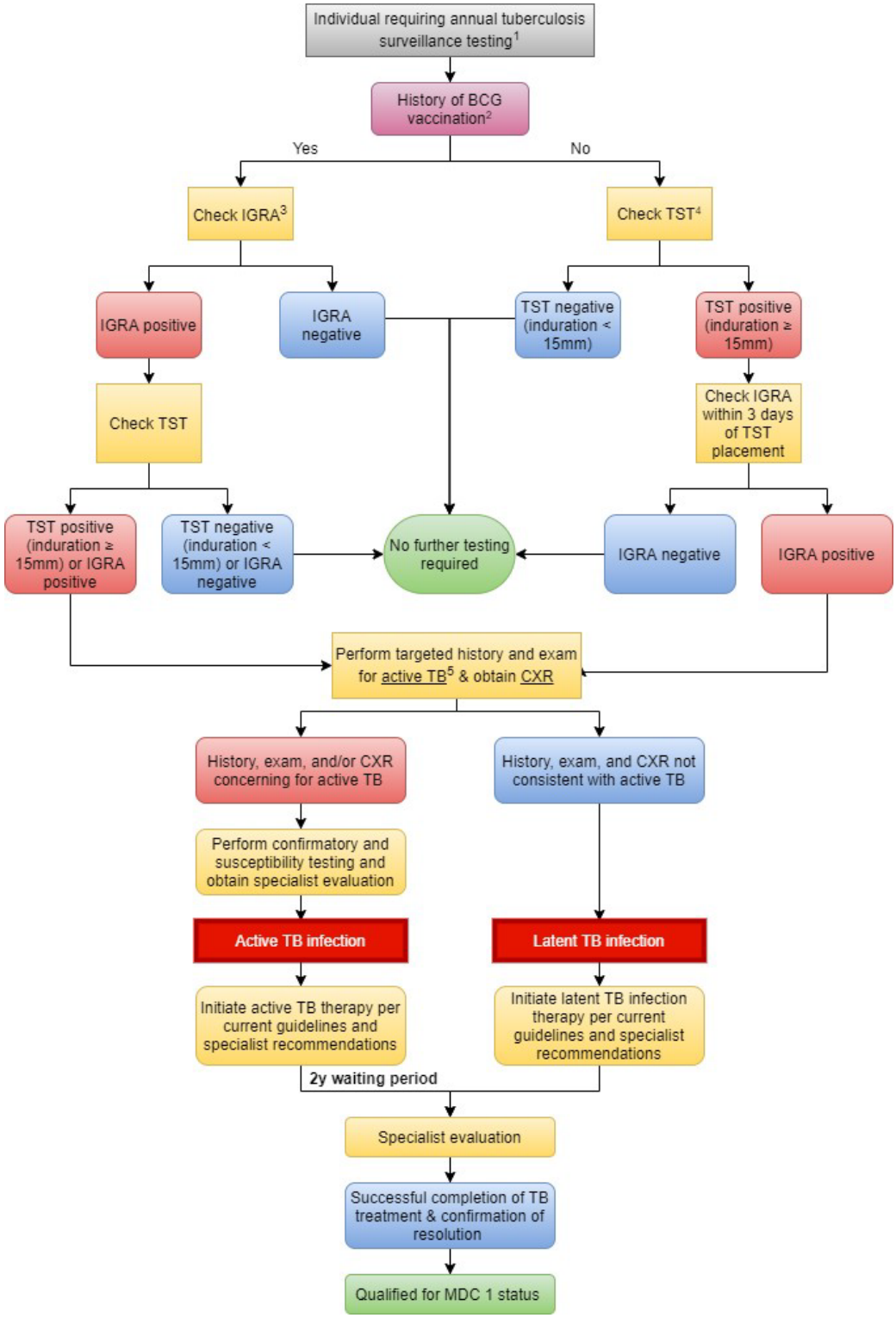
This Appendix provides guidance regarding tuberculosis (TB) testing and a flowchart summarizing the recommendations. This includes guidance on Bacille Calmette-Geurin (BCG) vaccination information, Interferon gamma release assay (IGRA) and Tuberculin skin test (TST) considerations, and recommendations on TST and IGRA.

B.2 Tuberculosis Screening & Management Guidance

IGRA assays detect the secretion of interferon-γ (INF-γ) by T-lymphocytes which are stimulated by TB-specific antigens. Every effort should be made to confirm positivity (i.e., latent or active TB) before undertaking a treatment regimen.

- If prior BCG vaccination, the initial screening test should be with IGRA, not TST.
- If no prior BCG, initial screening test can be with either TST or IGRA.
- If the initial IGRA is positive, to rule out a false positive (and thus avoid unnecessary treatment), a follow-up with TST or a different IGRA is required.
- If the initial TST is positive, perform a confirmatory IGRA to rule out false positives from non-tuberculous mycobacterial infection within 3 days of TST placement. (This timing is to prevent boosting and false positives on the post-TST IGRA).

B.3 Tuberculosis Screening & Management Flowchart



Abbreviations
BCG – Bacillus Calmette-Guérin
CXR – chest X-ray
IGRA – Interferon gamma release assay TB – tuberculosis
TST – tuberculin skin test

Figure 1—Tuberculosis (TB) Testing Flowchart

B.4 Assumptions

- Astronauts are comparable to health care workers (HCWs) in the articles addressing the challenges of latent tuberculosis infection (LTBI) testing in these low-risk populations.
- Astronauts are unlikely to be infected with Mycobacterium TB.
- Astronauts will be undergoing serial testing in the absence of known exposure.
- The majority of newly positive TSTs and IGRAs are due to false positive tests[3].

B.5 BCG Vaccination

- Consensus is to use IGRAs for determining TB infection status in BCG-vaccinated individuals because BCG vaccination reduces the specificity of TST[11].

B.6 IGRA Considerations

- Among health care workers tested serially for LTBI, conversions from negative to positive and reversions from positive to negative are more commonly identified with IGRA than with TST[1,5,11].
    - Routine serial testing of HCWs at low risk for TB infection is likely to result in FP conversions, which occur 6-9 times more frequently with IGRAs than with TST and must be balanced against any logistical advantages from using IGRAs[3].
    - More concerned about false positive seroconversion in low risk populations[6] sub-bullet.
    - Instability of IGRA results in annual retesting of HCWs and other low risk cohorts[2,4].

B.7 TST Considerations

- Cut-off matters: TST specificity is 99.3% when using the 15-mm cut-off for positive test results recommended by the CDC for persons at low risk of exposure or 96.8% when using the 10-mm cut-off[7].

B.8 Diagnosis

- The diagnosis of pulmonary TB should be suspected in patients with relevant clinical manifestations (cough > 2 to 3 weeks' duration, lymphadenopathy, fevers, night sweats, weight loss) and relevant epidemiologic factors (history of prior TB infection or disease, known or possible TB exposure, and/or past or present residence in or travel to an area where TB is endemic).

B.9 Recommendations on TST and IGRA

- Annual or serial testing of astronauts: To standardize the interpretation of results, the same test should be used for the baseline and the later tests.
- Unless astronaut has had BCG immunization, recommend TST for serial testing because of decreased likelihood of false positive conversions[8].

- Use a 15-mm cut-off for a positive TST7.

- Because the prevalence of LTBI is very low in our populations, all positive TST and IGRA tests should be confirmed to reduce the likelihood of a false positive test diagnosis.
  - If initial test is IGRA and the result is positive, either repeat IGRA or perform a TST to confirm positive results before initiating treatment for LTBI.
  - If initial test is a TST and the result is positive, perform IGRA within 3 days of the TST to minimize boosting the IGRA results. The person is considered infected only if both tests are positive[2,6].
  - Modify the up-to-date table "Approach to diagnosis of latent tuberculosis infection (tuberculosis screening) in individuals who require serial testing"[8]
    - If TST is positive with > 15 mm induration.
    - Perform IGRA within 3 days of the TST.
    - If IGRA is positive, treat for LTBI after excluding active TB.
    - If IGRA is negative, the TST is most likely a false positive result.

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APPENDIX C. MEDICAL CERTIFICATION SPECIFIC TO MISSIONS TO THE INTERNATIONAL SPACE STATION

NOTE: This standard OCHMO-STD-100.1A uses the term "Private Astronaut" instead of "spaceflight participant." This appendix is provided for historical/information purposes only.

The following is provided for informational purposes as an overview of the international medical certification process that is followed when NASA (career) astronauts or private individuals sponsored for flight by a government space agency, fly to the International Space Station (ISS).

A set of international medical policy boards govern international spaceflight medical oversight activities. These boards and their organization are described in the Memorandum of Understanding (MOU) between NASA and the IPs (see Article 11.4).

The Multilateral Medical Operations Panel (MMOP) develops the medical requirements for selection and certification of all ISS astronauts (NASA career astronauts and IP government astronauts), spaceflight participants (SFPs), and astronauts training at international facilities. Please note that the definition of spaceflight participant as used in these international documents is different from its definition in this standard. This standard uses the term private astronaut.

"ISS SFPs are individuals who are transported either by Soyuz or Space Transportation System (STS, Space Shuttle) to the ISS for commercial visitation or other purposes for short-term habitation (less than 30 days). Such individuals are generally fare-paying passengers. SFPs will not have primary operational duties or assignments, but may, in conjunction with supporting ISS agencies, be involved in short-term research activities. They will be trained in all applicable emergency and egress procedures".

The following standards and requirements are used for international medical selection and evaluation for the ISS:

a. SSP 50667, Medical Evaluation Document (MED), Volume A, Medical Standards for ISS Crewmembers—an international document that contains the ISS selection and retention standards for government career astronauts (NASA or IP).

b. SSP 50667, Medical Evaluation Document (MED), Volume B, Preflight, In-flight, and Postflight Medical Evaluation Requirements for Increment-Assigned ISS Crewmembers—the international document that contains the pre-, in-, and postflight medical testing and evaluations for long-duration missions.

c. SSP 50667, Medical Evaluation Document (MED), Volume C, Medical Standards and Certification Procedures for Spaceflight Participants—the international document that contains the medical standards and certification procedures for short-duration spaceflight participant missions.

The Multilateral Space Medicine Board (MSMB) reviews the pertinent medical information for all individuals assigned to or visiting the ISS or training at international facilities and determines individual medical certification.

A waiver or restriction may also be assigned, if appropriate.

All IPs may follow their own procedures in conducting selection, annual, and pre- and post-flight medical evaluations for ISS astronauts and long-duration candidates, as long as the evaluation requirements and standards outlined in SSP 50667, MED, Volumes A, B, and C, are followed.

Medical certification by the MSMB is valid for a period of 1 year following the last medical examination. Temporary extensions of MSMB medical certification may be authorized for a period of up to 90 days by CHMO.

APPENDIX D. REQUIREMENTS COMPLIANCE MATRIX

D.1 Purpose

Due to the complexity and uniqueness of spaceflight, it is unlikely that all of the requirements in a NASA Medical Standard will apply. The Requirements Compliance Matrix below contains this NASA Medical Standard's technical authority requirements and may be used by programs and projects to indicate requirements that are applicable or not applicable. Follow the process for waiver in section 4.7 in this NASA Medical Standard. Enter "Yes" in the "Applicable" column if the requirement is applicable to the program or project or "No" if the requirement is not applicable to the program or project. The "Comments" column may be used to provide specific instructions on how to apply the requirement or to specify proposed waiver.

Requirement	Description	Requirement in this Standard	Applicable (Enter Yes or No)	Comments
[4001]	AMB Evaluation and Certification	The examining physician **shall** present a candidate's evaluation results to the AMB.		
[4002]	AMB Evaluation and Certification	The AMB **shall** determine if the candidate does or does not meet medical standards or requires further evaluations before disposition can be made.		
[4003]	AMB Evaluation and Certification for NASA (career) Astronauts	The AMB will review the medical records of all NASA astronaut applicants at selection, and of each NASA astronaut annually, and **shall** recommend qualification, disqualification, or conditional qualification (waiver for active astronauts) to the CHMO.		
[4004]	CHMO Final Disposition for NASA (career) Astronauts	The Chief Health and Medical Officer (CHMO) **shall** make the final disposition on qualifications and disqualifications of NASA astronauts, based on review of the AMB recommendations.		
[4005]	Waiver of Medical Standards	The term "waiver" **shall** be used when a disqualifying condition is waived, and the NASA astronaut is conditionally medically certified.		
[4006]	No Waiver on Selection	No waiver **shall** be granted on selection of NASA astronauts.		

[4007]	Waiver of Medical Standards	For a NASA (career) astronaut waiver request, the examining physician **shall** provide a detailed presentation to the AMB of all relevant medical data and also address the following: a. An evidence-based review with data derived from the medical and aeromedical literature, as well as specialist consultant opinions detailing the potential risks associated with the condition, complications, and sequelae. b. A thorough consideration of the potential consequences of related medical events on mission safety and mission completion and on the potential incremental health risk to the individual in the space environment.		
[4008]	Waiver of Medical Standards	The examining physician **shall** notify the NASA astronaut that his/her medical condition is being considered for waiver or disqualification from flight status.		
[4009]	Waiver of Medical Standards	The Chief Health and Medical Officer (CHMO) **shall** make the final disposition based on review of the AMB recommendations. The CHMO may delegate waiver decision authority to the AMB Chair for routine medication waiver renewal.		
[5001]	Medical Screening NASA Astronauts	The examining physician **shall** perform medical screening, including the procedures and consultations in Table 2, Medical Evaluation Procedures, at selection and for annual recertification as indicated.		
[5002]	Medical Conditions to Consider for Selection and Annual Recertification of NASA Astronauts	The examining physician **shall** determine the suitability for selection and retention of NASA astronauts, using the conditions for disqualification specified in Appendix A.		
[6001]	Pre- and Post-flight Physical Examination for > 30 Days Crews	NASA Astronauts **shall** undergo clinical examinations with the Crew Surgeon (CS), Deputy Crew Surgeon, or Partner Flight Surgeon (FS) according to the specifications and schedule described below.		
[6002]	Crew Medical Officer Health Status Evaluations	Crewmembers **shall** complete periodic health status evaluations in-flight.		
[6003]	Private Medical Conference	Crewmembers **shall** participate in private medical conferences with a mission assigned FS.		
[6004]	Neurological Assessment	Crewmembers **shall** undergo a neurological assessment before and after flight.		
[6005]	Neurovestibular Platform Test	Crewmembers **shall** undergo an objective assessment of neuro-vestibular function before and after flight.		

[6006]	Resting ECG	Each crewmember **shall** complete a resting ECG prior to launch to provide a baseline study.		
[6007]	Hearing Assessment	Crewmembers will be tested with conventional audiometry before and after flight. Crewmembers **shall** also conduct pre-flight and in-flight hearing assessments utilizing in-flight hardware.		
[6008]	Hearing Protection	Crewmembers **shall** be fitted for and provided with hearing protection earwear.		
[6009]	Dental Examination	The dental health of each crewmember **shall** be assessed before launch.		
[6010]	Dental Orthopantomogram or Full Mouth X-Ray Series	A full dental orthopantomogram x-ray or full mouth x-ray series **shall** be performed within two years of launch.		
[6011]	Ophthalmology/Optometry Examinations	Each crewmember **shall** undergo ophthalmological exams before and after flight in addition to regular annual checkups.		
[6012]	Specialized Ocular Assessments	To assess the effects of exposure to the space-flight environment on ocular health, crewmembers **shall** undergo specialized eye examinations pre-flight, in-flight, and post-flight.		
[6013]	Bone Densitometry	Pre- and post-flight measurements of bone mineral density (BMD) **shall** be performed.		
[6014]	Ultrasound Imaging (Sonography)	Ultrasound imaging **shall** be conducted for each crewmember.		
[6015]	Body Mass Measurement	Crewmembers **shall** evaluate body mass periodically while in-flight.		
[6016]	Photodocumentation of Skin	The Crew Medical Officer or Crew Surgeon **shall** document, through photographic imaging, the condition of the crewmember's skin, including any signs of skin disease or injury.		
[6017]	MRI Brain and MR Angiography	Each crewmember **shall** undergo an MRI study of the brain and MR angiographic study of the supra-aortic and intracranial vessels		
[6018]	MRI Cervical and Lumbar Spine Imaging	Each crewmember **shall** undergo pre- and post-flight non-contrast MRI studies of the cervical and lumbar spine		
[6019]	Laboratory Testing	A clinical laboratory assessment **shall** be completed for each crewmember before and after flight		
[6020]	Methicillin Resistant Staphylococcus aureus (MRSA) Screening and Suppression	Nasal cultures for Staphylococcus aureus **shall** be conducted on all crewmembers at L-90/30 days.		

[6021]	Group A Beta-Hemolytic Streptococcus (GABHS, Strep pyogenes) carrier state	Throat swab for Group A Beta-Hemolytic Streptococcus carriage **shall** be conducted on all crewmembers at L-90/30 days.		
[6022]	Radiation Monitoring/Personal Physical Dosimetry	In-flight radiation monitoring **shall** be performed with crew personal dosimetry according to the specifications in NASA-STD-3001, Volume 2.		
[6023]	Active postural stand tests	Each crewmember **shall** undergo orthostatic tolerance testing by means of an active stand test.		
[6024]	Functional Fitness Assessments	Each crewmember **shall** complete a series of tests designed to establish functional fitness before and after flight.		
[6025]	On-Orbit Strength and Conditioning Monitoring	Each crewmember **shall** undergo strength and conditioning monitoring during flight.		
[6028]	Test for Aerobic Functional Capacity	Each crewmember **shall** complete tests to assess aerobic functional capacity and exercise induced arrhythmias before flight, periodically in-flight and post-flight. Prior to an EVA or at any point during the mission, this test may be requested by the Crew Surgeon.		
[6029]	Pre- and Post-EVA Medical Examinations	All EVAs **shall** be preceded and followed by an assessment of medical fitness by the Crew Surgeon.		
[6030]	Monitoring during EVA	Crewmembers **shall** undergo EVA monitoring as per the requirements in NASA-STD-3001, Volume 2.		
[6032]	Pre-flight Psychiatric/Psychological Status Check	Crewmembers **shall** be evaluated by designated experts to confirm psychiatric/psychological readiness for flight.		
[6033]	Private Psychological Conference	Crewmembers **shall** participate in a private psychological conference, performed by a specialist, according to the specifications and schedule described below.		
[6034]	Post-flight Psychiatric/Psychological Status Check	Crewmembers **shall** undergo psychiatric/psychological clinical interview post-flight by a specialist to assess behavioral health and performance mission support and behavioral re-adaptation.		
[6035]	Cognitive Assessment	Crewmembers **shall** undergo a cognitive assessment before, during, and after flight.		
[6036]	Behavioral Observation of Training	Training events of crewmember (preferably of whole assigned crews) **shall** be observed by behavioral specialists.		

[6037]	Vitamin D Testing and Treatment Protocol	Crewmembers **shall** be evaluated and treated prior to a long-duration mission. The timing of the testing will be at the discretion of the Crew Surgeon. The optimal/desired range for 25-OH Vitamin D is 35-90 ng/ml. The recommended maintenance dose of Vitamin D3 is 1,000 I.U. daily or 5000 I.U. once a week.		
[6038]	Nutritional Status Assessments	Crewmembers **shall** undergo nutritional assessment testing according to the specifications and schedule described below.		
[6039]	Sleep Assessment	Each crewmember **shall** provide a daily assessment of sleep quality and quantity for a 2-week pre-flight period, 1 week pre-launch, weekly in-flight via Private Medical Conference, and 1 week post-flight to supply daily sleep data to the crewmember and Crew Surgeon.		
[6040]	Sleep Medication Ground Testing	Each crewmember **shall** undergo a baseline assessment of program approved sleep medications prior to in-flight use.		
[6041]	Screening for deep vein thrombosis and venous flow anomalies	Every crewmember **shall** be screened for deep vein thrombosis (DVT) and flow anomalies of the internal jugular veins.		
[6042]	Space Motion Sickness Medication Ground Testing	Each crewmember **shall** undergo a baseline assessment of program approved space motion sickness medications prior to in-flight use.		
[7001]	Private Astronaut Medical Requirements	Private astronauts **shall** have the medical screening, including the procedures and consultations in Table 9, Medical Evaluation Procedures, completed and evaluated prior to flight.		
[8001]	Medical Evaluation Procedures for NASA Suborbital Research Specialists	NSRS **shall** have the medical screening, including the procedures as listed below, completed and forwarded to the AMB prior to flight. o FAA Class III Exam or equivalent o Plus: EKG, Standard Blood (CBC, BMP) & Urine Analysis o Valid for 1 year		

APPENDIX E. REFERENCES

Purpose

This Appendix provides references to guidance documents related to this NASA Medical Standard.

References

Health Insurance Portability and Accountability Act (HIPAA) (https://www.hhs.gov/hipaa/for-professionals/security/laws- regulations/index.html)

Memorandum of Understanding (MOU) between NASA and the IPs (Article 11.4)

NPD 1382.17, NASA Privacy Policy

SSP 50667, Medical Evaluation Document (MED), Volume A, Medical Standards for ISS Crewmembers

SSP 50667, Medical Evaluation Document (MED), Volume B, Preflight, In-flight, and Postflight Medical Evaluation Requirements for Increment-Assigned ISS Crewmembers

SSP 50667, Medical Evaluation Document (MED), Volume C, Medical Standards and Certification Procedures for Spaceflight Participants

Langston—Legal, Ethical & Medical Implications for Commercial Spaceflight

Langston, Sara M. *Commercial Space Travel: Understanding the Legal, Ethical, and Medical Implications for Commercial Spaceflight Participants and Crew.* International Aerospace Strategies / Senmurv Consulting LLC, Arlington, VA, 2025, pp. 489–494.

Overview: Evaluates participant rights, crew responsibilities, and regulatory gaps shaping commercial human spaceflight governance.

COMMERCIAL SPACE TRAVEL

UNDERSTANDING THE LEGAL, ETHICAL AND MEDICAL IMPLICATIONS FOR COMMERCIAL SPACEFLIGHT PARTICIPANTS AND CREW

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Abstract— Commercial human spaceflight raises numerous medical, legal and ethical considerations with regard to the health and safety of civilian spaceflight participants (SFPs) and commercial crew. New and emerging space transportation companies are proposing a range of commercial suborbital, orbital, interplanetary and point-to-point space transportation. However, the diversity in mission architecture, operation, flight purpose and duration make it difficult to establish a solitary risk assessment or approach towards spaceflight as a homogeneous activity. Even after 50 years in space, there is no denying that a great deal of scientific, technological and medical uncertainty exists with spaceflight. While some hazards have been identified (e.g. acceleration, microgravity, radiation and meteorites), physiological risks and uncertainties for spacefarers remain and are accentuated in opening space access to a wide demographic of individuals with varying levels of fitness and no standardized medical criteria for selection. In addition, the scope of physiological risks spans pre-flight, in-flight and post-flight operations and activities this in turn triggers practical mitigation measures and bioethical-legal duties, such as full disclosure and informed consent. This paper will provide an overview of the applicable laws, underlying values and duties of care intertwined with spaceflight and addresses prominent concerns of medical uncertainty and human risk factors. The aim of which is to assist in establishing a practical, prudent and sustainable framework for human expansion into space.

Keywords—law; ethics; space medicine; human spaceflight;

I. INTRODUCTION

Commercial human spaceflight raises numerous medical, legal and ethical considerations with regard to the health and safety of civilian spaceflight participants (SFPs) and commercial crew. New and emerging space transportation companies are proposing a range of commercial suborbital, orbital, interplanetary and point-to-point space transportation. However, the diversity in mission architecture, operation, flight purpose and duration make it difficult to establish a solitary risk assessment or approach towards spaceflight as a homogeneous activity. Even after 50 years in space, there is no denying that a great deal of scientific, technological and medical uncertainty exists with spaceflight. While some hazards have been identified (e.g. acceleration, microgravity, radiation and meteorites), physiological risks and uncertainties for spacefarers remain and are accentuated in opening space access to a wide demographic of individuals with varying levels of fitness and no standardized medical criteria for selection.

In addition, the scope of physiological risks spans pre-flight, in-flight and post-flight operations and activities, this in turn triggers practical mitigation measures and bioethical-legal duties, such as full disclosure and informed consent. At the present time, the U.S. is leading the commercial human spaceflight industry and has established a regulatory framework for commercial spaceflights and civilian participants. This paper provides an interdisciplinary overview of the applicable laws, underlying values and duties concerning spaceflight and addresses prominent concerns of medical uncertainty and human risk factors. Economic implications can also be seen from insurance and contractual practices within the industry. The aim of this work is to assist in establishing a practical, prudent and sustainable framework for the future of human space transportation.

II. MEDICAL AND BIOETHICAL IMPLICATIONS

Space medicine is a broad term that encompasses both medical support and monitoring of astronaut health in space as well as medical evaluation, health and related training requirements on Earth for space activities. *Space surgery*, is another aspect of space medicine. As a whole, space medicine can be seen as part operational medicine, part medical research and part education [1]. *Bioethics* specifically relates to practical ethics and issues arising in medicine and biology. In spaceflight, prominent bioethical concerns include, but are not limited to: SFP patient rights (e.g. consent, full disclosure, data privacy, autonomy over one's own body and risk); professional responsibility for medical practitioners; the use of human subjects in studies and scientific experiments; medical data exchange; medical monitoring and telemedicine; and mission design, architecture and technology where human life-support systems and necessary accommodations are concerned.

Significantly in biomedicine, law and ethics often intertwine and ethical concerns can overlap with legal requirements and regulations. Thus, it behooves a commercial launch operator to always comply with ethical dictates for

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human spaceflight, regardless of whether a law exists to regulate the issue or not. By following analogous ethical duties of care for other transportation carriers where possible (cruise liners, for instance) a commercial operator may protect itself from negligence claims where a party sustains injury or harm. Thus, for practical application, both law and ethics are addressed here in discussing human spaceflight.

It is well known that space presents environmental hazards and adverse impacts to human health and safety, which can trigger a range of physiological responses requiring different countermeasures [Table 1]. Medical mitigation therefore includes internal and external countermeasures, including preflight medical treatment and customized training to in-flight pharmacological therapies and psychological support, to spacesuits, anti-G suits, exercise, artificial gravity and technological designs/ systems (*e.g.* thermal control, acoustic insulation, radiation shielding) [2]. It is also known that pharmaceutical drugs metabolize differently in microgravity and can affect people differently, both in space and upon return to Earth [3]. The Federal Aviation Administration (FAA) Centers of Excellence have been working on narrowing medical uncertainties for suborbital spaceflights by testing acceleration forces on particular pathologies, utilizing centrifuge simulations [4]. Consequently, our knowledge of prophylactic and in-space medical treatments is an ongoing work in progress.

TABLE I. SELECTED SPACE THREATS[1]

Environmental Hazards	Physiological Impact on Human Systems
Acceleration G-forces Vibration and noise Reduced atmospheric pressure, microgravity/ weightlessness Extreme temperatures Impact with meteroids and debris mitigation Confinement and isolation Extraterrestrial dust (e.g. Lunar regolith, Martian dust)	Neurovestibular Cardiovascular Musculosketetal Hematological and Immunological Pharmacobiological

[1]M. Grenon *(Footnote 2)*

A. *Medical Criteria and Training*

In regards to commercial space crew, U.S. regulations stipulate baseline medical criteria and training to ensure that the crew can adequately perform their functions. However, the screening, selection, and detailed training criteria for SFPs remain ungoverned. The lack of uniform standards does raise issues of concern for medical forum shopping and limited understanding of the risks, among other things. Ultimately, commercial launch operators are responsible for evaluating candidates for relevant spaceflight options [Table 2] and ensuring the general welfare and safety of all concerned.

1) Commercial Crew: U.S. regulations require commercial space crews with critical-safety functions to meet the requirements of a Class II airman's medical certificate [5]. In the 2014 Recommended Practices for Human Space Flight Occupant Safety (Recommended Practices), the FAA further suggests that crews undergo medical examinations every twelve (12) months for suborbital flights, and six (6) months for orbital flights, by a licensed physician board certified in aerospace medicine [6]. Like airlines, spaceflight crew must also monitor their own health for the ability to perform their safety-critical functions and exercise caution in the use of pharmaceutical drugs which may impair judgment or motor function. In addition, pilots must possess an FAA pilot certificate with instrument rating and the aeronautical knowledge, experience and skills necessary to pilot and control the space vehicle [7].

2) Spaceflight Participants: Currently, no standardized medical selection criteria exist for SFPs. The Commercial Space Launch Act (as amended) (CSLA) remains silent on the issue, and the FAA outlines some very general guidance on human spaceflight in its Recommended Practices. However concerning the medical "No Go" criteria issue, the FAA states [8]:

> This document does not include any medical criterial that would limit who should fly in space as a spaceflight participant. Medical consultation for space flight participants is recommended to inform them of risks and to ensure they will not be a danger to other occupants. However, spaceflight participants would be free to make decisions about their own individual risk.

The FAA reasoning is that "there is little clear statistical evidence on the actual impact of space flight on the health of an occupant with pre-existing conditions" [9]. The FAA recommends that SFPs receive a medical consultation within twelve (12) months of flight from a physician trained or experienced in aerospace medicine to ascertain the medical risks of spaceflight. However, the Recommended Practices do not constitute legal obligations, and unlike for crewmembers there are no professional board requirements or specific expertise legally required for the medical practitioners certifying SFPs for spaceflight.

Similarly, the regulations do require that launch operators instruct SFPs on basic emergency procedures but that is the extent of formal training requirements [10]. Currently, commercial launch operators, to include Virgin Galactic, XCOR Aerospace and Bigelow Aerospace, are advertising training programs of three to four days which may include pre-flight briefings, basic emergency response training, parabolic flights and exercise techniques (for *g*-force preparation) [11]. Specific training details on these programs, however, are still not publicly available.

B. *Duties of Care*

The levels and priorities of care associated with commercial human spaceflight activities may differ depending on the type of launch and reentry, vehicle design and flight technology, trajectory, and duration of the spaceflight. The complexities involving possible commercial space missions, operations, and architectures make it difficult to apply a solitary framework for risk to spaceflight as a homogeneous activity. In the Recommended Practices, the FAA directly

TABLE II. EXAMPLES OF COMMERCIAL SPACEFLIGHT ACTIVITIES

Air (near space)	**Suborbital**	**Orbital**	**Interplanetary**
Stratospheric balloon flights (20 mi/ 32 km)	Air-launched (glide reentry)	Low Earth orbit flights/ space stations	Flights to/from Moon
Parabolic flights	Rocket launched (glide reentry/ module landing)	Beyond low Earth orbit flights/ space stations	Flights to/from asteroids
	Point-to-point transportation (space hops)	Superorbital flights	Flights to/from Mars

acknowledged the convolution of risk and levels of care with commercial human spaceflight systems: "Because of the wide variety of commercial human space flight activities that are likely to take place in the future, with differing destinations, purposes, and architectures, different risk levels may be appropriate in different situations. In addition, establishing a single level of risk may inadvertently limit innovation" [12].

The FAA Recommended Practices therefore suggest a very basic management approach to risk and three (3) corresponding levels of care to be afforded to all occupants of spaceflight vehicles. However, as guidance these do not constitute legal obligations for launch operators.

Level 1 Overall environment: the spacecraft environment should not pose a danger of serious injury or fatality. This is a low standard of care.

Level 2 Safety critical operations: commercial flight crews have safety critical functions. Consequently, the level of care is raised during these operations. The same applies to limited safety-critical tasks performed by SFPs, such as engaging seat restraints and emergency evacuation.

Level 3 Emergencies: in emergencies the duty of care is raised to a reasonable chance of survival.

It is significant to note that U.S. government guidance and regulations is aimed at preserving the health and safety of the public, and to an extent the SFPs, alongside the fostering of commercial enterprise. From the onset, spaceflight has been deemed an inherently dangerous activity, and the spaceflight industry has a distance to go to reach the safety statistics of airlines and transportation carriers. For these reasons, the regulatory provisions on commercial crew qualifications and training focus on crewmembers' ability to withstand the stresses of spaceflight (acceleration, deceleration, microgravity, vibration, etc.) and skillful conduct specifically targeted to shield the public from harm. In contrast, obligatory SFP training is limited to emergency response (smoke, fire, loss of cabin pressure etc.) and egress.

C. Uncertainty and Risk

Even after 50 years in space, there is no denying that a great deal of scientific, technological, and medical uncertainty exists with spaceflight. While there are *known* hazards (for instance, acceleration, microgravity, radiation, and meteorites), what we do not know or the *known unknowns* are highlighted in opening the passenger manifest to a wide demographic of individuals as space tourism companies intend to do, along with diversity of language, comprehension, age, ability and fitness.

Risk as a social construct, is also a determination subjective to culture, context, perception and communication of an identifiable or potential hazard versus opportunity [13]. Understanding the overall cultural perspective on risk-taking is pertinent to the understanding of societal attitudes towards individuals interested in engaging in human spaceflight which has always been deemed an ultra-hazardous activity. Overall, the U.S. and Russia both generally share a cultural recognition of a person's right of autonomy to engage in risky ventures.

Still, a risk assessment must be made by the national launch authorities to ascertain all known risks inherent in any spaceflight architecture. These include the likelihood of the harm to human spacefarers, third parties, the environment, as well as the impact of spaceflight (to include emergency response) on the economy and judiciary. Bioethicists can also help in evaluating the risks by clarifying scale points and values for heightened risk requiring an ethical assessment and decision-making approach [14].

1) Decision-making Framework: There are three main stages of risk evaluation:

- Identification, for risk assessment – Ask: is it safe?
- Mitigation, for risk management – Ask: if not safe, how can we make it safe?
- Hindsight, for improvement – Ask: was it safe? If not, what can we do about it?

NASA, for instance, frequently confronts bioethical concerns in its human spaceflight program, which requires a procedural approach to uncertainty, evaluating and balancing the actual and prospective risk of harm to astronauts with the prospective benefits and mission objectives. The scoring criteria used ranges from no risks of impairment to crew health and mission, to increasing levels of significant, long-term, irreversible, and catastrophic harm (impairment, death, and loss of mission objectives) [15]. Commercial launch operators will likely also need to employ similar assessments and criteria.

2) IOM Ethical Decision-Making Framework: In 2014, the Institute of Medicine (IOM) published an ethical decision-making framework for NASA's long duration spaceflight program [16]. The fundamental ethics outlined there may

likewise be applied to private/ commercial spaceflight. For instance:

a) Avoid harm – by preventing harm, exercising caution, and removing or mitigating harms that occur.

b) Uphold beneficence – using spaceflight to benefit society; this includes transportation, entertainment, scientific research and exploration.

*c) S*eek and maintain a favorable and acceptable balance of risk of harm and potential for benefit in spaceflight operations.

d) Respect for individual crew and SFP autonomy - particularly, concerning voluntary decision-making.

e) Ensure fairness – in company procedures and operations; and

f) Fidelity – recognize individual contributions of crew and SFPs as appropriate, and honor societal obligations to employees.

The significance of adopting an ethical approach besides legal obligations is that law is concerned with liability, mostly this means pecuniary compensation for when something goes wrong. Whereas, ethics is concerned with people, human relationships, and doing the right thing. As a result, compliance with ethical conduct benefits both individuals and the rule of law, and moral frameworks benefit society when law is silent or lacking on an issue.

3) Precautionary Principle: The Precautionary Principle holds that where threats of serious or irreversible damage exits, the lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent the harm/damage from occurring [17]. Consequently, the precautionary principle provides a valuable framing strategy for interpreting risk and caution rather than constituting a *de facto* legal principle [18] and has been applied to environmental policy, health, medicine and many other fields as a social, ethical and legal approach.

Likewise, it can be applied to commercial spaceflight. Particularly, where questions of increased risk exist the principle may be applied to limit the participation of an individual for health, safety and security. For instance, in 2009, a prospective Japanese space tourist, Daisuke Enomoto, was dismissed by Russian doctors from participating in a ten day visit to the *International Space Station* (ISS), due to persisting kidney stones [19]. Rather than risk jeopardizing the mission, the safety of the space tourist himself or other astronauts, six months of training and $40 million ticket were forfeited. In essence, it's better to be safe than sorry! This can likewise be applied to future decision-making, such as when questions arise as to the scope of future human activity in space as well as planetary protection.

4) Informed Consent: Informed consent is a major concern in both bioethics and law particularly in regard to personal risk taking. Even occupationally hazardous professions (e.g. firefighters, military, law enforcement) recognize and appreciate the significance of voluntary consent to participate in high-risk missions and individual contributions. The IOM decision making framework specifically integrates these concerns in two of the six foundational principles: a) respect for an astronaut's individual autonomy and the right to voluntarily make decisions on participation in proposed missions, and b) Agency recognition and respect for individual sacrifices and contributions to society [20]. The ISS Astronaut Code of Conduct also reiterates this principle of respect for autonomy by requiring informed written consent for human test subjects on the ISS as well as research approval from the human ethics board [21].

Informed consent for members of the general public requires clear communication and transparency—and consent applies to all stages of the activity, before, during and after (given potential residual effects). Unlike other extreme sport activities, a SFP is limited in withdrawing consent once the launch or space flight commences. In this regard, spaceflight is more akin to an experimental medical treatment rather than an extreme sport. One cannot withdraw consent for any residual effects which may manifest in the future from treatment or spaceflight. This dictates that consent to engage in a risky activity at one point in time implies consent for repercussions and consequences that can arise later, as a result of the initial consent. For instance, long-term effects of microgravity and radiation can persist beyond flight and manifest an array of medical events. Unlike an airline passenger who declines the higher risk and duties of an emergency row seat, there are no alternative safer options for SFP participation [22].

For these reasons, U.S. law requires that licensed spaceflight operators inform the commercial crews and SFPs that the U.S. government does not certify the spaceflight and space vehicle as safe for carrying humans. The operator must also inform the SFP in writing on the risks of launch/ reentry, the safety record of the vehicle, and that the hazards and risk could result in serious injury, death, disability, or total/ partial loss of physical and mental function, as well as the existence of unknown hazards [23]. The operator must present this information in a manner that can be readily understood by an SFP with no specialized education or training. These disclosure requirements are to ensure clarity and transparency in operator communications and to ensure the SFP maintains the requisite rational awareness for autonomous choice. As a result, the FAA currently interprets the law to mean minors (those under 18 years) cannot consent, and the FAA does not accept parental consent as a substitute for legal informed consent and voluntary participation [24], as is permitted in other high risk sports and medical procedures.

III. Legal Considerations

A. State Responsibility

Article VI of the Outer Space Treaty makes States inextricably responsible for authorizing and supervising nongovernmental space activities and ensuring compliance

with the treaty and international law [25]. States incorporate these obligations by passing domestic legislation and implementing regulations. In the U.S., the FAA Office of Commercial Space Transportation is responsible for issuing commercial launch operators with permits (research and development) and licenses (commercial operations). Due to a recent tabled legislative bill, the "American Space Commerce Free Enterprise Act," certification authority for non-transportation space related matters may soon fall under the purview of the Department of Commerce's Office of Space Commerce [26].

Interestingly, under U.S. statutory law, weapons are prohibited from commercial spaceflight but there is no mention or prohibition on alcohol or recreational drugs [27]. Indeed, some passengers may be interested in enhancing a spaceflight experience with recreational substances. In such cases, these questions will likely be determined under state law, and where state law may permit the SFP to partake of such substances (*e.g.* Colorado), the launch operator will ultimately have the final say as it is the entity legally responsible to ensure that the SFP does not jeopardize the safety and security of the flight as well as the public.

B. Distinguishing Common Carriage and Spaceflight

While commercial human spaceflight is deemed a method of 'transportation' it has not yet reached the status of *common carriage*, a legal and liability status attributable to transportation service providers (*e.g.* airline, trains, taxis) and establishes rights and duties between the carrier and passenger. In 2004, U.S. Congress excluded commercial spaceflight from the scope of common carriage and exercised a regime of cross-waivers and personal liability waivers for commercial operators and SFPs [28]. Notably, U.S. legislation also identifies commercial passengers as 'spaceflight participants' and not 'passengers' to further illustrate the distinction.

1) Cross-waivers: The CSLA manages the risk of potential liability and litigation arising from launch and reentry by stipulating a national bifurcated (two part) approach: First, a 3-tier liability regime for indemnification; and second, a risk-sharing system of reciprocal waivers of claims (cross-waivers) between parties [29].

A licensed launch operator is required to obtain insurance or demonstrate adequate financial ability. Where damage or harm is incurred, the operator liable for the maximum probable loss (MPL) capped at $500 million. The U.S. government will indemnify anything over the MPL up to $2 billion. Any liability exceeding that watershed is shifted back to the licensed operator. Under the reciprocal waiver scheme each party agrees to be responsible for personal injury, death, property damage or loss sustained by it or its employees resulting from a licensed activity. Traditionally, this cross-waiver system is based on the concept of *best efforts* by the parties. In short, (1) the operator signs cross-waivers with all commercial entities involved in the launch/reentry; (2) operator, crew and SFPs and associated contractors are required to sign a liability waiver indemnifying the U.S. government for any claims that may exceed the insurance of the operator.

2) Personal Liability Waivers: Up until recently, there was no Federal requirement for SFPs to sign a personal liability waiver with the launch operator. Efforts to provide operators and manufacturers with legal immunity to negligence claims only existed under state law to stimulate the nascent space transportation industry (this included Texas, Florida, New Mexico, Virginia, Colorado and Arizona) [30]. However, the U.S. Space Launch Competitiveness Act of 6 January 2015 amended the CSLA to include SFPs in the mandatory cross waiver scheme with launch operators [31]. Although, these waivers are controversial within the legal community and legally uncertain as they have yet to tried in a court of law. On the other hand, claims between SFPs are not precluded by statute and remain unregulated. So it is possible for one SFP to sue anther SFP where one causes harm or injury to the other [32].

C. Duties of Astronauts

The 1967 Outer Space Treaty applies only one requirement to individual spacefarers. Article V stipulates that astronauts in space shall "render all possible assistance" to other astronauts in space and on celestial bodies [33]. This is the only personal duty required of astronauts under the international space law regime, and stems from traditional maritime principles and law of the sea. However, no uniform definition of 'astronaut' currently exists and U.S. law is silent on this specific obligation for private spaceflight. Thus, it is unclear whether commercial launch operators and SFPs fall under this treaty provision.

Aside from a legal obligation, the underlying ethical question is whether a moral duty to render possible assistance to other persons in space exists, regardless of whether one is a professional astronaut, crewmember or SFP. This is also a question of public policy because if the answer is yes, it follows whether the 'Good Samaritan' principle should also be extended to commercial human spaceflight and in-space activities to promote and protect prospective rescuers. The international space community has yet to address these ethical and legal implications.

D. Private Insurance

Traditionally, space tourists to the *ISS* have been required to insure themselves in the event they cause damage to any one or thing on the station. Now, Allianz Global Assistance (Allianz) is the first insurance company to offer personal and corporate insurance for commercial SFPs. Allianz intends to actively engage with the spaceflight process and accompany SFPs from the first preparatory phase to "provide medical assistance solutions, as well as expert advice and personal services for space travelers" [34]. As of yet, it is unclear what role the insurance company will play in the screening and

selection process or how contract terms may affect doctor-patient confidentiality.

IV. Conclusion

Private/ commercial human spaceflight presents a myriad of medical, bioethical and legal implications for consideration. As the U.S. is leading in developing national regulations specifically for commercial human spaceflight, in many cases the ethical and legal issues overlap and jointly form legally binding requirements. In other instances, voluntary guidance is provided to encourage optimal operator conduct. Significantly, the inherent risks involved in human space activities calls for incorporating ethical risk management strategies into industry standards and best practices, even where the law is silent or absent. As technology advances and spaceflight increases in safety, it is possible that spaceflight operators will become common carriers and SFPs will eventually be afforded traditional passenger rights and higher standards of care. However, as of now all major risks of spaceflight – medical and legal – are borne by the licensed operator and SFPs. For this reason, the dangers and risks need be communicated clearly and procedurally to crewmembers and SFPs to ensure legal and ethical informed consent as well as voluntary action throughout the various stages of spaceflight.

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Whitehouse—OSHA & Neoliberal Market Conflicts (2025)

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Overview: Analyzes tensions between commercial space expansion and worker protections, highlighting OSHA limitations.

Bioethics

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SPECIAL ISSUE ARTICLE

Workers' Rights in the Space Race: OSHA and Neoliberal Market Conflicts

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ABSTRACT

This paper presents a synthesis of pragmatic and ethical concerns with the Occupational Safety and Health Administration (OSHA), a US government agency, in the context of exploration, colonization, and monetization (with an emphasis on critical metals). OSHA provides worker safety regulations on a federal level, and proponents state that these regulations protect workers, while opponents state that OSHA either does not do enough to protect worker safety or that the increase in worker safety rates is due to market competition rather than federal regulation. This paper aims to state the importance of preemptive regulation in the context of the space race, in lieu of historical reactionary regulations, and to note the intersection of neoliberalism and colonialism that dictates market values, including space exploration. Finally, the paper posits that OSHA can utilize decolonizing ethics to increase worker safety and decrease health disparities associated with race.

1 | The Contentious Nature of Space in the 21st Century

As Blue Origin, a company founded by Jeff Bezos, had its first female flight, the discourse surrounding the flight ranged from female empowerment to decrying it as a "morally vacuous" publicity stunt [1]. Privately owned aerospace manufacturers range the gamut from SpaceX to Blue Origin, with owners having motivations from colonizing Mars to using space as a manufacturing hub [2, 3]. Private space and technology companies have been criticized for polluting the planet [4] and for having rockets explode [5].

2 | Philosophy and Methodology

This article is theoretical, synthesizing and exploring previously published works. Based on the ethos of Campa et al. transdisciplinary research is a vital element for technological forecasting, based on drawing from different sources of data, information, and knowledge derived from a variety of different fields [6].

Furthermore, with the importance of health in particular, which OSHA is geared to protect, Gehlert et al. promulgate the importance of transdisciplinary collaborations for understanding and resolving health disparities. The determinants of health disparities vary "from the molecular to the societal," which necessitates multilevel frameworks for addressing said inequalities [7].

The multilevel framework of health determinants developed by Kaplan, Everson, and Lynch [8] includes pathophysiological pathways, genetic factors, individual risk factors, social relationships, living conditions, institutions, and economic policies. Smedley, Syme [7, 9]. OSHA, a US government agency, regulates to protect human health and lives and can reduce healthcare disparities when implemented correctly.

3 | Over 50 Years of OSHA

Fellner et al. state in the debate "Is OSHA a Failed Agency or an Unheralded Success?" that the Occupational Safety and Health

Administration [10] was founded in 1970, the same year as the Environmental Protection Agency, and occupational injuries fell by 60% since OSHA was founded. OSHA engages with hundreds of thousands of employers and provides hundreds of thousands of employers with free advice on how to improve working conditions [11]. For the purpose of this paper, the focus will be on OSHA, as "U.S. companies account for 50 percent of all space-related private investment and for 87 percent of launch-specific investment" [12]. Furthermore, while the FAA does regulate space launches [13], the focus of this paper is on occupational health, safety, and historically marginalized communities within this context.

And while OSHA has eliminated some occupational diseases, such as "brown lung" disease in the textile industry, "the agency has not clearly controlled toxic substances that cause chronic disease as broadly as the EPA has." OSHA has only set exposure limits for 18 hazardous substances, while there are roughly 70,000 chemicals in commerce, and while the German equivalent of OSHA has set limits for over 1000 substances [11].

In the article, Fellner explains that the agency provides occupational safety and health on a federal level, much to the chagrin of some states. Furthermore, contention surrounds OSHA's objective to "regulate by shaming," which is exemplified by press releases and expensive penalties. Furthermore, the agency posited the idea of publishing "hundreds of thousands of employer injuries and illnesses on OSHA's website" with the supposed goal of persuading employees, customers, and vendors not to work with companies based on their injury records. But, Fellner also states that even though OSHA has gone a bridge too far from time to time, OSHA has created a culture of safety that is exemplified in pre-work safety talks and risk analysis. "Employers have dramatically reduced injury rates simply because of OSHA, with all its excesses" [11].

In contrast, in the article, Finkle writes that OSHA has done little to reduce the risk of illness and injury of workers, with occupational disease becoming the eighth leading cause of death. According to the judicial interpretations of the Occupational Safety and Health Act of 1970, OSHA is allowed to:

- reduce excess risks of chronic disease to far below 1 chance in 1000, even if there are as few as several hundred exposed workers nationwide;
- impose costs high enough to threaten some firms' viability, so long as the costs don't "threaten the profitability of an industry as a whole";
- impose a "general duty" on employers to remedy safety or health hazards even when no specific OSHA regulations exist, or even when obviously weak and antiquated rules apply;
- force industries, if necessary, to install novel risk-reducing technologies that go "beyond what the industry is presently capable of producing"; and
- change the fundamental nature of certain jobs (e.g., farms can no longer employ people to stand within grain silos to loosen the product) [11].

But, Finkle states that despite these capabilities, OSHA defends its "won-lost" percentage more energetically than it provides support to the departmental infrastructure that protects workers, refusing to impose costs that exceed 1% of any firm's revenue, severely limiting the capabilities of the department. Furthermore, in the article, Rabinowitz writes that many standards are woefully out of date and based on information from the 1960s or earlier. It takes OSHA 7 years to complete a new standard, and since 1970, OSHA has issued only 37 major health standards and 55 major safety standards, with the average penalty for a serious violation (death or serious physical harm) being just $2148 [11].

4 | A New Frontier, a New OSHA

In the context of the space race, from exploration to possible colonization, optimizing OSHA for a new frontier will be imperative to protect workers from new dangers. Private establishments that are "primarily engaged in the operation of space flights on their own account are classified in Transportation and Public Utilities, Industry 4789." Industry examples range from cabs, horse-drawn, sleeping cars, and other passenger car operations to space flight operations, except for government [14].

Industry category 4789 is underprepared to protect workers who are involved in space flight operations, both in terms of risks to workers and potential financial incentives to protect worker safety. Space, as an environment, is not compatible with life, with astronauts and space tourists being exposed to galactic cosmic rays that are composed of high-energy protons and high charge (Z) and energy (E) that can increase fatal cancer risks [15]. Furthermore, it is impossible to maintain homeostasis in the crushing vacuum of space without mechanical intervention, visual disturbances, cognitive impairment, a shift in circulation, and a change in immunological mediators. Additionally, psychological issues can arise from living in confined areas for prolonged periods of time [16].

Under the Occupational Safety and Health Act of 1970, employers have a responsibility to provide a safe workplace, and it currently covers all 50 states, DC, and other US jurisdictions [14]. In this context, under the Outer Space Treaty of 1967, space and celestial bodies cannot be appropriated by nations, but objects launched into space and personnel on board these objects remain under the jurisdiction of the state of registry [17]. Objects launched into space, from research stations to tourist flights, are under the jurisdiction of OSHA.

And there are early signs of space regulations in OSHA's A-Z registry. Despite Industry Code 4789 encapsulating space flight operations, the A-Z registry, which provides a comprehensive index of OSHA regulations, does encapsulate some space-specific risks to workers. More specifically, "radiation" just encapsulates nonionizing radiation (from extremely low-frequency radiation to radiofrequency and microwave radiation, to infrared radiation, to visible light radiation, to ultraviolet radiation, to laser hazards) and ionizing radiation (where sources are air and space travel and transport). The page "Ionizing Radiation" states that standards to protect workers from ionizing radiation, but "OSHA's Ionizing Radiation standards have not been substantially revised from the provisions in

the original 1971 version of 29 CFR 1910.1096." Updating OSHA's ionizing radiation standards to protect workers in a new technological paradigm, protecting them from both the short-term and long-term damages of radiation, suits the ethos of the department.

Calling back to the Environmental Law Institute, in which the article states that OSHA has only set exposure limits for 18 hazardous substances, versus the German equivalent of OSHA, which has set limits for over 1000 substances, the importance of preventive regulation to protect human health and lives is clear. Historically, protective measures tend to be reactionary rather than anticipatory. From the public's reaction to *The Jungle*, a 1906 novel by Upton Sinclair that denoted the hazards of the meat-packing industry, was a precursor variable to the creation of the Food and Drug Administration in 1927, to *Silent Spring*, a 1962 novel by Rachel Carson that denoted the impact of indiscriminate use of pesticides, which caused discussion that resulted in the formulation of the EPA in 1970, the United States has a history of reactionary legislation after documented harm [18, 19].

Furthermore, penalties need to be monetarily incentivizing enough to ensure that corners will not be cut; $2,148 pales in comparison to the 2025 evaluation of SpaceX and Blue Origin, the current leaders in the privatized space race. SpaceX is currently valued at $350 billion, and Blue Origin is a private company, owned by Jeff Bezos, with a net worth of approximately $190 billion [20, 21].

5 | The Critical Mineral Crisis, Mining, and the Space Race

> *Few areas of competitive activity so dramatize the contemporary struggle among nations for power and prestige as does outer space [22].*

And space—from exploration to possible colonization to the economic incentives surrounding mining for metals and minerals—may very well turn into a highly industrialized zone, rather than the barely tangible biome it is today. Critical metals and minerals are used for technology and manufacturing needs. These are vital for the computing, transportation, and energy sectors. Furthermore, the United States is over 50% net import reliant on metals and minerals in 2022, according to the 2023 US Department of the Interior Geological Survey [23, 24].

According to Jeff Bezos, owner of Amazon and Blue Origin, he envisions a "future in which Earth is zoned residential and light industry, with heavy industry and mining moving to space" [2]. Furthermore, in the face of the 2025 tariff trade war, the Trump administration is drafting an executive order to enable the stockpiling of metal found on the Pacific Ocean seabed. It is clear that the critical mineral crisis is leading to an expansion of traditional mining [25].

Furthermore, start-ups such as AstroForge, founded in 2021, and Planetary Resources, formed in 2009, aim to mine asteroids. Asteroids contain critical minerals that are used in consumer electronics. Widespread adoption of this sector, and the advent of the technology needed to implement it, may not be possible in the immediate future, according to Richard Binzel, an astronomer who taught planetary science at the Massachusetts Institute of Technology, but rather a "resource for the space economy of the 22nd century." Meanwhile, other academics, such as Khairutdinov et al. denote the direction that technologies must develop to extract minerals from space [26].

Regardless of the implementation of space mining, forecasting threats and mitigating risk to workers is imperative. Terrestrial mining is associated with silicosis, black lung, hearing loss, strains, sprains, fires and explosions, machinery struck by injuries [27], and death, with an average of 30 fatalities in the past decade [28]. Additionally, the Department of Energy also has an incentive to invest in space, as indicated by a webpage denoting its interest in space-based solar technologies [29].

6 | Neoliberal Market Conflicts: Safety and Economic Incentives

Neoliberalism, a market philosophy that has dominated American economic policy, is a model that emphasizes the value of free market competition and is associated with laissez-faire economics; neoliberalism is characterized in terms of its belief in economic growth as tantamount to human progress, its confidence in free markets as the most efficient allocation of resources, and its emphasis on minimal state intervention in economic and social affairs, as well as its commitment to the freedom of trade and capital [30]. Neoliberalism can also be defined as the refusal of Keynesian policies, which advocate for increased government intervention in the economy, to stabilize capitalism and protect citizens and the Marxist precepts of a centralized state planning system [31].

Chapman states that neoliberalism has been the dominant political ideology for the past 40 years and poses significant challenges to human rights, particularly economic, social, and cultural rights. Neoliberal doctrine reduces the role of the state, in which human rights are dependent on protection and implementation, and may diminish or eliminate social and welfare programs as a safety net for the poor, with policymakers often arguing for the privatization of infrastructure, utilities, and social services [32]. Meanwhile, neoliberal philosophy is so dominant in the United States to such an extent that the United States is not a party to the United Nations' International Covenant on Economic, Social, and Cultural Rights 33. This resolution states numerous rights that nations should try to provide for their citizens, including the right to maternal leave before and after childbirth, consent with marriage, adequate food, clothing, and housing, and the right to education (United Nations, n.d.).

In the United States, colonialism and neoliberalism are closely related. The history of colonialism—from the genocide of Indigenous Americans to the advent of chattel slavery, subjugating millions of enslaved people, to Manifest Destiny in the 19th century, originated from the idea that the United States had the God-given directive to expand its reach, spreading democracy and capitalism; this idea of economic capital being

God, and cultural capital being myopically American, have hundreds of years of history.

Forjwuor explains that the geologies of these terms showcase how self-governance under a liberal democracy works to accomplish neoliberal objectives, which curtail the legitimacy of ipseity (individual identity), which is essential for democratic values. The sense of dominant hegemony that Western neoliberal values attempt to create across the globe showcases how "what took violent colonial oppressive rule to accomplish is now accomplished with ease under neoliberal mandates" [31]. This sense of control and abuse can be seen through rhetoric, such as "maldevelopment," "corruption," and "the third world." Colonialism, which in the United States has led to long-term inequalities with race and class that are still seen to this day [34].

OSHA can play a role in reducing the legacy of colonialism in the neoliberal American marketplace. While the Equal Employment Program, OSHA prohibits race-based discrimination, there are still reports of bias with OSHA protections, with a Union in South Carolina filing a claim that OSHA failed to protect Black workers, failing to adequately inspect workplaces that are dangerous for employees and employ a large number of Black Americans. An estimated 416,000 South Carolinians are employed in the state's food, beverage, general merchandise, food service, and warehouse industries, with a disproportionate number of employees being Black. "But, between 2018 and 2022, [S. C. OSHA] conducted only two scheduled inspections of facilities in those industries combined." Meanwhile, S.C. OSHA conducted 499 inspections of the construction and specialty trade contracting industry, where Black workers are underrepresented [35].

In the report, a worker in the food industry described how she was required to work in a kitchen without water breaks in August after the air conditioning went out. In another incident, a worker in a store reported that the emergency exits were blocked and "the store was infested with mold and rats," but the report was closed after the company submitted a response with photos from a different location [35].

It is impossible to know what space exploration and colonization will look like, but dismantling existing biases and improving existing operations to create a more equitable and just world is vital [36]. explain that there is an invisibility to racism in the global neoliberal area, but that "racism can be internalised and seen through individual actions and structural inequalities." Racial inequalities in healthcare can be understood through a lack of access to opportunities, stereotypes, prejudice, and discrimination against certain minority groups [35].

Some theorists, such as Campa et al. posit that space colonization will be fully automated, as humans cannot live for very long periods of time in outer space, limiting the prospects for human space colonization. Crewed missions will have an ancillary function, in which machines or human/machine avatars will inhabit other celestial bodies to pursue economic enterprises and progress scientific discovery. The authors argue that since humans decided not to settle en masse in the Sahara desert, "we can hardly expect that they will settle on Mars..." and only see that as a possibility in case of a catastrophe on Earth [6].

While full automation is a possibility, Finney states that space is being humanized, with people learning to live and work in orbit, with the actual settlement being developed in another portion of the solar system seemingly almost at hand. She states that settling on the Moon, or further, represents an extension of our Earthly behavior, not a departure, and that life in space is already becoming more complicated as physicians, physicists, engineers, and other specialists begin to outnumber the traditional staff. She also discussed norms surrounding reproduction in space [37], implying that the colonization of space will not be fully automated.

There are drastically different visions around what the expansion of humanity into space will look like. Some may advocate for a fully automated workforce, while others see humanity itself living in space. Worker safety will have to be considered, with a particular emphasis on extraterrestrial safety if humans decide to populate space ourselves.

6.1 | Reframing Neoliberal Market Values and Challenging Delocality Through Indigenous Philosophy

OSHA can challenge the ethical framework that the United States' economic and social system is rooted in neoliberalism and colonialism, ensuring room for plurality, recognizing disparities in power within the United States, and potentially allowing for Rawlsian rule within the 21st-century space race. Ethics are not separate from policy. Holahan and Bardakh explore the relationship between ethics and public policy, finding that evaluating a healthcare scenario from an ethical perspective can "provide a framework that can guide decision-making toward a good or, at a minimum, morally permissible outcome" [38]. By implementing indigenous philosophy into policy, stakeholders can make more inclusive policies that emphasize the heritage of, and protection of, BIPOC individuals.

According to Burkhart, in "Refragmenting Philosophy through the Land: What Black Elk and Iktomi Can Teach Us about Locality," the Western ideals that place absolute value on the unchangeable and rationality are due to a false sense of security caused by delocality and coloniality, leading to the false sense that Western thought is the only valid thought. Burkhart states:

> *Joseph Marshall, in his book on Lakota stories, recounts another story of Iktomi (the Spider Trickster) tricking Mato (the bear) by playing on the latter's honor and honesty. Marshall opines, "our current method of choosing leaders reminds me too much of Mato's loss at the hands of the clever Iktomi.... As a society we reward arrogance and 'attitude,' and our heroes tend to be loud and brash sports figures, millionaire developers, movie stars, and the like—those kinds of people who don't know, or don't want to know, what humility is [39].*

This sense of disconnect from I-Thou or I-We can be seen firstly in the need for OSHA regulations and the punitive nature of regulations. Instead of the sense of protection being inherent in our social and economic structure, it needs to be built in externally. It can secondly be seen in the disconnect between the stated goals of OSHA and the protection of vulnerable populations in the United States, as denoted by the failure of S.C. OSHA to protect Black employees. By focusing on the I-We and I-Thou relationship between employers and employees, instead of profit maximization, and having equitable audits, OSHA can help support the exploration and settlement of space, perhaps leading people to eschew the word colonization of space in this context as well.

7 | Conclusion

Stakeholders will need to decide what acceptable levels of risk are in the exploration, colonization, and commodification of space. Existing infrastructure exists to quantify risk on our planet—thousands of years of social norms, policy, and debate that shape a finite globe. But, with the space race, acceptable risk and personal autonomy will have to be considered alongside federal regulations to govern immensely wealthy and transnational companies that are morally obligated to their stakeholders, not to Earthly citizens. OSHA's potential utilization of decolonizing ethics and preemptively having federal regulations in place before the widespread exploration, colonization, and monetization of space, will protect vulnerable communities in a new biome in which one's very existence is tenuous. Furthermore, setting strict environmental safety regulations on space-specific health risks, such as ionizing radiation, will be vital.

Space may not change humanity—all the pitfalls, hopes, dreams, aspirations, and ambitions—but rather magnify the scale to something that is incalculable and incomprehensible to our current society. Preemptively building a strong social infrastructure will allow us to scale a safe, just, and equitable social system from the Earth to the stars.

Conflicts of Interest

The author declares no conflicts of interest.

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Overview: Assesses ethical debates around genetic and technological human enhancement through feminist and non-feminist frameworks.

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The bioethics of biomodification for the future of space exploration: Evaluating insights from feminist and non-feminist approaches

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ABSTRACT

This article analyzes the bioethical challenges raised by applying human enhancement to future space missions. We first outline mission-specific justifications for bioenhancement –framed within a utilitarian approach tailored to space policy – while rejecting the view that the space environment is morally discontinuous from Earth. We argue instead that moral evaluation should be continuous across environments, even if operational constraints differ. Our central claim is a conditional defense of bioenhancement: under clearly specified mission profiles, expected welfare gains can outweigh risks, provided stringent safeguards are in place. The strength of this justification varies with mission type (exploration, long-duration settlement, in-situ resource utilization, and reproduction in space). We identify uneven risk burdens for particular groups, especially women, people with disabilities, and private-sector spaceworkers, and specify where risk-transfer and consent problems are most acute. We also introduce a feminist lens that both broadens the problem space and surfaces concerns neglected in mainstream space ethics and bioethics (e.g., labor exploitation, reproductive justice, and design biases). While this lens substantially improves risk detection and governance design, we show that a fully comprehensive feminist framework may resist endorsing space expansion under non-ideal social conditions. The paper concludes by mapping policy levers that can reconcile a mission-sensitive utilitarian rationale for enhancement with feminist requirements of fairness and non-domination.

1. Introduction

Human space exploration and exploitation can be undertaken for a variety of reasons. Among the main reasons for undertaking space exploration, as well as planning for it in the future, are scientific investigations, commercial purposes, or, more often within the philosophy and ethics of space exploration and risk and disaster studies, space exploration is viewed as a solution to saving humanity from future global catastrophe on Earth (Munévar, 2023). Perhaps all these reasons seem too idealistic and naive when confronted with the realities of a non-ideal world. In this non-ideal world, the real motivations are political, in a sense nationalistic, and military, accompanied by profit motivations. However, at present, there seems to be insufficient political motivation to commit national space agencies to large-scale human mission projects. The most likely drivers of future space expansion are profit-driven private initiatives

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known as Space 4.0 (Chatzitheodoridis et al., 2024).

This article examines whether, and to what extent, the ethical case for radical biomedical enhancement of future deep-space crews should track the rationale of specific mission types. After situating bioethics within futures thinking, we develop a consequentialist, non-feminist analysis of enhancement options and treat germline interventions as a special case. We then show how justificatory standards shift with mission purpose, offering targeted analyses of research missions, space mining and commercial exploitation, and space settlement. Throughout, we use thought experiments to test claims about risk, utility, and consent, and we argue that although reasons for applying controversial procedures often should be assessed against mission goals, rights-based claims do not always depend on purposes – for example, the justification for abortion should not hinge on expected outcomes (Kendal, 2023). This sets up a rights-based pivot: if hazard mitigation can underwrite a right to biomodification in space, parity of reasoning forces us to ask why closely analogous rights, most clearly reproductive autonomy, remain so contested on Earth.

Against that backdrop, from a feminist bioethics perspective, pregnancy and childbirth remain high-risk forms of bodily labor, and abortion functions as a risk-avoidance measure for those likely to face serious gestational harms. If we are prepared to recognize a right to biomodification for astronauts on grounds of bodily integrity and hazard mitigation in an extreme environment, parity of reasoning supports at least as strong a right to abortion in ordinary, gendered environments. Rights grounded in protection against grave, non-consensual risk should not depend on whether the risks serve prestige projects or social expectations of reproduction. The anticipated ease with which biomodification may attract universal acceptance, compared with abortion, exposes androcentric and pronatalist bias and suggests that normative priority should run from reproductive risk-mitigation to spacefaring enhancement, not vice versa. Thus, if the right to human enhancement is recognized as a procedure with a status analogous to those behaviors that are considered human rights, the problem of its moral justification will disappear. And even if the right to human enhancement does not gain the status of one of our human rights, human enhancement as such may lose its controversial status, analogous to the status of organ transplantation, formerly controversial, or in vitro fertilization. The latter is usually no longer controversial to the public, while it faces criticism from some religions and conservative governments.

Arguing for a moral justification for human enhancement within the non-feminist bioethical tradition and linking bioethics to futures studies, we use a thought experiment. The thought experiment is one of the main tools of the speculative method in bioethics and is also useful for designing future scenarios. Speculation in bioethics makes it possible to test our moral intuitions, highlights current bioethical and social issues, as well as enables a cautious approach to the phenomenon of technological determinism, which is the recognition of technologies as inevitable (Johnson & Romanis, 2023). Finally, we outline a potential framework for a feminist approach to the philosophy and bioethics of space exploration and show how it differs from traditional space mission philosophy and bioethics with respect to the issues of human enhancement and justification for space missions discussed.

We present the feminist approach to space exploration at the end only as an alternative, because from the interpretation of feminism we present, expansion into space is difficult to justify morally. Feminism is marked by internal diversity. Feminists often reach divergent judgments about the same practices and institutions (Jenkins, 2024). This pluralism is standard in feminist philosophy and ethics, as seen in disagreements over sex work, pornography, assisted reproduction, and related issues. While some feminists do not oppose space exploration, we adopt a critical feminist interpretation. Our rationale is programmatic: contemporary space efforts are entangled with a capitalist–nationalist–military power nexus, entail significant opportunity costs amid urgent global needs, and predictably exacerbate global injustice and harms to vulnerable groups. Moreover, biomodification and reproductive governance in small, closed populations risk gendered domination and consent deficits. On this view, space exploration is difficult to justify, and the justificatory burden rests with its proponents to rebut these justice-based concerns.

2. Bioethical thinking about the future in space

One of the main purposes of this paper is to highlight the importance of futures thinking for the development of bioethics in relation to future space missions. We contend that bioethics is the most important of the branches of philosophical reflection about our future in space. Other branches of the philosophy and ethics of space exploration include the ethics of astrobiological issues, ethical evaluation of the justification for space expansion, environmental ethics and the issue of terraforming space objects, as well as feminist philosophy and ethics applied to space exploration plans in relation to social justice, global exclusion, the costliness and exclusivity of this endeavor, and candidate selection (Szocik, 2023a, 2024). Feminism has an important role to play in reflecting on the morality and meaningfulness of space exploration, for regardless of its conclusions, feminism always contains an important critical element that other, non-feminist perspectives often lack. Bioethics matters here because it interrogates the moral trajectory of any prospective spacefaring society, even if permanent settlement remains distant and uncertain. Our contribution to futures thinking is present-oriented: near-term governance of biomedical procedures for space missions will set path-dependencies for the norms of any future workforce and communities off-world. Drawing on Martin Sand's notion of "not having a future," we highlight an exclusion risk: under the current nation–capital–military impetus, access to space, and thus to key loci of future opportunity and security, may be reserved for elites, leaving most without a meaningful share in the future (Sand, 2019). This strengthens the justice-based case for precaution now: evaluate human enhancement, selection, and reproductive governance for how they distribute futurity itself, not only immediate mission risk. Solutions implemented in the space at the beginning, according to the dynamics of the "founder effect," can be difficult to modify and affect future generations (Elvis et al., 2022). These biomedical procedures and issues concern the concept of

human enhancement of future astronauts and future space settlers, the criteria for selecting participants in space missions based on a certain concept of the norm, as well as several issues concerning human reproduction.

We argue that the balance of benefits and losses suggests that a future world in which biomedical human enhancement procedures are applied is a better world than one without permission for human enhancement. In what follows, we discuss the consequentialist argument[1] for the use of human enhancement, considering the potential use of germline gene editing. We then point out the potential similarity between the bioethics of future space missions and present-day military bioethics. Finally, we analyze how the justification for the use of biomedical modifications may depend on the purpose and rationale of specific types of space missions. We are building on our previous publications, where we only outlined the potential dependence of human enhancement on mission type, as well as the potential similarity to military ethics and bioethics (Szocik & Braddock, 2022; Szocik, 2023a, 2023b). In comparison with these publications, we here expand our consequentialist argument by showing that consequentialism and utilitarianism[2] find strong justification in the context of future space exploration. It is worth adding that the consequentialist orientation is not an ethical profile specific only to the sphere of space exploration. Consequentialism is appropriate for public policies in general. Despite our consequentialist perspective, we also note the problems raised in recent discussions on the bioethics of space missions, which tend to apply a utilitarian perspective. These comments mainly concern the objection of moral exceptionalism in the way we think about the environment of space missions (Balistreri & Umbrello, 2022a).

While outlining the case in favor of justifying genetic modification for future space exploration, we also consider the possibilities of what can go wrong in justifying this procedure. We note that modifying future participants in space missions is a good idea in principle, but when an intersectional feminist lens is applied to consider certain configurations of events, it can be seen that groups that do not meet the norm, which is usually the (white) male body and (white) male psyche, may come under particular pressure, i.e. women, queer and trans people, people with disabilities, indigenous people and people of color, to name but a few. People with disabilities may be excluded from participating in space missions at all, which until now at least have involved having a non-disabled background. People with disabilities thus collide with the paradigm of a participant in space exploration, and it can be doubted whether the political in-roads made by feminism and disability studies and activism will be enough to influence mission planners and organizers to convince them to be fully inclusive during selection processes. Paradoxically, human enhancement may be a tool which, ostensibly serving empowerment, may in practice be a source of female disempowerment and a tool of oppression. Feminist bioethicists point to the dangers caused by the development and popularization of digital health technologies (Paton, 2022). Analogous oppression may apply to people with disabilities (Scully, 2008, 2022). An intersectional feminist approach, i.e., a form of thinking that considers the ways in which gender intersects with issues of race, ability, sexuality, class and belief, is a useful conceptual tool for exposing the complexity of mechanisms of oppression and exclusion (Crenshaw, 1991; Hunt, 2017; Ciurria, 2020). The fact of having any characteristic defined in an ableist society as a disability conflicts with our idea of the cosmos as a demanding place for the best prepared. Human enhancement policies may further exclude candidates with disabilities if biomedical enhancements are given to people without disabilities. Being disabled will not fit into this logic of ableism. In turn, regarding the rationale for carrying out specific missions, we point out that a group particularly vulnerable to exploitation will be employees of space business corporations.

In our paper, we essentially present a perspective specific to the non-feminist bioethical tradition, that is, one that does not take the categories of gender and exclusion as its starting point. Consistent with our broader view, adopting a feminist lens to evaluate present-day and near-future space exploration and biomodification may lead us to question the moral justification of any mission (Szocik, 2025b; Szocik & Abylkasymova, 2025). Similarly, from a feminist perspective, a morally unacceptable procedure may be radical human enhancement, where, given certain social and political dynamics, biomedical emerging technologies will increase rather than decrease the oppression of women and other marginalized groups (Szocik, 2024; Abylkasymova & Szocik, 2024). Many feminists warn of the negative impact of biotechnology on women. Feminist bioethics shows how reproductive technologies can be used to commodify and control women's reproductive capacities (Corea, 1985), how prenatal testing technologies can pressure women and transfer control of pregnancy to medical institutions (Rothman, 1993), and how scientific narratives about the female body shape women's experiences of reproduction and medicalization (Martin, 1987). Finally, Catherine Waldby and Robert Mitchell show how biotechnologies extract value from the human body, especially through the unequal mobilization of female and racialized bodies. They dispel doubts that emerging technologies – at least some of them, and at least in certain alignments of power – are not only not neutral but are also harmful. This is because they are deeply entangled with social hierarchies of gender, race and class – transforming the body into a site of labor, value and exploitation of neoliberal global capitalism (Waldby & Mitchell, 2006). As we stressed in the introduction, feminism is a heterogeneous current of thought, and among feminists there are also serious critical thinkers who associate with technology the possibility of enhanced agency for women (Firestone, 1971; Braidotti, 2013; Haraway, 2016; Veit & Browning, 2024). It is worth noting, however, that even the aforementioned feminists do not view technology with unreserved optimism, recognizing the risk of technology dominating women's bodies (Haraway, 1991), as well as augmenting patriarchal control (Firestone, 1971). In the article, however, we want to consider the variant in which humanity will and perhaps should explore space. Therefore, adopting an exclusively feminist perspective, at least our highly critical interpretation of feminism, may actually undermine our ability in this paper to uncover the normative ways in which debates on space exploration and biomodification are currently unfolding.

[1] Consequentialism is a normative theory that assumes that the morality of an act depends on the consequences of that act (Sinnott-Armstrong, 2023).

[2] Utilitarianism is a form of consequentialism that states that the criterion for evaluating the morality of an act is its effect on maximizing the overall good (Driver, 2022).

3. Human enhancement and gene editing in long-term space flights[3]

The space environment contains several dangerous factors to humans, with cosmic radiation at the forefront, which can be difficult or impossible to fully neutralize during long-term missions. Long-term missions refer to future hypothetical missions beyond the limits of Earth's orbit, that is, missions that are interplanetary, such as to Mars, and that will last at least several years. Improving the biomedical condition of future participants in such missions through pharmacological means and gene editing may be a reasonable option considering the difficulties and dangers that characterize the space environment. The idea of human enhancement considered for space missions seems to offer a much stronger rationale than analogous proposals for the terrestrial context. The difficulty of the space environment and the lack of entirely effective alternatives thus distinguish the context of bioethical discussion in space from the analogous discussion concerning earthly applications. Perhaps this peculiarity of the space environment will make future long-term space missions the first area of application of biomedical human enhancement on a larger scale.

Human enhancement through genetic modification may include the following genes and functions. In terms of enhancing resistance to cosmic radiation, TP53 genes that regulate the cell cycle and prevent cancer can be modified. Modifications can enhance DNA repair mechanisms; NRF2 (NFE2L2), which are involved in the antioxidant response, reducing oxidative stress caused by radiation exposure; Dsup (Damage Suppressor, from tardigrades), a protein that protects DNA from radiation damage. In terms of bone and muscle maintenance, modifications may include: MSTN (myostatin) inhibiting muscle growth. Eliminating this protein could prevent muscle loss in microgravity; SOST (sclerostatin), which regulates bone density. Suppressing it could prevent osteoporosis in space; COL1A1 and COL1A2 involved in collagen production and bone strength. Regarding enhancing the immune system, modifications may include FOXO3 associated with longevity and immune resistance. Enhancing its function may improve immune responses; as well as IL7R (interleukin-7 receptor), which is important for T-lymphocyte production, which is impaired in space. Worth considering are gene editing for neuroprotection and cognitive function, such as BDNF (brain-derived neurotrophic factor), which supports brain plasticity and function, counteracting cognitive decline, such as CLOCK AND PER2, which regulate circadian rhythms that are disrupted in space (Borg & Baker, 2021; Hadhazy, 2019; Mason, 2021, 2023; Kendal, 2024a).

One of the most popular understandings of human enhancement considers enhancement to be those modifications that improve cognitive and physiological functions to a level beyond the species norm (Lewens, 2015). The term enhancement postulates the creation of a better version of us, improvement of the biological organism in relation to what is considered its normal, healthy state (Bostrom & Roache, 2008). Bioethics of human enhancement discusses issues such as the norm and going beyond the norm, justification for modification, its scope and purpose. Some authors emphasize the importance of the degree of modification, while others expose the role played by how the modification is carried out. An important distinction is that between therapy and enhancement, which is not related to health. Usually the former is justified, while the latter is often prohibited or requires special justification. Although this distinction has been widely criticized, its preservation is pragmatic, in part because it establishes the range of modifications possible for public funding. The issue of public fudging is important if only from the perspective of social justice. However, it does not protect against the possibility that human enhancements can be used by the rich and privileged to gain advantages that guarantee an advantage over the rest of society, such as longer life, greater fitness, better health, or perhaps in the future modifications affecting cognition, morality or intelligence.

What is meant by radical human enhancement is such biomodifications that are carried out by biomedical means requiring intervention in the human body, and therefore are invasive, may be irreversible, and even hereditary. These measures must also result in some significant modifications, although these need not necessarily be modifications that violate so-called human nature. The argument concerning the need to protect human nature and render it inviolate is one of the strongest and most popular arguments against the idea of human enhancement (Roduit et al., 2013). We, on the other hand, are inclined to the views of those theorists who reject the notion of human nature as an empty concept (Hull, 1986; Caplan, 2004). We also argue that even if such a metaphysical construct as human nature existed, human enhancement would not influence it.

An interesting context for the discussion of human enhancement is the issue of human redesign. The issue of redesigning through biomodification, especially through gene editing, both somatic and especially germline, can be understood in at least two ways. In one approach, human redesign, which means changes so advanced that they significantly alter several parameters and may even lead to the evolution of a new species, may be a side effect that was not intentionally planned by the initiators of genetic modification. In the second option, such advanced changes may be planned intentionally. In the latter approach, human redesign would be understood as the implementation of an ideological program.

In our article, we reject the concept of human redesign. When considering the concept of human enhancement, we treat it in terms of preventive and therapeutic activities. None of the biomedical human enhancements we consider would lead to functions not possessed by unmodified persons, since the only effect of these modifications would be only to improve certain abilities and modalities inherent in humans, such as resistance to cosmic radiation or the microgravity environment. Even the introduction of genetic modifications such as biomedical moral enhancement, however controversial, would lead neither to the redesign of humans nor to the creation of a new species, for it would be geared toward the exposition of selected traits of behavior, conduct, motivation or emotion that fall within the spectrum of human characteristics. The possibility of evolving a new species cannot be ruled out, however, this

[3] Some works discussing the concept of human enhancement for space flights include (Szocik, 2015, 2019a, 2019b, 2020a, 2020b, 2020c, 2021, 2023a, 2023b, 2024; Szocik et al., 2018; Szocik & Braddock, 2019; Szocik et al., 2019; Szocik & Tachibana, 2019; Szocik & Wójtowicz, 2019; Szocik, Norman, et al., 2020; Szocik, Wójtowicz, et al., 2020; Abney & Lin, 2015; Mason, 2021; Balistreri & Umbrello, 2022a; Balistreri & Umbrello, 2022b; Balistreri & Umbrello, 2023).

seems significantly hampered by the need to meet several factors, among which are the need to remain in isolation, as well as the long-term significant impact of selection pressures. It is worth emphasizing that human enhancement – perhaps somewhat paradoxically from the point of view of those convinced that biomedical human enhancement would lead to the emergence of a new human species – will be a factor that may precisely inhibit such evolution.

Consequently, the changes that will be initiated because of the genetic modifications that will be carried out will not lead to radical changes, nor will they have a population range that would justify talking about the creation of a new species. Potential side effects should be minimized, so it is important to prioritize the mission and assess whether sending humans – who, in addition to the standard risks inherent in space missions, may also face risks from biomedical human enhancement – is morally justified by the significance of the mission objectives. Issues related to the risks and challenges of applying human enhancement in space, as well as the possibility of evolving a new species and redesigning humans, have been analyzed elsewhere (Szocik, 2020c, 2023a, 2024).

In conclusion, according to the traditional philosophical approach to bioethics, the idea of human enhancement considered for future space exploration and exploitation finds justification on many levels. It is justified medically and from the point of view of risk safety, it is justified nationally and politically from the point of view of imperial government space agency policy, and it has an economic rationale – not only can such modification be cheaper than alternative infrastructure modifications, but it will also be required by the mission success criterion. If the criteria for safety and efficacy are met, with a traditional, that is, non-feminist perspective, it is difficult to find arguments against the use of human enhancement in space. As Evie Kendal points out, there are good reasons in principle for postulating a kind of moral obligation to biomedical human enhancement for future space exploration. The need to be concerned about eliminating potential risks such as the safety of applied modifications, equal access and the risk of genetic discrimination do not preclude a moral justification for a human enhancement program for space missions (Kendal, 2024a).

Nevertheless, let us consider three hypothetical scenarios of a future world in which human enhancement remains forbidden, as well as a world in which human enhancement is allowed. These scenarios are based on an idealist non-feminist understanding of bioethics. They do not consider feminist criticism, which we will refer to later.

4. Thought experiment 1: a world without human enhancement

Suppose the normative demand of opponents to human enhancement is accepted at the political and legal level, and we live in a society where human enhancement is banned. Given the strong opposition to human enhancement and gene editing, this is a possible scenario. To demonstrate that banning human enhancement is morally undesirable, we assume that such a ban could be effectively maintained and enforced at the population level, and that no exceptions would ever be permitted, regardless of future rationales or emerging interests. What, then, would be the consequences of a ban rooted – at least in part – in people's moral intuitions? Consider three hypothetical scenarios of a non-preferred future.

4.1. Scenario 1: population-based diseases

Human enhancement can be used for disease prevention. Imagine being able to make such changes in the genome of an embryo that genetically modified humans will be resistant to many diseases. We live in a society in which we are not allowed to inflict human enhancement, especially one as radical as germline gene editing (GGE). The cost paid for being faithful to our moral principle, which is the idea of the immutability of our nature is the suffering and death of the sick, as well as the attendant costs and losses. This is a scenario that is difficult to imagine from the perspective of utilitarian ethics.

4.2. Scenario 2: climate change

Let us imagine that a way to mitigate the negative effects of climate change is biomedical moral enhancement. Imagine that there are tools to biomedically modify our morality in such a way that our decisions and actions do not harm the environment. The goal of such biomodification would be to make the concept of climate change, the negative effects of global warming, and overpopulation a close idea to us, as deeply felt as one's desire to do good for one's genetically related relatives. Imagine if biomedical moral enhancement led to mechanisms that worked the same way as kin selection. Only that our inclusive fitness after modification would include not only ourselves and our relatives, but all of humanity, and the modus operandi would be to care for the environment.

But our deep-seated moral intuitions make the concept of moral bioenhancement incompatible with our principle of immutability of our nature. We therefore admit that it is not in our nature to act pro-environmentally, nor to act for the good of the population, an endeavor which overlaps significantly with pro-environmental action. Since we are unable as a population to change our habits regarding energy consumption as well as reproduction – although the latter is a controversial issue and at the outset violates reproductive rights and reproductive freedom – we are inevitably headed for disaster. Moreover, even if this climate catastrophe does not lead to our extinction in the sense of literal extinction, at the very least it will significantly worsen the quality of our lives and especially the lives of future generations.

4.3. Scenario 3: space settlement

In the third scenario, we envision a near future in which humanity is either compelled to abandon Earth or chooses to remain while space-based living offers a comparatively superior quality of life. As such, residing in a space habitat may yield greater prospects for well-being and human flourishing than continued life on Earth. Crucially, however, we assume that participation in such space

missions is contingent upon undergoing biomedical human enhancement. Within a speculative society governed by moral bioconservatism, such interventions are categorically rejected. This raises pressing ethical questions about autonomy, distributive justice, and the legitimacy of restricting access to potentially life-improving futures based on resistance to enhancement technologies. Humanity may be aware of the risks of continuing to remain on Earth and is aware of the need to evacuate, but its energy and efforts are focused on even more intensive development of space technology and medicine. These efforts do not include human enhancement. As a result, humanity is annihilated, however not completely, and the survivors have lives barely worth living. Alternatively, instead of a single catastrophe of global proportions, humans experience steadily worsening living conditions; at the same time, they perhaps know that life in a space settlement they did not have time to build would be a life more worth living.

5. Thought experiment 2: a world with human enhancement

Imagine a world in the not-too-distant future where human enhancement is widely accepted and used just like education or therapeutic methods. No one notices its controversial nature. In such a society, the appearance of new diseases is not a problem if they can be prevented by somatic or germline gene editing. Humanity simply embraces the available means, seeing nothing immoral in them and instead seeing the positive effects of preventing or even eliminating disease.

At some point, humanity will realize that the only way to confront climate change, and incidentally perhaps solve the overpopulation problem, is to apply moral bioenhancement. Humanity on a global level chooses to undergo such modification so that pro-environmental and pro-population behavior becomes intuitive. Consequently, no one even recognizes that environmental concern involves giving up every day conveniences and requires perhaps a major modification of habits.

Finally, space settlement will not be hampered by the adaptive limitations of the human body. Under the quite realistic assumption that the only obstacle will remain the ability to effectively protect human health and life from the harmful effects of cosmic radiation and altered gravity, and that the only alternative for a long time will be human enhancement alone, humanity will be ready to pursue long-term space exploration leading to the establishment of space settlement. If it turns out that at a given time of implementation of the plan for the settlement of space will require the application of human enhancement, this will not be treated as an obstacle that must not be crossed.

We assume that the role of the state is to expand, rather than restrict, individual opportunities. Just as this principle underlies rights to abortion, euthanasia, and assisted suicide, it should likewise apply to biomedical human enhancement. This position is supported by the thought experiments discussed above, which suggest that access to enhancement technologies is likely to yield greater benefits than harms. However, this does not discount the possibility of significant negative consequences arising from the legalization and widespread use of biomedical human enhancement. We will address this concern in the final section, which offers a critical analysis of space exploration and human enhancement through the lens of feminist bioethics.

6. The consequentialist argument for human enhancement

The above thinking expresses consequentialism, or utility-based ethical reasoning, which justifies applying different means and solutions to achieve morally desirable outcomes. The principle of utility, Lewis Vaughn suggests, is not so much a stand-alone principle like other traditional bioethical principles, such as the principle of autonomy, justice, beneficence and non-maleficence, as it serves a supplementary function to them. The principle of utility is a fundamental principle used in public policies, especially in health policy (Vaughn, 2023, 11–12). With respect to the three scenarios discussed above, we consider such outcomes to be: a population free of major diseases, rather than a population plagued by diseases (assuming human enhancement can free us from these diseases); a population that can last as long as possible on Earth having a life worth living above the zero or lexical level (Mulgan, 2006) (assuming that moral bioenhancement, universally applied, will enhance the quality of life by reducing the negative effects of climate change, assuming that it is not too late); a population that, if the effect described above is not possible, will be able to continue to live a life worth living in a space base (assuming that life in space will guarantee a life more worth living than remaining on Earth, and will be both technically and medically possible from the standpoint of being able to apply human enhancement).

We would consider our position controversial if the above-mentioned outcomes are challenged and their alternatives are proposed as a more desirable state of the world.

We also believe that human enhancement can solve the problems generated by traditional consequentialism and rule consequentialism, problems related to the concept of reproductive choice generated, in particular, by the latter. That is, we have in mind here the zero reproductive choice rule and the lexical reproduction rule (Mulgan, 2006). According to these rules, we can reproduce whenever we want if we are able to provide life to our offspring that is life worth living above the zero level or above the lexical level. It is difficult to foresee all the possible accidents in life, and even the most privileged parents who can provide a good life from a financial point of view may conceive a child with a serious illness that will reduce her quality of life. Thus, human enhancement is a tool that may not solve risk and uncertainty, but it would certainly offset at least some degree of risk and uncertainty assumed by the precautionary postulate proposed by the aforementioned reproductive choice rules. The alternative to consequentialism understood in this way is antinatalism, according to which in such situations of uncertainty about the quality of life of future human beings and the risk of suffering, which according to antinatalism is inevitable in the life of every human being, the only moral and rational reproductive choice is not to procreate (Szocik, 2025a).

Human enhancement can therefore at least partially solve not only the problems of population ethics, but also the problems identified by intergenerational ethics, the theory of intergenerational collective action, and perhaps even antinatalism. Let us stop for a moment at the latter. Antinatalism concludes that since suffering is inevitable, and it is in an asymmetrical relation to suffering (it is

better to avoid suffering and not experience pleasure than to experience pleasure but also unavoidable suffering), then we should not procreate, since the people who would be born are unaware of the possible pleasures they could experience as humans anyway before they are born (Benatar, 2006). Thus, they cannot regret not being born. Human enhancement can mitigate and somewhat modify these seemingly inevitable conclusions to which antinatalism leads because, at least in theory, for those hypothetical scenarios we have proposed, it offers possibilities for making life more worth living, especially at the population level. Admittedly, it is difficult to imagine a situation in which the human population, estimated in 60 years' time to be more than 10 billion (Lam, 2025), will not experience suffering as a result of effective, mass-implemented biomedical human enhancement. This is not possible at the level of humanity as a whole, nor, even if it were, would it be unlikely to design such biomedical human enhancements that would eliminate all types of suffering and protect against all. But this does not necessarily constitute an argument in favor of antinatalism, since antinatalism is a radical philosophy, and as a pro-extinctionist philosophy – due to its advocacy of the abandonment of reproduction – it has far less claim to becoming a widely shared philosophy.

7. Bioethics of space exploration and human enhancement

What new ideas does the bioethics of space exploration offer in considering the ethical status of human enhancement? The main difference from terrestrial issues discussed by bioethicists is the preventive nature of enhancement considered for space missions, mainly aimed at counteracting the negative effects of cosmic radiation and altered gravity. Human enhancement in relation to Earth is usually considered a form of positive selection, which aims to create or enhance a desired trait. This understanding does not exclude preventive or therapeutic functions if immune enhancement is also a desirable trait. However, preventive and therapeutic functions are the domain of negative selection, while the creation or enhancement of a desirable trait is the domain of positive selection. Human enhancement for space missions changes this paradigm because it implies modifications that are closer to the idea of negative selection than the positive selection traditionally associated with human enhancement.

Space bioethics in the way it conceives of human enhancement challenges the therapy/enhancement distinction. For example, some authors suggest that CRISPR-Cas9 (considered as one of the most basic and feasible forms of genetic modification) application for reproductive purposes is not therapeutic (Rulli, 2019). However, this would lead to the removal of the only type of justification acceptable today (Palacios-González, 2021). Therapy is understood as an effort to match the norm (Greenbaum & Cabrera, 2020). The distinction itself may be challenged when advances in medicine and genetics allow the genome to be freely manipulated to the point where all diseases are eliminated. In such a situation, disease will lose its status as an irremovable phenomenon whose appearance we cannot prevent and often cannot effectively cure. If genetics gives us the possibility of unlimited genetic manipulation, then, as Christopher E. Mason suggests, instead of talking about diseases, we will be talking about limitations which, if we wish, we can remove with genetic modification (Mason, 2021).

The argument that there is a similarity between bioethics in space exploration and the ethics and bioethics of extreme environments, Arctic expeditions, and military ethics is partly justified (Szocik & Reiss, 2023). Consider the similarity between space environments and Arctic expeditions. Difficult environmental conditions, the inability to provide immediate aid, and immediate evacuation are elements common to both environments. Can we imagine a situation in which, for an Arctic expedition, participants must be subjected to human enhancement? The opponents of applying human enhancement may rightly point out that an Arctic expedition is not obligatory for any important reasons. Instead of applying a controversial biomedical procedure, we should avoid situations that may require its application. Necessary situations are an exception, but Arctic expeditions are unlikely to be one of them.

Are space missions different in this respect? In the short term they are similar, in the long term their status is different. In the former case, the necessity of human missions for scientific or commercial purposes can be questioned. If a scientific space exploration is not strategic for the human species, and if the commercial exploitation of space is not important for the survival of humanity or even a partial solution to environmental problems on Earth, space missions are not necessary in the sense of justifying the acceptance of these missions requiring human enhancement.

However, their status changes when considered from a long-term perspective – one that envisions the ultimate goal of human activity in space as the creation of sustainable habitats to ensure the continued existence of the human species. If we accept that any activity in space should be viewed as part of a gradual, somewhat haphazard, yet necessary process leading to the development of technologies that enable long-term space settlement, then even scientific and commercial missions can be regarded as essential steps in this broader trajectory. Within this framework, the application of human enhancement may be morally justified by reference to this overarching objective. But when we relate this reasoning to Arctic expeditions, our conclusions may be similar. If human presence is strategic, then applying human enhancement gains moral justification even if it is normally considered controversial and forbidden. Perhaps, then, space bioethics is not unique in comparison with the bioethics of extreme environments. Perhaps working in dangerous places on Earth would also meet these criteria. What Earth and space extreme environments have in common is the need to provide a compelling rationale for the necessity of these tasks. However, one can imagine a situation where the ethical minimum is the need to follow the rule of informed consent regardless of the justification for the mission or work requiring human enhancement.

What unites and differentiates space bioethics from military ethics? Military ethics is, in certain circumstances, such as the battlefield, the ethics of extreme environments. However, if the tasks performed by soldiers are not directly related to the implementation of combat operations, military ethics loses its status as an ethics of extreme environments justifying the application of human enhancement.

Let us consider the unique characteristics of the battlefield. This setting presents a distinct context for both military ethics and bioethics, setting it apart from other extreme environments on Earth or in space. What distinguishes the battlefield is not only the heightened risk of loss of life – qualitatively different from environmental risks in other extreme settings – but also the fact that soldiers

are required to make decisions about the life and death of others. This latter aspect holds a different ethical weight than in other extreme environments, where such decisions are typically indirect or absent. The act of making life-and-death decisions in the way soldiers must on the battlefield constitutes an exceptionally complex and morally demanding situation, one that requires specific ethical safeguards and support mechanisms. Imagine that cognitive and moral bioenhancement is available that enhances a soldier's relevant cognitive and moral/behavioral functions in ways that improve her decisions and actions involving the life and death of others. Let us assume that only bioenhancements can guarantee such a high level of correctness in decisions and actions. If the effect of the applied modification is to improve the soldier's effectiveness in a situation leading to a decision about the life and death of others, this can be considered a strong justification for applying even such a controversial type of enhancement as cognitive and moral.

The space environment does not involve direct life-and-death decision-making in the way that is characteristic of battlefield ethics. However, it does present indirect analogues, wherein performance, cognitive abilities, and behavior can significantly influence mission success or, conversely, contribute to mission failure. One factor that weakens the justification for applying cognitive and moral bio-enhancement in space missions is the lack of empirical evidence that such enhancements alone can ensure success or meaningfully reduce the risk of failure. It is reasonable to anticipate that the conditions of long-term space missions – such as confinement, isolation, and vast distance from Earth – will generate extreme psychological stress and increase the risk of interpersonal conflict. Nonetheless, in the absence of empirical data concerning the moral and social functioning of individuals under such conditions, critics of cognitive and moral bioenhancement may argue in favor of conventional, non-invasive methods of support. Unlike physiological enhancements, cognitive – particularly moral and behavioral – modifications are far more difficult to predict, control, and evaluate.

One of the more interesting questions in the bioethics of space exploration is whether the rationale for human enhancement for space missions is different from the rationale for human enhancements on Earth. In a sense, the above question can be answered in the affirmative, pointing out the peculiarities of the space environment, which, unlike extreme environments on Earth, will be permanently difficult. One position assumes that the space mission environment provides a special justification that is not necessarily applicable on Earth. The dissenting position, on the other hand, assumes that the same elements regarding principles, rules and values should be paid attention to in both contexts, and the context of application becomes less significant. In a feminist bioethics of space exploration, context is central: assessments foreground sex, gender, power structures, oppression, and domination (Szocik, 2024). Mission purposes may inform evaluation but do not confer moral license. The permissibility of biomedical procedures turns on whether they avoid coercion, unequal burdens, and governance that entrenches domination. Accordingly, space moral exceptionalism cannot override baseline constraints of consent and justice. What we have in mind here is the specific moral situation of the space environment, in which we would not want to allow the right to lower moral standards in the name of the exceptionally harsh conditions in space precisely because of the uniqueness of the space environment. Feminist bioethics as presented by us elsewhere (Szocik, 2024) emphasizes the need to protect the weak and excluded on a global scale, as well as the pursuit of equality and inclusion in all areas of society. Feminist ethics is broadly skeptical of moral exceptionalism – the claim that extraordinary contexts license suspending baseline constraints of consent, non-maleficence, and justice. Feminist analyses of abortion exceptionalism and of emergency health governance show that such framings typically entrench coercion and unequal burdens rather than justify departures from ordinary norms (Parsons & Romanis, 2021; Romanis & Horn, 2020; Wenham, 2021). Appeals to space exceptionalism alone do not justify controversial biomedical procedures. For advocates of sterilization of those considered socially problematic, their sterilization, as well as the promotion of abortion, is justified by context and social goals. Bioethics that allows for the principle of moral exceptionalism, usually non-feminist, will tend to justify the moral use of controversial procedures by purpose, effect, or specific context, ignoring the immorality of a particular procedure or ignoring its harmfulness, as in the case of eugenics policies involving forced abortion and sterilization.

The idea of moral exceptionalism is characteristic of military ethics, which justifies special treatment of soldiers, allowing more to be done to them than to civilians, as well as allowing radical biomedical modification under the super-soldier concept. Maurizio Balistreri and Steven Umbrello criticize the idea of moral exceptionalism, but for reasons other than those characteristics of feminist bioethics. They point out that living conditions on Earth are also likely to deteriorate significantly, as well as that there are many contexts and good reasons for using biomodification on Earth. In their view, therefore, there is no basis for treating space as the only unique environment justifying the application of human enhancements (Balistreri & Umbrello, 2022a). The authors make a strong case for applying human enhancement to space missions rather than modifying the space environment, while stressing that emphasizing the acceptability of human enhancement only or primarily for space missions runs the risk of falling into the aforementioned moral exceptionalism and seeing human enhancement as something requiring exceptionally strong justification, hardly, if at all, acceptable on Earth (Balistreri & Umbrello, 2023).

Even if we accept that the unique conditions of the space environment justify the application of biomedical physiological – and potentially moral – enhancements, the central point of ethical controversy remains the means by which such enhancements are implemented. Let us assume that the space mission community acknowledges the necessity of biomedical enhancements but agrees to permit only somatic gene editing (SGE) and implants. Further, let us assume that SGE, provided it is medically safe, remains ethically uncontroversial. A particularly compelling case for space bioethics, however, involves germline gene editing (GGE). The space environment introduces novel circumstances and ethical considerations that warrant renewed discussion of GGE within bioethical frameworks.

8. GGE in space missions

Since GGE includes editing of gametes, zygotes and embryos, it is considered more controversial than SGE because of its impact on future generations. Assume that human reproduction in space will be possible. A space settlement in which humanity will not

reproduce loses justification if it is seen in terms of a means to guarantee the continuation of humanity, assuming that life on Earth will be threatened or impossible, and migration between Earth and the space base will be hindered or impossible.

The very issue of the duty to reproduce in space is controversial. We can assume that humans will reproduce in any environment. But we can imagine a hypothetical situation in which humans in a space settlement, for some reason, will not want to reproduce. The need to prolong the existence of the human species may therefore interfere with the reproductive autonomy and reproductive rights of members of the population living in space, not all of whom will want to reproduce. The impact falls disproportionately on women and other individuals capable of pregnancy, implicating access to abortion care and the full exercise of reproductive autonomy (Szocik, 2025b). Since reproduction in space carries special risks for pregnant people, both medically and from the point of view of compounding oppression and enslavement, it is worth considering new technologies aimed at replacing biological pregnancy with pregnancy in an artificial womb (Firestone, 1971; Kendal, 2024b).

What ethical challenges does the concept of germline gene editing generate in the context of long-term space missions? Imagine a scenario in which humanity is pursuing an ambitious space program, and GGE is established as medically safe. Participation in space missions is perceived as desirable, as it expands the range of opportunities available to individuals living on Earth. Additionally, assume that life on Earth in the near future will be marked by significant challenges arising from environmental degradation and population pressures. Furthermore, suppose that the successful realization of space missions considered attractive will require the use of GGE – since alternative enhancements either fail to guarantee the same level of functionality and performance or are altogether insufficient. Consequently, a future adult who has not undergone GGE at the embryonic stage would be excluded from participating in space missions or would face significant health issues and diminished capabilities compared to those who were genetically modified during embryonic development. Let us assume that in the future discussed in this example, individual reproductive rights will not be affected by any environmental or population challenges. What decision should future parents make? If the application of GGE to a future child will not adversely affect the child's ability to live and develop on Earth at any stage, it is difficult to formulate an argument against the application of GGE. But if the application of GGE will negatively affect the future child's life on Earth at any stage, or even exclude it at any stage, a serious moral problem arises (Szocik, 2023b).

Parents guided by the principle of procreative beneficence in good faith may decide to apply germline gene editing, assuming that life in space will provide greater well-being for their future child than life on Earth. However, the concept of well-being is abstract and multifaceted; while it is a valid guiding principle, it can be defined in various ways and must consider many conflicting factors. The well-being of a genetically modified future child who participates in space missions as an adult may be higher in terms of socioeconomic status. Yet, this potential advantage may not compensate for the loss of psychological and emotional connections with people on Earth, the very experience of living on Earth itself, or the love and friendships the individual might have formed before embarking on a space mission. In this sense, the individual may be irreversibly committed to such a mission by virtue of having undergone embryonic modification. If we accept both the irreversibility of GGE and the precautionary principle, we should oppose the use of GGE under these circumstances. On the other hand, however, we face uncertainty regarding the future conditions of a child's life on Earth as environmental and social conditions continue to deteriorate. The thought experiment presented here shows a special case of applying GGE. Another scenario is the application of GGE in a population living in space. What space bioethics finds controversial is the possibility of coercion. Voluntary GGE is not controversial, at least not in a space environment.[4] On the other hand, can we accept a situation in which, due to harsh environmental conditions, GGE will be compulsorily applied to all future children to be born in space?

The analogy to mandatory vaccinations on Earth is quite useful here. Suppose that on Earth all newborns must be vaccinated against disease A. The need for universal compulsory vaccination against disease A is justified by the risk of disease, complications and even death, mass morbidity, as well as the negative social and economic consequences of mass morbidity. Imagine that GGE is required in a space settlement to increase immunity to cosmic radiation, to which all inhabitants of the space base are exposed in a sizable dose. The alternative remains permanent residence in a subsurface shelter, which, however, can accommodate a small number of space settlement residents. Living below the surface also reduces the quality of life. In addition, it makes it difficult for the space base to function because certain activities require being on the surface. The rationale for applying GGE is to protect individual and population health and life, as well as to avoid negative social and economic impacts on the entire space settlement. If a certain minimum level of risk of living in space remains relatively high, a rational decision is a GGE understood as a measure to prevent or at least minimize predictable risks to the future development of children from the beginning of their lives (Balistreri & Umbrello, 2022b). Such a GGE could guarantee immediate protection from the harmful conditions of life in space, unlike individual SGEs, which could be applied only at different periods in the lives of future children born in space.

The rationale in both cases is the need to protect against a hazardous environmental factor. This rationale is stronger for space than for Earth, because any human in space will be exposed constantly to cosmic radiation, whereas the risk of contracting a disease on Earth is less than one hundred percent. If GGE is the only countermeasure, it is difficult to find legitimate counterarguments for its use. But even if GGE were one alternative, it should not be ruled out if it offers more reliable, cheaper, and permanent protection from cosmic radiation than living in subsurface shelters.

However, it is worth keeping in mind the risks associated with the idea of reproduction in space. While for the concept of saving the human species – under the assumption of a catastrophe scenario, for which continued existence on Earth is not possible – reproduction in space is necessary, under other variants of permanent space settlement operation reproduction in space is not necessary, however it

[4] One can envision special circumstances when voluntary GGE in space would be controversial because of potential social and economic impacts in the form of inequality in labor market access. However, this scenario requires the assumption that the social structure in space will evolve toward the competitiveness inherent in capitalism as known on Earth.

may be recommended for various reasons. One of the most serious risks is the risk of bringing new children to life under relatively low living conditions. GGE can improve this quality of life to some extent, preventing the onset of diseases and adapting to harmful and harsh environmental conditions, but it cannot offset or neutralize the very fact of living in an extremely and permanently dangerous environment such as space. Therefore, Balistreri and Umbrello (2022b) suggest that in a situation where it is impossible to guarantee a sufficiently high quality of life, especially in the early days of space settlement, reproduction in space should be postponed for the future. The principle of parental responsibility should become the main bioethical principle deciding whether reproduction in space would be morally permissible. In a similar vein, JS Johnson-Schwartz argues that our philosophy of thinking about future habitat in space should be very demanding, and we should not accept a lowering of ethical standards, let alone accept any degree of sacrifice on the part of future space settlers (Johnson-Schwartz, 2022).

The use of human enhancement, including GGE, should be guided by core bioethical principles: autonomy, beneficence, non-maleficence, justice, and utility. With respect to the principle of autonomy, full knowledge and adherence to the informed consent standard are considered the ethical minimum. In the case of GGE, the parents of future children should possess comprehensive knowledge not only of the potential risks, but also of the purpose and broader significance of the mission, as well as any viable alternatives to GGE. As Vaughn (2023, 10) points out, one of the greatest threats to respecting autonomy is strong paternalism, in which a patient's knowledge and consent are disregarded in the name of their supposed well-being. According to the informed consent rule, disclosure must include details about the procedure, potential risks, available alternatives, anticipated benefits, and the likelihood of success (Vaughn, 2023, 202).

The principle of respect for autonomy has been criticized for its narrow interpretation. An alternative approach is the concept of relational autonomy, which considers the social and interpersonal contexts that shape individual decision-making. Feminist bioethicists argue that many decisions deemed autonomous in non-feminist frameworks often involve hidden dependencies and relational constraints (Stoljar & Mackenzie, 2022). James F. Childress (2020, 34–35) acknowledges that relational autonomy provides a valuable perspective in evaluating the moral quality of individual decisions. However, he cautions that an overly demanding application of this model could undermine traditional understandings of autonomy and risk legitimizing paternalistic interventions. Thus, relational autonomy should inform, but not replace, the classical principle of autonomy.

The principle of nonmaleficence poses particular challenges for experimental and radical forms of human enhancement. It remains unclear whether GGE can be implemented without causing at least minimal adverse effects. This concern aligns with the precautionary principle, which advises against action in the absence of clear evidence of safety. At the same time, the motivation for GGE is rooted in nonmaleficence – the desire to protect future astronauts and space settlers from the known harms of prolonged exposure to cosmic radiation and altered gravity. The principle compels us to avoid inflicting unnecessary harm.

The principle of beneficence requires promoting the welfare of others and enhancing their well-being. Although there is no universal duty to actively benefit others, the application of this principle is often limited to specific relationships, such as those between parents and children or between medical professionals and patients (Vaughn, 2023, 11). GGE may represent a specific instantiation of beneficence – namely, the principle of procreative beneficence. While the notion of moral exceptionalism is often viewed with skepticism in space bioethics and debates over human enhancement, the principle of procreative beneficence may gain ethical traction in the space context. In this setting, GGE could be justified as a morally responsible act aimed at optimizing the well-being of future children expected to inhabit challenging space environments.

The principle of utility, which derives from the principle of beneficence, emphasizes the generation of the greatest possible positive outcomes while mitigating inevitable negative consequences. Like other forms of consequentialist ethics, the principle of utility frequently underpins ethical justification in the bioethics of extreme environments, including both military bioethics and space bioethics. The principle of justice, when applied to human enhancement for space exploration, concerns the equitable distribution of enhancement technologies. As long as space missions remain elite in character – comprising small, specifically selected groups such as state-sponsored astronauts – the selection of a particular theory of justice, whether libertarian or egalitarian, may not pose significant moral dilemmas. However, justice becomes a more pressing concern in the realm of space policy, particularly when evaluating whether the financial and material resources devoted to space exploration might be more justly allocated to alternative purposes. Although such resource-allocation issues are not strictly within the scope of bioethics, they are particularly relevant in the context of global bioethics and cannot be overlooked. Justice emerges as a direct bioethical challenge when space missions become more widespread and accessible. If space travel becomes increasingly popular and desirable, yet contingent on the use of radical and potentially expensive human enhancements, concerns regarding fair access will intensify. Participation in such missions may be limited to individuals who can afford or are willing to undergo mandatory biomedical modifications. In this scenario, the settlement of space – along with associated requirements for biomedical enhancement – could evolve into a public health issue. Specifically, individuals who are unable or unwilling to undergo enhancement may be left with inferior health outcomes or diminished life opportunities compared to those participating in space settlement (Szocik, 2025b).

In summary, GGE represents one of the most radical and morally contested forms of biomedical human enhancement. Within the framework of non-feminist space bioethics, we argue that GGE can be morally justified. If the long-term presence of humans in space is essential for the survival of the species – and if we reject proextinctionist (antinatalist) positions – then we may hold a moral obligation to pursue GGE. In such a scenario, GGE could be viewed as a necessary tool to enhance the quality of life in space and to provide protection against at least some of the environmental hazards associated with extraterrestrial living (Szocik et al., 2024).

9. Bioethics and rationale for space missions

The philosophy and bioethics of human enhancement outlined above treat enhancement as a potentially inevitable consequence of

scientific and technological advancement. This progression may serve to improve human adaptability to increasingly harsh environmental conditions on Earth, and, in the case of space expansion, to facilitate adaptation to extraterrestrial environments. In the following section, we examine the main rationales for human space missions, including scientific exploration, commercial exploitation, and the concepts of space settlement and refuge. We aim to demonstrate how the ethical and bioethical evaluation of these missions is shaped by their underlying justifications. Depending on the rationale behind a given mission and the extent of human enhancement required, enhancement may be regarded as either obligatory or desirable. In some cases, missions may need to be postponed or canceled altogether due to ethical concerns.

9.1. Research missions and scientific exploration of space

What is interesting and relevant for bioethical issues in the value of scientific exploration of space is the following question: if any human space research mission, to Mars and beyond, requires application of human enhancement, then should we allow for such modification? Does the value of science in space exploration justify human enhancement? We agree that scientific purposes are not trivial. We also agree that scientific exploration as such has a high value in human axiological hierarchy. There are strong rationales in favor of human space missions that could be carried out for scientific reasons, both for human exploration in space and for the study of the universe (Shelhamer, 2017; Schwartz, 2020). However, we cannot sacrifice everything that we have or who we are to make possible progress in scientific explanation. We do not accept tests on some animal species, and we strongly criticize the infliction of suffering on those animals that, at least for now, science needs. We also usually agree that the moral status of human beings is higher than all other non-human animal species. If we are opposed to the use of animals for scientific research, perhaps we should be even more opposed to the use of humans.

Scientists argue for or against robotic or human missions. While some of them prefer automated missions, some scientists emphasize the advantages of human astronauts in the field. This is ethically neutral as far as no human enhancement is required even for relatively short research missions. Factors reinforcing the rationale in favor of automated missions are that they are less costly, pose no risk to human life, and threaten the space environment less than the presence of humans will threaten it (Goldsmith & Rees, 2022). But if human enhancement is mandatory even for short research missions, are we not treating the modified astronaut in a very instrumental way? But, on the other hand, the previous history of space missions, especially the space race of the Cold War era, also implied instrumental treatment of astronauts, however they were not subjected to the kind of modifications discussed in our paper. This becomes clearer in the context of the dispute between supporters of human and robotic missions. We can assume that due to the high risk and high costs of space missions, automated missions should be treated as a default mode of operation, at least to conduct research in space. We can also assume that humans are sent to undertake research in space only when really needed, when no currently available robot is able to conduct the planned research as well as a human. This is an instrumentalization of the human astronaut, which is not bad or, at least, morally challenging as far as no enhancement is required. But the ethical issue arises if the scientific purposes of space exploration justify radical human enhancement of astronauts. If yes, we should ask what kind of scientific objectives are so valuable (and why). There is at least one justification for human enhancement for research missions. If we assume that due to the risk of contamination and distortion of the pristine environment on Mars or other astronomical objects by space mining or space settlement, this environment will obviously lose its scientific value, it is rational to precede these missions with a scientific mission. If, however, humanity cannot wait for the invention of effective countermeasures against space radiation and microgravity, and either space mining or space settlement require immediate implementation, then there is a justification for modifying astronauts for a purely scientific mission. Then such modified astronauts realize as soon as possible the scientific goals, and after they are achieved, we move as soon as possible to space mining and/or space settlement, if they are urgent.

The practical effect of sending genetically modified astronauts to conduct a scientific mission – setting aside the question of whether a mission to Mars could be exclusively, or even primarily, scientific – would be the termination of debates concerning Mars' scientific value, its pristine nature, and the protection of its environmental integrity. If the discovery of potential biosignatures, particularly of past life, as well as the advancement of knowledge about planetary geology and evolution, necessitates the physical presence of human explorers, it is reasonable to approach the study of Mars in a manner analogous to scientific investigations conducted in remote or extreme locations on Earth. In this context, subjecting Mars-bound astronaut-explorers to genetic modification should be regarded as a standard, albeit radical, preparation for a scientific mission. The extremity of the procedure stems from the unique and hazardous nature of the Martian environment rather than the scientific objectives themselves.

9.2. Space mining and commercial exploitation of space

At least two distinct phases can be identified in the development of space mining. The first is a current or near-term phase, during which humanity remains Earth-bound, and human activities in space – while potentially beneficial – are not essential for our survival and are often seen as a form of human extravagance. This phase includes not only space mining but also space tourism, including orbital flights and space hotels. The second phase envisions the beginning of space settlement, wherein the issue of in situ resource utilization becomes a matter of necessity and survival. The ethical and practical status of human enhancement may differ significantly between these two phases. A third scenario envisions a distant future in which humans live exclusively in space settlements, and the exploitation of space resources is taken for granted as a routine aspect of existence.

Can it be considered ethically controversial to subject workers – sent to various parts of the solar system for resource exploitation – to radical forms of human enhancement? One approach to this question is to treat labor in space analogously to conventional forms of employment, where specific physical and cognitive requirements are established for job applicants and employees. In an ideal society,

such requirements would fall within the realm of free and informed choice, exercised autonomously by individuals interested in pursuing such work. However, in a non-ideal world, at least two key concerns emerge. The first pertains to the genuine autonomy and freedom of prospective workers. A variety of socio-economic pressures could influence individuals to accept employment that demands radical, potentially unsafe biomedical modifications with unpredictable long-term consequences. The second concern involves the potential for exploitative practices by employers in the commercial space sector. Given that employers often seek to maximize productivity, and that operating in space involves high costs and considerable risk, there is a non-negligible danger that biomedical enhancement technologies might be employed not primarily to safeguard workers' health and safety, but rather to augment their performance and economic efficiency. Such a trajectory raises significant ethical questions concerning consent, coercion, and the moral limits of human enhancement in the context of labor.

9.3. Space refuge and space settlement

A range of ethical issues arises around this topic (Szocik, 2019b; Schwartz et al., 2021). Two fundamental assumptions underpinning the concept of space refuge warrant scrutiny. The first is the belief that the survival of the human species is worthy of protection or indeed ought to be protected. This belief exists in varying degrees. Some hold that humans should be protected by standard means and routines, while others argue that extraordinary measures are neither necessary nor deserved. Extraordinary measures might include cases such as a newborn with a rare disease requiring an expensive, complex surgery to survive. In wealthier societies, such interventions are typically pursued, but this approach becomes problematic if many severely affected individuals are born. Similar debates occur in the context of euthanasia and assisted dying. Some philosophers contend that humans, given their immoral behaviors and destructive tendencies – particularly regarding the potential harm to new extraterrestrial environments – do not deserve such extraordinary protection (Torres, 2024). In this paper, however, we align with the philosophical tradition advocating for the preservation of human life and efforts to save individuals. Yet, a significant challenge remains: the necessity of triage. Treating space exploration as a form of space refuge for humanity would necessitate selecting candidates qualified for evacuation. From today's perspective, it appears only a very limited number of Earth's inhabitants could be evacuated to such a space shelter.

The second contested assumption is that space refuge represents the sole means to protect the human species against certain disasters. There are compelling reasons to believe that terrestrial refuges could be equally effective. After all, what would distinguish a post-catastrophic Earth from the Martian or lunar landscape? In all scenarios, life without life-support systems would be impossible. Considering this perspective and reflecting on what life in a space settlement might entail, it becomes clear that it would likely be arduous and stressful, conducted in an environment of constant high risk. Two points deserve emphasis here. First, life in a space refuge may be even more challenging and hazardous than life for survivors on a post-catastrophic Earth. Earth's gravity and relative protection from cosmic radiation render it more hospitable than other celestial bodies where settlement might occur. Second, space settlement should not become humanity's primary goal. Instead, humanity ought to strive to survive on Earth as long as possible – whether through subterranean or aquatic refuges – while, perhaps in parallel, advancing space exploration and settlement programs.

However, if we accept the two premises mentioned above – that humanity is worthy of protection by extraordinary means, and that space refuge constitutes such a necessary means – we encounter several bioethical issues, some of which are particularly relevant to human enhancement. Johnson-Schwartz (2020) critically examines the core argument behind space settlement – our duty to extend human life. She argues that although space settlement may be necessary for long-term survival, it is not an urgent requirement in the near future and should yield to alternative strategies aimed at enhancing humanity's survival prospects on Earth. This is a crucial insight. If space settlement is not imminently necessary to ensure species survival, perhaps we should reconsider pursuing radical human enhancement, at least if the concept remains ethically contentious. Moreover, it is questionable whether mandatory radical modifications can be ethically required for survival purposes rather than for non-essential activities. Participation in scientific or commercial missions – even if they require human enhancement – is not strictly necessary for humanity's survival, whereas evacuation to a safe haven in the face of extinction arguably is. Thus, how far can we ethically justify invasive and controversial procedures on a mass scale?

In conclusion, framing a space mission as a means to save humanity provides the strongest possible moral justification, potentially legitimizing any form of action. Within this framework, a program of mandatory radical biomedical modification for all candidates loses much of its controversy if the alternative is the death of those who refuse to evacuate solely due to opposition to human enhancement. Biomedical human enhancement may then be regarded as the necessary measure – and price – to pay for preserving the continued existence of the human species and other life forms. Although the justification for biomedical enhancement in other types of space missions is weaker than for space settlement, it remains important to emphasize that, regardless of mission purpose, the bioethical evaluation must account for the inherently dangerous environment humans face in space. This reality demands the implementation of appropriate protective measures. To make space ethics and bioethics truly responsive to human and planetary futures, it must go beyond techno-optimism and individualistic autonomy. Feminist bioethics offers a critical lens that foregrounds embodiment, interdependence, justice, and care – values essential for evaluating the ethical legitimacy of space exploration and its broader consequences (Rogers et al., 2022).

10. Feminist bioethics and the critique of space exploration

In our article, we refer to the non-feminist philosophical tradition in bioethics, based primarily on principlism using the method of reflective equilibrium. We also refer to the tradition of consequentialism in thinking about bioethics and medical ethics. A different approach is offered by the feminist perspective, which occupies a marginal place in the philosophy of space exploration. This

perspective draws attention to the mechanisms of exclusion, oppression and discrimination that affect people of a particular gender, social class, race or degree of disability to a greater extent. The feminist perspective is revolutionizing the way we think about the future of humans in space. While the traditional approach sees basically nothing morally problematic in the idea of human enhancement applied to future space missions, as long as it is safe and effective, the feminist approach uncovers a number of problems that are invisible to the non-feminist perspective. These problems include the risk of increased oppression of women and people with disabilities (Szocik, 2024, 2025b; Szocik & Abylkasymova, 2025). In dominant biomedical and philosophical traditions, the male body has been treated as the norm – universal, rational, and neutral. In contrast, the female body is pathologized or marked as the "other." This normative bias not only distorts scientific understanding but also justifies systemic inequities in healthcare, research, and social policy. The concept of human enhancement applied to women could therefore serve to masculinize women in terms of desirable criteria so that they resemble as closely as possible the male model of strength, fitness, or other qualities desired by mission organizers (Szocik, 2023c).

Feminist bioethics reveals that enhancement technologies, rather than leveling the playing field, often function to enforce male-centric ideals of health, strength, and value. In contexts like space exploration, women's bodies are not simply included – they are often reshaped to conform to existing, masculinized paradigms of human excellence. For instance, in space travel, design decisions (spacesuits, mission length, physical training) have often assumed a male body norm. Enhancing women to match male metabolic rates or muscle mass may be seen as equalizing, but it risks erasing biological difference and marginalizing alternative strengths (e.g., women's typically greater resistance to radiation or superior adaptation to microgravity). Some feminist scholars critique biomedical design for universalizing the male body as the default norm, which often compels women to conform to these male-centered standards instead of prompting adaptations that accommodate female bodily diversity (Oudshoorn, 1994). Oppression and discrimination against women may increase when GGE is applied and humans reproduce in space. Depending on current population policies, anti-natalism or pronatalism will become the dominant philosophy, and women will be forced or induced to reproduce, or kept from it (Kendal, 2023). Another group particularly discriminated against by human enhancement in space will be people with disabilities (Wells-Jensen, 2023). The very logic of human enhancement may exclude anyone who reveals any deviation from the male-centric, ableist norm.

Feminist bioethics and the philosophy of space exploration adopts a fundamentally different paradigm and conceptual framework from non-feminist bioethics at its starting point, demonstrating unequal power structures, as well as the fact that what appears to benefit some stakeholder groups often harms and is based on the exploitation of others. On the other hand, a feminist analysis of our future in space does not always have to lead to exclusively negative conclusions. For, at the same time, feminists show what a just and equal exploration of space should look like. The methodological advantage of feminism is that it identifies problems, challenges and threats where often bioethics and non-feminist philosophy either fail to recognize these threats at all or consider them irrelevant.

The problems and dangers highlighted by feminism are very important and should be considered in futures studies in general and in thinking about our future in space in particular. We agree with Johnson-Schwartz, who says that the achievements of the humanities, especially in feminism, gender studies and postcolonial studies, in exposing and understanding mechanisms of oppression and discrimination, cannot be ignored (Schwartz, 2022). It is our moral epistemic duty to use this knowledge. The popularity of feminism in space exploration research is growing, and there is a growing awareness of the social and political risks that can accompany space exploration.

One of the key categories of feminist bioethics is intersectionality. This concept assumes that people are subject to many forms of oppression that interact simultaneously (Tomlinson, 2019). Intersectionality is a framework that examines how overlapping social identities – such as race, gender, class, sexuality, and ability – interact to shape individuals' experiences of oppression and privilege within systems of power. The concept of intersectionality also indicates that different oppressions combine to create a specific type of exclusion and marginalization that cannot be reduced to any single type of oppression (Hunt, 2017). Gender oppression, for women of color, intersects with racial and class discrimination, augmenting the types of inequality women of color face (Mohanty et al., 1991; Zinn & Dill, 1994). In our understanding of feminism, space exploration is a project that contradicts the idea of feminism, understood as the struggle to end sexist oppression (Hooks, 1984), by which we mean the oppression and exclusion of all those who suffer from injustice and exploitation caused by misogyny, sexism and the patriarchy (Mikkola, 2016). Space exploration will not only fail to end this oppression, but may even reinforce it, and will certainly not reduce it.

In our interpretation of feminism, which, as we have stated, takes a highly critical and more pessimistic approach to the consideration of ethical space futures, we arrive at a certain paradox. We believe that the morally necessary appeal of feminist philosophy and bioethics in the context of research into the future and space exploration, which cannot be ignored, significantly questions the morality of human expansion into space. Applying feminism to the ground of these considerations, the essential question is this: can any space exploration be justified on the grounds of feminism? Many feminists would answer this question in the affirmative (Boucher et al., 2024; Whitman Cobb, 2024; Gál & E. S., 2023; Steer, 2021; United Nations Office for Outer Space Affairs, 2024). Others, in turn, show that it will be very easy to apply exclusionary and conservative scenarios in space, which perpetuate sexist discrimination and gender-based inequality (Casper & Moore, 1995). As Ganser (2019, 41) argues, "the New Garden of Eden might turn out to be not a garden at all, not so new at all, and not produce unlimited growth and harmony but rather constitute another microcosm of struggle, strife, destruction, even genocide – or it might not turn out at all".

We take the position that space exploration and exploitation is such an activity that the very possibility of pursuing it and preparing for it sets in motion processes and mechanisms against of which feminism is skeptical. An example of this is the role played by the current private space business sector, embodied by Elon Musk, which makes deals with the state, receives huge subsidies from the budget that could address many existing social problems (in this case, the problems of gun violence, access to health care, extreme socioeconomic inequality plaguing the US), and pays no attention to global environmental problems, demanding precious resources

and causing pollution. Is subsidizing private space companies like SpaceX consistent with the feminist spirit, or does it serve to reduce oppression? Is it consistent with feminism to dispose of public assets in a country where there is an opioid epidemic largely caused by essentially no public health service? The case of Musk and the U.S. is not the only way in which space exploration exists and can be implemented, but it is one of its significant forms.

In this current climate, feminism, which in our understanding is a current critical and skeptical of space exploration, would fall somewhere between what Sid Simpson and co-authors call cosmic pessimism and cosmic neutrality. Cosmic pessimism opposes any space exploration, believing that it will bring negative consequences. Representatives of cosmic neutrality, on the other hand, do not reject space exploration per se, but argue that the resources devoted to it are almost always more needed on Earth (Simpson et al., 2024). The fact that there are feminists who are optimistic about our future in space does not preclude the more radical interpretation of feminism that we present in the article, which is closer to cosmic pessimism and skeptical of the current power arrangements (nationalism, capitalism, militarism, colonialism) on which the power of space faring states is based (Rubenstein, 2022). This is because we believe, looking at the nationalistic and militaristic policies of leading spacefaring superpowers such as the US, China, Russia and India, that the action models of these countries, as well as the goals of space expansion that guide them, have nothing to do with the realization of feminist ideals of equality, justice, peace or concern for the environment. Looking at the important role of publicly subsidized space businessmen, who represent the dynamics of exploitative global liberal capitalism, we criticize these dynamics as anti-feminist. Finally, looking at how difficult and dangerous the space environment is, we believe that – building on the dynamics described above – it cannot be a place that celebrates equality, justice and concern for the vulnerable, but will be a place that reinforces sexist and patriarchal trends, where the perfectly groomed male body and psyche will remain the model, not the woman or disabled person.

One can take a less radical and less consistent approach to feminism – as with any other philosophy or normative theory – and concede that feminist critique is valid yet nonetheless assume that the expansion into space will proceed anyway, because that is the driving dynamic (nationalist, capitalist, militaristic, colonial). One might also be content with measures like pursuing gender parity at space agencies or inviting racial and ethnic minorities and people with disabilities on spaceflights. However, such actions do nothing to transform the global, unjust structures of power, exclusion, and oppression. Moreover, paradoxically, space expansion may reinforce those structures, since it is intrinsically tied to states' nationalist and militaristic policies and serves their ends. The case of space weaponry shows that the militarization of space is inevitable, and it is hard to see this as any kind of feminization of space exploration.

Two space-policy fronts merit brief feminist scrutiny. First, neoliberal–libertarian framings, entwined with nationalist and militarist logics, organize extraction; discourse analysis should serve only as prologue to mapping power and objectives. Second, governance of biomedical enhancement and reproductive control in small, closed populations demands priority, as consent, equity, and accountability are especially fragile. Feminist philosophy makes it easier to criticize space millionaires such as Musk, Jeff Bezos and Richard Branson, because it reveals the dynamics of capitalism, which involves the relentless exploitation and accumulation of capital, which is essentially unstoppable (Billings, 2023).

Another issue revealed by the feminist perspective is the possible exploitation of workers on future space missions. Erika Nesvold shows that in virtually every possible variant of future human space exploration, where it becomes more common, workers will be exploited. They will be a very vulnerable group due to the distance, being in a confined environment, and the inability to migrate or return to Earth immediately. Their situation will likely be exacerbated by the unclear legal regulation of space enterprises, which may escape state jurisdiction on Earth. In addition, enforcement of rights will be difficult in space. Nesvold likens this hypothetical situation of future employees of space corporations to current workers in fishing in international waters, exploited especially because of isolation, distance from land, and problematic international law regarding worker protection (Nesvold, 2023a, 2023b).

These examples from the field of space politics show that feminism reveals to us in a new light what lies behind the space tourism practiced by space billionaires, their subsidization by state taxes, the risk of repeating expansionism, colonialist and exploitative policies. Feminism also reveals to us the specific vulnerability of future space workers. We agree with Tony Milligan that human space exploration will not be a watershed event in human history that will either solve the problems plaguing humanity or lead to disaster (Milligan, 2023). Space exploration will undoubtedly be characterized by forms of exploitation and oppression that feminism rightly identifies. Drawing on the philosophies of Chandra Talpade Mohanty (1984, 2003) and Gayatri Spivak (1987, 1988) – who highlight that so-called universal projects of humanity ignore the voices and needs of those in the Global South – we can, with a high degree of probability, conclude that future space exploration will not serve the so-called good of humanity, nor be carried out for the sake of reparative justice, but rather to advance the interests of spacefaring superpowers and space entrepreneurs.

Space exploitation itself causes environmental pollution both on Earth and littering the cosmos through space debris. Regarding the three thought experiment scenarios discussed in 'Thought Experiment 1: A World Without Human Enhancement' – 'Scenario 1: Population-Based Diseases', 'Scenario 2: Climate Change', and 'Scenario 3: Space Settlement' – imagining a future world without human enhancement, many proponents of feminist bioethics express strong opposition to radical biomedical human enhancement. Regarding human enhancements applied to combat disease, many feminists draw attention to the risk of oppression, exploitation and exclusion of the most vulnerable groups, namely women, indigenous people, people with disabilities and racial and ethnic minorities. Such people can be excluded from medical care, as well as be exploited in risky clinical trials. In the case of the thought experiment talking about applying biomedical moral enhancement for the purpose of better adapting to the fight against climate change, feminists draw attention to the risk of manipulation by state institutions or powerful private companies that would be the disposers of such moral bioenhancement. An additional risk is the notion of a norm regarding behavior and preferences deemed desirable to obtain. Exemplary moral ideals can be identified with one gender, either men or women, leading to the reinforcement of stereotypes, the empowerment of men and the deepening of the inferior status of women, which women already experience in many spheres.

Finally, many proponents of feminist bioethics oppose the biomedical human enhancement program applied to space missions,

pointing out the many dangers of manipulation, exploitation, use for nationalist, military and capitalist purposes, as well as the threat to women, trans and non-binary people, people of color and people with disabilities (Szocik, 2024). According to many thinkers in the field of feminist bioethics, discrimination and exploitation of these groups is inevitable, and therefore we should not engage in projects that lead to such discrimination. Since human space exploration in the sense of long-term missions beyond Earth orbit has not yet begun, feminist bioethics, critical and pessimistic, as we have defined it in this article, will argue in favor of not starting projects that are both based on and will also cause such exploitation and oppression. Because feminist bioethics insists that any technology or practice be evaluated considering its likely effects on power, oppression, and justice, a project that is essentially built on – and will inevitably reproduce – gendered, racial, and economic hierarchies will be judged ethically impermissible rather than merely in need of better guidelines.

Before we commit to multi-year projects of space exploration and exploitation, the culmination of which might be the permanent or semi-permanent settlement of humans beyond Earth orbit, two questions are key in our feminist bioethical interpretation of space exploration. The first is: who benefits from the exploration and exploitation of space, and who is put at risk? If it is only the already privileged who benefit, such as spacefaring states and wealthy space investors – then this entrenches injustice. The barrier to entry into space remains extremely high, confined to a few state actors and private entrepreneurs. Returning to Sand's concern about "not having a future," this concentration risks allocating futurity – opportunities, security, and voice – primarily to elites (Sand, 2019). The question, then, is whether exploration and exploitation can be re-conceived to center reparative justice and genuine inclusion. At minimum, projects should meet a futurity-access criterion: they must demonstrably broaden participation and benefits beyond elite constituencies or fail justificatory tests. If not, the default position should be to refuse to launch such an initiative rather than introduce tokenistic diversity measures. We take the position that, given the extraordinarily harsh conditions of space and the high barrier to entry, space exploration and exploitation are not projects that can be remolded in ways that realize feminist ideals deeply rather than superficially. We therefore maintain that, from the perspective of feminist bioethics, one should oppose embarking on human space exploration in its current, hierarchy-dominated form until the structures of funding, governance, design, and purpose of these ventures are reconfigured to dismantle, rather than reinforce, systemic oppression.

In conclusion, feminist bioethics in relation to the idea of human enhancement does not imply a strong opposition. There is, however, no doubt that feminist bioethics is incomparably more critical and skeptical than non-feminist bioethics, which is usually enthusiastically oriented, at least outside the bioconservative mainstream. One of the strengths of feminist bioethics of emerging technologies is that, as Walter Veit and Heather Browning emphasize, it is perhaps the only framework capable of detecting and analyzing all forms of inequality – not just the material ones that non-feminist discourse on biomedical human enhancement tends to focus on. Feminism sees positive elements in human enhancement in certain contexts and even points to the usefulness of applying human enhancement to the most discriminated groups (Veit & Browning, 2024). However, this pertains to the concept of biomedical human enhancement considered in an Earth-based context, not with a view toward future crewed space exploration. Regarding the application of human enhancements for space exploration, adopting the same feminist perspective, one can have well-founded doubts about the possibility of realizing feminist ideals in space. Veit and Browning rightly emphasize that human enhancement aligned with feminist values should serve the genuine benefit of the individual rather than society, must be implemented with full control and choice by the person being modified, and its policy should incorporate diverse viewpoints to achieve gender equality (Veit & Browning, 2024). Implementing these three feminist requirements is not possible in space. The nature of space missions is focused on mission success and task fulfillment, not on individual well-being. Astronauts already operate under conditions of incomplete informed consent, since participation in missions requires agreement to undergo experiments and various medical procedures. Regarding human enhancement, they would be compelled to accept all biomodifications deemed necessary by mission organizers and planners for the mission's success. Gender equality is irrelevant to space missions. In such an extremely harsh and largely inaccessible environment – where national interests also come into play – other objectives will take precedence over gender equality. Finally, it should also be noted that when we speak of gender equality, we mean equality of all genders, including queer, trans, cis and non-binary individuals. Whether such persons – and all those who break the model of a heterosexual male-female pair – will find a place in humanity's future in space, especially if reproduction is involved, is highly doubtful.

11. Conclusions

Human enhancement through biomedical means remains a controversial procedure. Despite the anticipated and promised benefits – consistent with the belief in scientific and technological progress, as well as the expectation that science should serve to improve human living conditions – some ambiguities persist regarding possible side effects, particularly in the case of GGE. The social consequences, especially in terms of increasing inequality, cannot be ignored either. The space environment provides greater ethical justification for applying radical forms of human enhancement due to its harsh conditions and the relatively small group of individuals who would undergo such modifications. The relative isolation of biomodified astronauts from the broader population, combined with modifications designed specifically for the environment and tasks at hand – as opposed to enhancement for its own sake, which is often discussed in Earth-bound contexts – allows for minimizing criticisms of human enhancement from the perspectives of equality and social justice (Szocik, 2023a). However, this specific context of the space environment and the particularity of space missions should not lead to the notion of the moral exceptionalism of the space environment. It remains important to uphold appropriately stringent moral principles and to remain vigilant regarding the risks of violating ethical norms and rules potentially associated with human enhancement in space missions. Following the methodology of thought experiments and speculative bioethics, the analysis of the bioethical challenges related to applying human enhancement to future space settlers provides valuable insights into the current state of bioethics on Earth, our moral intuitions, and potential areas of risk linked to emerging technologies.

In this paper, we also demonstrated how feminism offers a useful analytical lens for examining the future presence of humans in space. Feminist theory enables the identification of hidden dynamics within certain processes and emphasizes the importance of critically assessing the justifications for specific types of missions. For instance, if a particular mission primarily aims to enrich corporations and bolster nationalist or military state power, does this vision of human presence in space genuinely translate into the wellbeing of all humanity and justify the use of controversial biomedical interventions? As we have shown, adopting a feminist perspective as the dominant framework for philosophy and public policy would likely render space exploration untenable, due to the persistence of unequal power structures, exclusion, and exploitation that it exposes. Feminists recognize the particularities of power structures in an imperfect world and therefore advocate for the gradual, process-oriented implementation of their demands – wherever possible – to integrate feminist ideals into public policy (Rogers, Scully, et al., 2022). However, assuming that expansion into space will proceed regardless – because we cannot alter the development trajectories of superpowers and corporations – and given that non-feminist bioethics and philosophies of space exploration (which by definition do not preclude moral justification for such expansion) offer no resistance, our moral obligation is to apply feminism as forcefully as possible to warn against the likely negative consequences of future deep-space exploration.

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CRediT authorship contribution statement

Szocik Konrad: Writing – review & editing, Writing – original draft, Supervision, Funding acquisition, Conceptualization. **Rakhat Abylkasymova:** Writing – review & editing, Writing – original draft, Methodology, Conceptualization.

Declaration of Competing Interest

The authors declare no conflict of interests.

Data availability

No data was used for the research described in the article.

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Seylani et al.—Ethical Issues in Non-Government Spaceflight (2024)

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Overview: Highlights ethical, legal, and medical issues related to participant selection and human research in private-sector missions.

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Perspective

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Ethical considerations for the age of non-governmental space exploration

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Mounting ambitions and capabilities for public and private, non-government sector crewed space exploration bring with them an increasingly diverse set of space travelers, raising new and nontrivial ethical, legal, and medical policy and practice concerns which are still relatively underexplored. In this piece, we lay out several pressing issues related to ethical considerations for selecting space travelers and conducting human subject research on them, especially in the context of non-governmental and commercial/private space operations.

It has been over 50 years since the first human walked on the Moon. Since then, most commercialized spaceflights have been contracts granted to private companies by various governments to launch satellites, e.g., communication and GPS devices, into Earth's orbit. In recent years, the definition of commercial spaceflight has expanded to include human transportation between Earth and habitats in Low Earth Orbit and future lunar or other extraterrestrial outposts. Once considered nearly impossible, commercial space travel is now a reality, due to rapid technological advancement in the private sector, large-scale investment from governments, and continued public interest. With the first crewed launch of SpaceX Dragon to the International Space Station (ISS), on May 30, 2020[1], a new era of public-private spaceflight partnership has emerged. Private companies such as Boeing, Virgin Galactic, Axiom, Sierra Space, and Blue Origin now create a

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steep commercial demand for crewed spaceflight, both for technological and recreational purposes. NASA has further partnered with Axiom Space for commercial utilization of the ISS until the world's first commercial space station is built by 2028[2]. There is currently a wide range of private/commercial spaceflights, ranging from suborbital flights lasting mere minutes to Axiom's 1-2 week ISS missions to the first all-civilian orbital commercial spaceflight mission referred to as 'Inspiration4' (I4), comparable in duration (and health risks) to orbital shuttle missions[1–3].

Historically, government-sponsored spaceflights were mission-based and geared towards national interests, e.g., technological leadership, improving national security, creating high-quality jobs, or advancements in research. After the Cold War era and the "Space Race," government investment in space exploration declined. In contrast, the idea of commercial spaceflight continues to gain significant popularity and the economic opportunities linked to this are enormous. This has been accompanied by an influx of investment and the development of new technology, such as initial viable Reusable Launch Vehicle models by SpaceX[4]. Despite this rapid technology development, governmental regulation of commercial spaceflight lags behind. There are some requirements commercial spaceflight providers have to meet, including requirements concerning environmental safety, payload, payload re-entry, financial stability, and coverage for maximum probable loss[5]. Yet, there has been only limited regulation concerning the selection and training of non-government-sponsored astronauts and no formal oversight governing medical research on such crews, whether orbital or suborbital. The United Nations Office for Outer Space Affairs has collated national space laws relating to space activities from 42 countries[6]. While the regulations listed there cover a wide range of fields, such as objects in space, radio-communication, and space activities, there is a general lack of health-associated regulations. This is a symptom of a bigger problem where there is little oversight of private sector spaceflight participants which, with Inspiration4, dearMoon[7], and the upcoming Polaris program[8], are already a reality.

An increase in commercial/private and civilian space missions with a more diverse crew may provide an opportunity to collect data on health issues in space. While these data could shape medical standards and improve treatment choices for prolonged spaceflight, their collection and management should require strict regulation. At the same time, as spacefarers shift from professionally trained astronauts to private individuals without rigorous preparation or with existing medical conditions, there is a need to refine selection criteria and training for non-governmental space travelers. Yet, despite their importance and urgency, these considerations have gone relatively unexplored[9].

In this paper, we will lay out several pressing issues related to ethical considerations for selecting space travelers and research practices, especially in the context of non-governmental and private space operations. Although there are many other ethical issues related to space exploration – both commercial and otherwise[10–19]– our focus here is on ethical considerations regarding selection and human subject research. Note that while some of the issues we raise might be covered by guidelines, regulations, or law, this does not diminish the ethical considerations we discuss. A good example illustrating this point is NASA's recent decision to unify the effective radiation exposure for male and female astronauts so as to not exceed 600 mSv, which translates to having to remain below 3% mean risk of cancer mortality above the non-exposed baseline mean, despite differences in male and female radiation-based cancer risk[20,21]. This decision is highly controversial, precisely because it is viewed by many as ethically problematic. Likewise, signing a consent form to undertake a certain activity (whether employer-mandated or not) does not make the proposed activity or consent process ethically unquestionable[21]. Indeed, our point here is that ethical considerations resulting from the increase in private and commercial spaceflight arise despite established rules and guidelines[22,23].

A note on terminology: SpaceX, Axiom, and others refer to their travelers as 'crew'. This has important consequences since the limited Federal Aviation Administration (FAA) guidelines[24] that are applicable to non-professional astronauts are somewhat more stringent for crew than 'ordinary' spaceflight occupants. To bypass ambiguity, we prefer the term 'spaceflight occupants' (SOs), using it to refer to non-professional space travelers lacking substantial spaceflight training. Further, we use the terms 'laws' and 'regulations' to refer to binding law and the neutral terms 'guidelines', 'recommendations', and 'policy' to refer to non-binding guiding instruments.

Considerations on governmental vs. non-governmental spaceflight

Biological hazards of spaceflight

The selection of professional astronauts is highly regulated because space travel and habitation are demanding and dangerous. Current space missions to the ISS in Low Earth Orbit and future missions pushing the boundaries of human space exploration towards the Moon and Mars are characterized by exposure to space radiation, such as galactic cosmic rays (GCR), solar particle events (SPE), and trapped radiation[25], changing gravity fields, acceleration/deceleration phenomena[26], isolation, and confinement[27] in a hostile and closed environment[28] and, finally, the increasingly far distance from Earth (Fig. 1). Exposure to GCR/SPE is potentially the most significant single health hazard for Low Earth Orbit; for deep-space crewed missions beyond the Earth's protective magnetic field this risk profile increases dramatically[28]. Recently, NASA increased an individual astronaut's total career effective radiation dose (independent of age at exposure and sex) due to spaceflight radiation exposure to less than 600 mSv, translating into a mean risk increase of cancer mortality (REID) of below 3% above the non-exposed baseline mean[21]. This change was implemented following a study carried out under the auspices of the National Academies of Sciences[29]. However, these standards remain controversial, especially in light of predicted REID ranging between 6-10% for females exposed at ages 20, 40, and 60 years for a simulated Mars Mission[20]. Of note, most international partners use a higher career dose limit of 1,000mSV (independent of sex and age).

Health concerns and ethical considerations regarding commercial space travel are of great importance considering that the aforementioned potential hazards can severely interfere with many physiological processes, such as physiological homeostasis on a cellular and

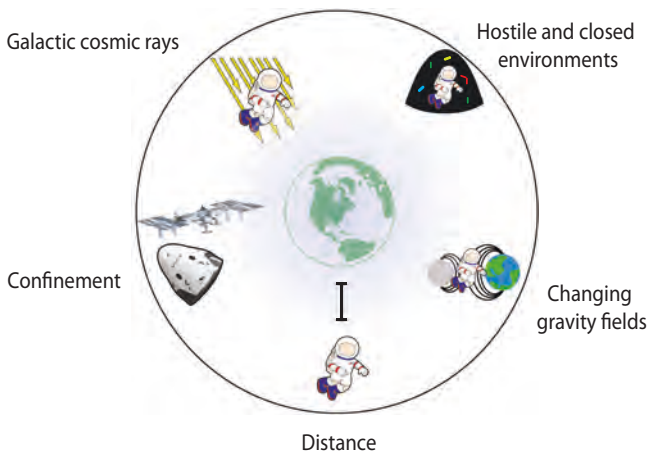

Fig. 1 | The Five Hazards in Space Contributing to Increased Health Risks. The figure exemplifies the main space flight hazards as used by NASA for the Human Research Road Map, such as distance, confinement, hostile and closed environments, galactic cosmic rays and space radiation, and changing gravity fields.

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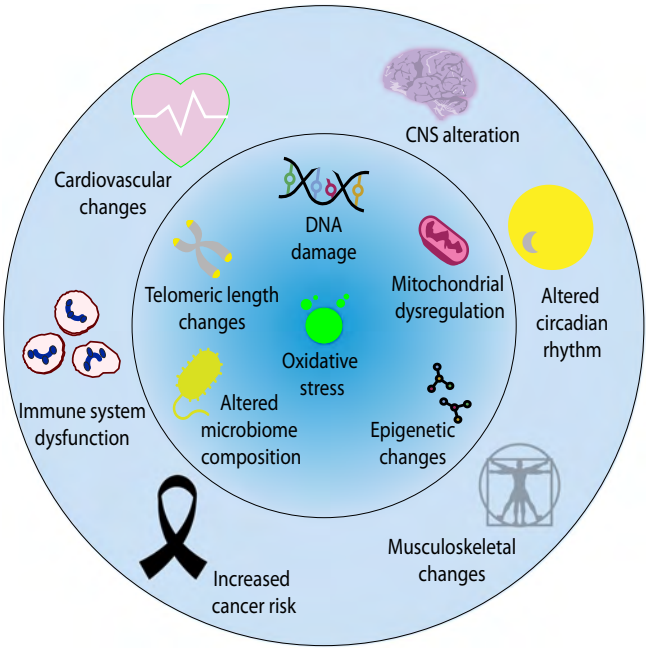

Fig. 2 | Biological and Health Features of Spaceflight. Space hazards, as outlined in Fig. 1, drive a diverse array of molecular and cellular changes observed during spaceflight, including DNA damage, oxidative stress, mitochondrial dysregulation, alteration in the microbiome composition, epigenetic changes, and telomere length changes. Such features will have the potential to induce pathophysiologic system changes affecting the central nervous system, the cardiovascular system, immune functions, musculoskeletal dynamics, the circadian rhythm, and cancer risk in SOs.

molecular level (Fig. 2), leading to microbiome shifts[30,31], inducing dysregulated mitochondrial function[32], and causing oxidative stress[33]. Furthermore, several space hazards cause DNA damage[28,30], affect telomere length[30], induce significant differences in DNA methylation, and alter accessibility of chromatin regions and specific DNA epitopes[30,34]. Such cellular and molecular effects lead to serious pathophysiology and health consequences[25], including but not limited to: changes in the cardiovascular system including fluid shifts, orthostatic intolerance, reduced ventricle size, thrombus formation[28,35–39], musculoskeletal defects defined as muscle atrophy and bone loss[30,40–42], central nervous system alterations including fluid shifts, neurocognitive and psychiatric alteration and Space-Associated Neuro-ocular Syndrome (SANS)[43,44], immune system dysfunction, initiation of malignant processes[45] due to loss of DNA integrity, failed DNA repair mechanisms, mutations, and chromosomal rearrangements[46]. Nevertheless, while knowledge mounts, there remains a lack of data addressing individual differences among astronauts, such as age, sex, and genetic background, contributing to the challenges of accurately predicting radiation hazards and outcomes[28].

Ethical issues related to the dangers and selection of SOs

Given these significant spaceflight hazards, stringent selection criteria are important to protect astronaut and SO health and to help ensure that missions can be completed successfully. For instance, the ISS Multilateral Space Medicine Board provides guidance about travel to the ISS by private individuals[47,48] and NASA has significantly strengthened its health-oriented recommendations and guidelines over the last two decades. Similarly, independent organizations such as the Aerospace Medical Association, have issued policies and guidelines taking into consideration not just the physical health of SOs but also their mental health[49]. There are not only expansive rules and guidelines at the selection and annual re-evaluation stage for astronauts, but also stringent health monitoring before, during, and after spaceflight[50]. However, with increasing commercial and private spaceflight opportunities, it is no longer just trained and pre-screened astronauts who travel to space. Since existing guidance in its various forms applies mostly to government-sponsored or -employed professional astronauts, the question arises as to who determines whether the potential health risks associated with spaceflight are acceptable or not in the case of SOs.

Current guidance on its own is not in a good position to resolve some of the issues that will arise in these new contexts. Both medical and scientific research communities as well as a number of governments have long and carefully deliberated about medical and ethical scenarios and questions that might arise during spaceflight. However, while some of their guidelines might apply to certain instances of, say, paying SOs (for example, private astronauts travelling to the ISS and therefore covered by ISS rules), there is still a relative dearth of discussion concerning how to extend these important deliberations to the new types of SO that we are likely to see in the coming decades.

Moreover, since existing law and policy frameworks were designed mostly with government-employed or -sponsored astronauts in mind, their scope does not always extend neatly to their non-governmental counterparts. For instance, federal space agencies form an employer-employee relationship with their astronauts. While this might be applicable to some kinds of potential commercial SOs, it will not be applicable to private SOs. For example, while the International Commission on Radiological Protection stresses the importance of radiological protection, in the U.S. the National Council on Radiation Protection and Measurements (NCRP)[51] explicitly states that its purview is "NASA selection of astronauts for participation in space missions" and that "the measures suggested in this Report may be unique to NASA and not generalizable". Although the refinements proposed by the NCRP to NASA's shared decision-making framework do not directly pertain to commercial and private SOs, their relevance is evident and should be taken into consideration.

One might think that general documents of medical research ethics could provide some help here. For example, the World Medical Association's (WMA) "Declaration of Helsinki" (DoH)[52] is one of the most influential and important sets of ethical principles concerning medical research involving human subjects. While the WMA has no formal authority or binding status, it is still often expected that guidelines concerning research ethics will look to the DoH as a guiding document. However, the DoH is neither accepted by all countries nor uncontroversial. For example, Schüklenk and Ashcroft[53] have highlighted both the "absence of a consensus over the actual content of the Declaration and its status", and stressed its "continuing lack of a serious consultation with the relevant stakeholders", while also emphasizing the more general "absence of a consensus among knowledgeable, well-intentioned bioethicists, scientists and political activists over the central issue of research ethics standards". There is also a heated debate about whether there exists an international consensus opinion that violates and diverges from the DoH's principles[54,55]. Macklin has argued that, even with revisions, the DoH "cannot resolve ongoing controversies", since "it simply does not address other aspects of international research about which people disagree"[56]. Macklin has further stressed conflicts between the DoH and "official regulations promulgated by a federal agency, with enforcement mechanisms and sanctions for noncompliance" and pointed out that "it is hardly surprising that researchers, ethical review bodies, and governmental agencies do not consider the Declaration of Helsinki to be a necessary adjunct to the "official" Common Rule, which governs most federally funded research in the United States"[56]. Indeed, the US FDA first rejected the 2000 and later revisions, before eliminating all references to the DoH in 2006[57]. The situation is not dissimilar in many other countries and regions. Documents such as the

DoH – regardless of its controversies – are much too general to resolve particular ethical conundrums related to human space travel. Thus, while they might provide some necessary restrictions and sometimes even positive guidance, the question of how such general principles apply to specific and concrete cases, especially when there is little precedent, requires further examination. This of course is just one reason why agencies around the world spend enormous efforts on crafting guidelines and recommendations about the ethics of human subject research in space. But who will do the same for those space travelers to whom these do not apply?

The relevant international legal framework, i.e. the five UN Space Treaties, do not specifically address the health of astronauts or other spaceflight participants[6]. The Outer Space Treaty (OST) of 1967 introduces the concept of "envoys of mankind" for astronauts[58]; the Rescue and Return Agreement (RRA) extends this protection to "personnel of spacecraft". However, neither of these terms is clearly defined and terminological inconsistencies have led to a broad interpretation, suggesting that the Agreement extends to human life in outer space or spaceflight generally, covering both professional and non-professional space travelers, including tourists. However, these agreements were drafted at a time when activities such as space tourism were unforeseen, posing challenges in predicting and regulating health concerns for modern space activities. Thus, these agreements lack explicit health regulations for individuals that are part of the private space industry and, even if such regulations existed, enforcing them would be challenging due to the absence of robust enforcement mechanisms in international law.

To address issues such as these at the US-level, the FAA[59] and NASA entered a Memorandum of Understanding in June 2012, to coordinate standards for commercial government or non-government astronaut transport to and from Low Earth Orbit and the ISS. The goal was to foster both public and crew safety, avoid conflicting rules and guidelines, as well as to provide a framework for the American space industry. Despite this, the clearance of 'ordinary' SOs for spaceflight is currently the responsibility of commercial providers, with limited oversight, and a lack of standardized screening procedures and protocols[60]. The US is currently the main country providing such guidance in the form of the FAA *Recommended Practices for Human Space Flight Occupant Safety*. However, due to the limits of FAA jurisdiction, these guidelines only apply to launch and reentry[61]. Further, the FAA guidance comes not in the form of mandatory requirements but rather as (minimal) recommendations, suggesting merely that "[p]roximate to flight, the operator should require each space flight participant to consult with a physician, trained or experienced in aerospace medicine, to ascertain their personal medical risks from the space flight profile and vehicle" (2023: B. 4.4.2). It also explicitly states that "[t]his document does not include any specific medical criteria that would limit who should fly in space as a space flight participant." (2023: A. 6.1). Thus, given that medical consultation is only a recommendation, in principle anyone capable of giving written informed consent can fly, regardless of their health profile, as long as they meet specified spaceflight operator criteria (Fig. 3). This raises a number of issues.

First, if an SO fails to be cleared by one physician, can they get clearance from a more lenient provider elsewhere?[62] As Langston points out, "[m]edical forum shopping is a foreseeable ethical and legal concern where regulatory standardization is lacking or is inconsistent between jurisdictions… [which] could lead to increased risk of harm for the individual (in-flight/post-flight), spaceflight and crew, as well as uninvolved third parties"[63]. This scenario parallels a situation seen in the Federal Motor Carrier Safety Administration[64], where a disqualified driver can apply for a resolution if a disagreement exists in regard to the medical qualification exam. However, to oversee potential medical forum shopping, all results from medical examinations have to be entered into the centralized National Registry, preventing the continued medical examination until a desired result is achieved and certified.

Second, there might be tension between the potential clearance requirements desirable for a commercial spaceflight operator or provider – who might have an interest in lenient requirements to sell as many seats as possible to the limited pool of individuals who can afford them – and those desirable from the health standpoint of a particular SO. One might argue that SOs should undergo relevant medical consultations and decide on the risks they are willing to take, similar to making choices about risky adventures on Earth. So why should they not be in a position to make similar decisions for space? Nonetheless,

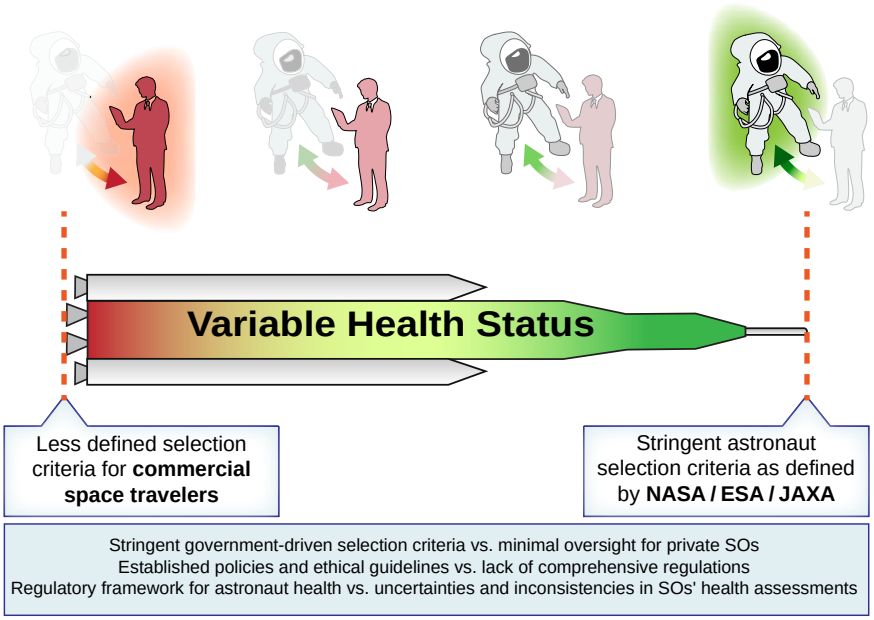

Fig. 3 | Differential Approaches to Selecting SOs. Stringent selection criteria (green) for government-sponsored astronauts (i.e., NASA, ESA, JAXA), including a hard stop mechanism are depicted on the right of the schematic (right dashed red line). Less defined commercial space traveler criteria for civilians (red) finally leading to rejection (left dashed red line) are indicated. The green-red color-coded middle area symbolizes the health-related risks, where the array of potential commercial space selection criteria is located.

while legal and social norms allow people to engage in some risks, the same norms do not give blanket allowance for people to do anything they want, instead exercising various degrees of paternalistic oversight both in people's private and public lives (for an overview of paternalism and its issues, see Dworkin 2020)[65]. For example, many governments require drivers and passengers to wear seatbelts, they require motorcyclists to wear helmets, forbid the sale of certain drugs, they forbid people to enter into certain kinds of contracts (for selling organs, gambling debts, etc.). Questions thus arise about the appropriate degree of paternalistic oversight for space travel, as well as questions about who has the power to enforce relevant policies and regulations. A further complication – and again one that speaks in favor of increased guidance or regulation – is that compromised SO health might also affect fellow passengers. In fact, the September 2023 revisions of the FAA recommendations now recognize this problem at least partially, stating that "[m]edical consultation for space flight participants is recommended … to help prevent them from endangering other occupants …. [and] commercial operators will be challenged to control hazards to space flight participants from other space flight participants with medical conditions."[61] This is, of course, also a problem with respect to various forms of ground and air transportation; however, it is exacerbated in the case of space travel. For one, providing assistance in space is more difficult than on the ground or in the air, thus putting fellow travelers in a position in which they are more likely to compromise their own safety during the course of providing help, especially in the absence of mandatory training. Further, space travel has inherent limits about the amount and kind of medical equipment that can be transported and effectively used in a spaceflight environment.

Third, even if stringent screening requirements are in place, substantial uncertainties remain regarding the various health consequences of space travel, making it virtually impossible for specific individuals to understand what their actual health risks are, even if advised by someone "trained or experienced in aerospace medicine"[61]. Current data insufficiently address individual differences among astronauts such as age, sex, and genetic background[66], which translates into significant uncertainty in predicting individualized space radiation hazards and outcomes for both astronauts and SOs[67]. In addition, while it is known that individuals metabolize drugs and supplements differently in space[68–70], little to nothing is known about the physiology underlying these changes. Limited available data[70] suggests that even relatively common prescription drugs might work differently in space. Furthermore, the reduced and often unknown stability of pharmacologic ingredients and supplements over the course of exploration-rated space missions becomes even more critical[70]. Specially prepared space medications, appropriate repackaging to improve pharmaceutical stability, and more insight into individual pharmacokinetics are needed to supply both astronauts and SOs with effective pharmaceuticals and/or other treatment options.

All of these considerations strongly suggest that some guidance and/or oversight with respect to potential SO screening and clearance would be highly beneficial (Fig. 3). In fact, this is not just so for the SOs, but also for the commercial providers who agree to transport them. While SOs are currently required to sign liability waivers, the legal status of these waivers is unclear, and so binding rules might also provide a way for providers to indemnify themselves against future lawsuits[71]. However, such rules should be sensitive to the diversity and variety of potential spaceflight endeavors: there is a difference between a private citizen enjoying a suborbital flight and a commercial crew member spending prolonged time in space for research purposes, perhaps on a commercial space station.

Human subject research

As our technical and research abilities evolve, so do the ethical considerations for using human subjects for research. While NASA estimated the chance of survival of the first mission to the Moon (Apollo 8) at 50-50, such odds for harm would not be accepted for any present-day study involving human subjects (recollection quoted from Ref. 72). NASA's ethical principles are defined to ensure human research subject welfare and minimize health risks. Further, research protocols can be implemented only if a risk/benefit analysis demonstrates that the risks to the subjects are reasonable in relation to the anticipated benefits and the expected importance of new knowledge. This will become even more important for missions to Mars[73]. In addition to the prevention of direct harm, other important considerations include protecting privacy, ensuring strict data security, and maximizing the positive social impacts of research.

Human Subject Research projects in space, supported or otherwise subject to regulation by any US federal department or agency, are strictly regulated under the Code of Federal Regulations (14 CFR pt 123069). Based on this, the implementation, procedures, and requirements to conduct space-related research involving human subjects is tightly controlled within a binding framework. NASA Institutional Review Board (IRB) committees review such research proposals to guarantee enforcement of these policies and the ethical, safe, and equitable treatment of human research subjects. In addition, the Office of Research Assurance ensures that all activities comply with applicable federal regulations and guidelines, ensuring that human subject welfare and minimal health risk are prioritized for all decisions. Such analysis will not take into account potential long-term effects on public policies. An interesting variation from non-NASA research protocols is the requirement that the responsible flight surgeon maintains the duty to intervene and terminate ongoing research if the health and welfare of astronaut research subjects is in question.

While the NASA IRB process adheres to standard practices for IRBs, it has unique aspects focused on human subjects' well-being beyond typical standards. The highest level of concern involves human subject research studies involving genetic testing. NASA defines genetic testing based on the Genetic Information Nondiscrimination Act[74]. Studies involving genetic testing in human subjects are deemed of the highest concern and automatically categorized as "greater than minimal risk", according to NASA[75]. These studies require additional measures to protect the research subjects, including policies that prohibit the public release of genetic data without prior approval from the individual or their direct family members, in accordance with NASA policy. NASA enforces strict rules as genetic data must be stored separately, and cross-referencing is forbidden without IRB approval. After genetic testing, all electronic data is deleted and given solely to NASA. However, commercial institutions or providers using services at NASA facilities to launch a space vehicle do not have to adhere to such rules in the same way.

While the above-described scenarios are focused on NASA, the processes for international ISS partner research are not demonstrating significant national differences. In general, plans for research involving human research subjects are carefully examined by the ethics committee of the researcher's university or institute, the space agency proposing the research, and the space agency of the astronaut subject. Furthermore, the Human Research Multilateral Review Board (HRMRB), comprising the representatives of space agencies involved in the ISS (NASA, ESA, CSA, JAXA), is tasked with investigating and reviewing ethical matters on the ISS. For all research conducted on an astronaut, the HRMRB looks at whether the safety and health of the astronaut are assured and whether the appropriate ethical considerations have been made. As necessary, the HRMRB then issues recommendations or modification requests. While government-sponsored human subject research is strictly regulated, it is still unclear whether future commercial SOs will be covered under such regulations, or if adherence to government regulations needs to be amended to reflect the new reality of space human subject research.

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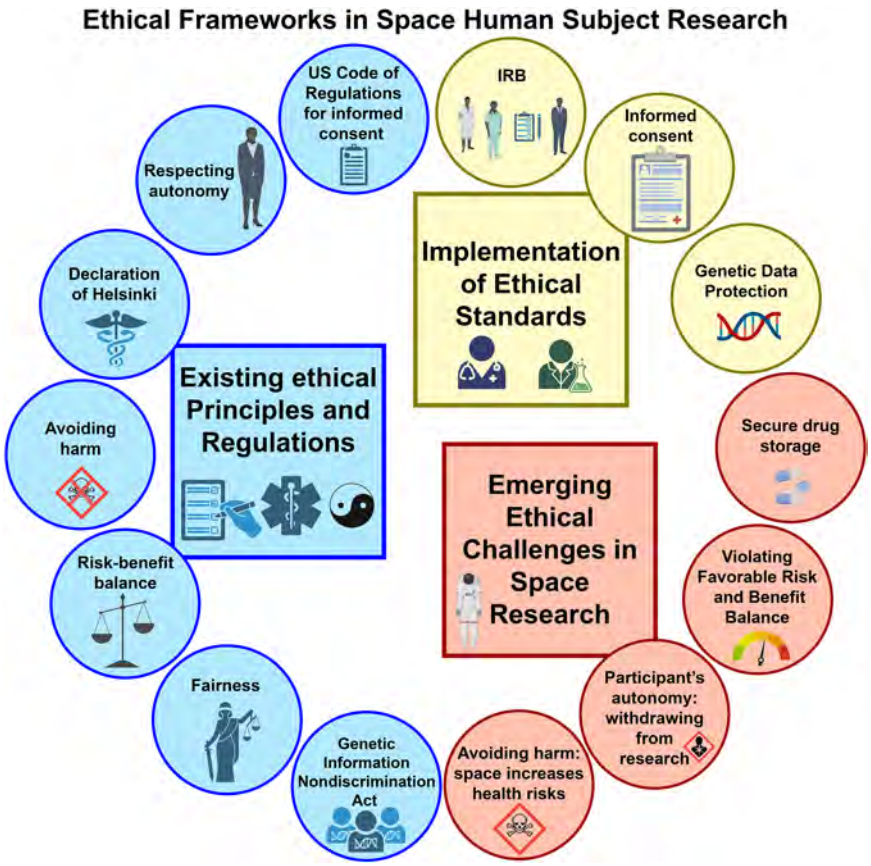

Fig. 4 | Human Subject Research Ethical and Operational Guidelines. A schematic for the ethical framework for space human subject research. This framework defines the key existing principles and regulations that currently exist in human research (in blue), the implementation of these ethical standards in the clinic and research laboratory (in yellow), and the challenges that should be considered and will arise for human research in space (in orange).

Ethical considerations

To date, our knowledge regarding the effects of spaceflight on humans, as well as the efficacy and safety of select medical interventions and pharmaceuticals in space, comes from government-sponsored missions, a small number of astronauts, and, more recently, civilians (Inspiration4, MS-20, Axiom-1)[76,77]. Increasing this type of knowledge is vital to ensuring the safety of future astronauts and SOs, especially considering the limited opportunities for medical treatment in space. It is therefore likely that astronauts and SOs will need to monitor, diagnose, and treat themselves at least part of the time. Increased commercial and private spaceflight opportunities will bring with them an expanding diversity of SOs with different health profiles, most of them likely not in the same physical and psychological shape as highly trained career astronauts[78–80]. By necessity, increasing knowledge about the effects of the spaceflight environment on human molecular biology, physiology, and psychology, as well as on the chemical composition of pharmaceuticals, involves human subject research. With the success of the recent Inspiration4 mission in defining a wide range of biomedical data, the role of commercial and private SOs in such research is likely to increase.

As previously outlined, government-sponsored spaceflights adhere to stringent criteria with respect to human subject research, through their respective IRBs, ethics committees, and groups. In the case of Inspiration4, research was conducted through Weill Cornell Medicine, the Translational Research Institute for Space Health of the Baylor College of Medicine[81], California Institute of Technology, and Massachusetts Institute of Technology and underwent similarly rigorous approval processes[82]. As the general standard for human subject research requires compliance with ethics approvals, it is expected that commercial spaceflight-based human subject research will continue to follow these and other applicable internationally ratified processes (Fig. 4).

However, commercial spaceflight also raises new ethical issues. In the past, human subject research in space was mostly a secondary concern of overall missions whereas now missions are increasingly conducted explicitly for this purpose. Ethical recruitment for biomedical research requires informed consent. For space travel, this requires participants to have a good understanding of the space environment, the nature of associated environmental hazards, as well as the potential side effects of any drugs under study[51]. But to what extent is such consent really possible with respect to space travel?[83] Exposure to high radiation, microgravity, and galactic rays may compromise participant safety in a number of unknown ways. Further, the effect of radiation and other extra-terrestrial factors on the chemical composition of pharmaceutical ingredients is largely unknown, thus making it especially difficult to inform potential subjects about likely side effects. The US Code of Regulations for informed consent requires a "description of any reasonably foreseeable risks or discomforts to the subject" (Title 45, A.A. Part 46.116, b2[82]). In the case of space travel, where many or most risks are unknown, it is unclear to what extent – if at all – this requirement can be met. Thus, there is a need to incorporate new and emerging ethical issues into existing frameworks in ways that are based on the same underlying ethical principles that gave rise to these and similar regulations in the first place and that are applicable to space travel. This is all the more urgent since civilians are already involved in such research[51]. Note also that the aforementioned problems are exacerbated for non-astronaut SOs: most of the existing data is not from a random population, but rather from an elite force

markedly dissimilar to average citizens in terms of training, age, health, and biomedical and behavioral profiles. Additionally, it has been established that even highly trained individuals respond quite differently to the zero-gravity environment[84]. Moreover, existing research was conducted on a population with a high degree of sex, gender, and ethnic homogeneity and relatively low diversity. Currently, it is therefore unclear to what extent this research generalizes to SOs beyond the relatively narrow population that has been studied so far.

Furthermore, principles of health ethics encompass avoiding harm, beneficence, achieving a favorable risk-benefit balance, respecting autonomy, fairness, and fidelity[85]. Terrestrial clinical trials rely on large participant numbers, secure drug storage, and timely sample collection, which are difficult to replicate in space. How to ensure compliance with these principles in space thus remains uncertain. There are also some concerns about individual principles: For example, human subject research in space may violate a participant's autonomy, should the individual decide to withdraw from the study. In terrestrial medical research, subjects may at any time withdraw their consent, even if the study is already in progress. Such withdrawal, however, is much more complicated in space. Even if individuals are able to drop out, return to Earth will not be immediate. There is also no way for individuals to withdraw from the possible (unknown) long-term effects of the spaceflight environment, and any consent thus involves not just consent to the study itself, but consent to any future effects that might result from spaceflight activities. This might also lead to violating the Avoiding Harm principle, since remaining in space is unhealthy for participants, especially if the desired withdrawal occurs as the result of unforeseen health problems. In turn, these conditions might then violate the Favorable Risk and Benefit Balance, due to the changing circumstances during the course of research. In NASA's case, the responsible flight surgeon can interrupt trials. However, in the absence of official, government-sanctioned flight surgeons with extensive spaceflight experience, who assumes the equivalent responsibilities for SO healthcare, ensuring subjects' best interests are met?

These problems represent only a small subset of issues, demonstrating the urgent need for guidance on non-government space research on human subjects (for further issues relating to privacy and behavioral health, see[86,87]). Such research should follow strict ethics committee review and otherwise meet the same stringent standards that NASA, ESA, and JAXA currently adhere to[88], including following suggestions by international medical research bodies, such as the DoH, The Council for International Organizations of Medical Sciences' International Ethical Guidelines for Health-Related Research Involving Humans[89], and others.

Conclusion

We are entering an exciting new era of space exploration previously only thought of as science fiction. Commercial/private and civilian spaceflights, such as Inspiration4 and the Polaris missions are no longer just a possibility but a reality. Exciting as these opportunities are, they also come with the burden of ensuring that future space travel will be as safe and ethical as possible. While governmental oversight has historically governed space activities, the emergence of non-governmental initiatives calls for unified ethical guidelines, safeguarding human well-being during selection, research, and decision-making in space. Since non-governmental outfits are not bound by the same rules in the same way, we as a community must ensure that the guidelines we set will guide space exploration according to the highest ethical and medical standards for humans that are currently possible, including selection of SOs, medical research ranging from human subject research to discussion of in-flight triage decisions. The added difficulties of non-universal terminology referring to different kinds of space travelers and of making guidelines sensitive to the diversity and variety of potential spaceflight endeavors will add further layers of complexity. The earlier and better any such guidelines can be implemented, the better the chances that space travel can be performed according to the safest and most optimal standards.

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Competing interests

The authors declare no competing interests.

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Rahimzadeh et al.—Research Ethics in Commercial Spaceflight (2023)

Rahimzadeh, Vasiliki, Jennifer Fogarty, Timothy Caulfield, et al. *Ethically Cleared to Launch? Rules Are Needed for Human Research in Commercial Spaceflight.* Science, 2023, 381(6665):1408–1411. doi:10.1126/science.adh9028

Overview: Calls for a dedicated regulatory framework for human research in commercial spaceflight.

INSIGHTS

POLICY FORUM

SPACEFLIGHT

Ethically cleared to launch?

Rules are needed for human research in commercial spaceflight

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Massive public and private investment in scientific research has enabled the commercial spaceflight industry to expand opportunities in space beyond primarily government-sponsored missions (*1*). Commercial companies endeavor to fly thousands of commercial spaceflight participants (cSFPs) and workers to space in the decades ahead (*2*). Although the future of safe commercial spaceflight depends on rigorous and inclusive research, the ethical conduct of such research is complicated by scientific uncertainty, high attendant risks (*3*), and poorly defined rules for research ethics oversight within the commercial spaceflight industry. Now is the opportune time to develop clear rules for ethical cSFP

PHOTO: JOE RAEDLE/GETTY IMAGES

The SpaceX Falcon 9 rocket with the Crew Dragon spacecraft lifts off from the Kennedy Space Center in Cape Canaveral, Florida, on 21 May 2023.

research while space activities are ramping up and the regulatory environment for commercial spaceflight is actively being shaped. We propose an ethical framework based on terrestrial human research that is anchored in four guiding principles—social responsibility, scientific excellence, proportionality, and global stewardship—and is applicable to the responsible conduct of research in commercial spaceflight.

Well-established norms, policies, and national regulations guide the ethical conduct of most traditional research involving humans on Earth. There is also consensus on ethical principles guiding research with government astronauts (*4*). However, there are no clear frameworks that govern privately funded research with civilians on commercial space vehicles. Existing research ethics safeguards may not apply because of gaps in how research regulations govern private industry, and international space research must contend with interjurisdictional issues. Many of the regulatory and ethics challenges we identify for commercial spaceflight research are amplified by the rare opportunity cSFPs have to travel to space and the outsized social value that only they can provide through research participation (see the box).

The emerging commercial spaceflight sector will have global impact, but the United States currently leads the world in overall spending on space programs, including investment in developing the commercial arm of spaceflight. We therefore highlight ethical tensions posed by the regulatory vacuum for responsible research conduct, primarily in the United States. For example, the US Federal Aviation Administration (FAA) moratorium on occupant safety regulations aboard commercial space vehicles is set to sunset in October 2023 (*5*). The FAA is working to encourage the development of industry consensus standards and revise the US government's human spaceflight safety practices (*6*), and has established an aerospace rule-making committee to garner industry input on a new safety framework. Meanwhile, the Biden administration confirmed that the United States will decommission the International Space Station as soon as 2030, which effectively ends decades of collaboration on the only microgravity research platform shared with other spacefaring nations. International agreements, including the Outer Space Treaty (OST)—signed and ratified by 112 countries—are silent on whether principles for peaceful human space exploration apply to human research sponsored by commercial firms (*7*), and diverse research partners and complex funding and sponsorship relationships can lead to redundancies in the science and provide insufficient oversight.

Gaps in policy intended to protect cSFP health and safety in commercial spaceflight research threaten the industry, hamstring scientific collaboration between public and private partners, and limit the translation of research benefits to society. To foster research safety and utility, our primary objectives are twofold: (i) create an expectation that commercial spaceflight companies provide the infrastructure and resources necessary to engage in high-quality human research, and (ii) inform approaches to safe and effective commercial spaceflight research by advocating for robust ethical principles and standards that reflect consensus among diverse stakeholders and account for the distinct research environments to which future cSFPs will be exposed.

GUIDING PRINCIPLES

Social responsibility

Most commercial flights currently depend on cofunding from the government and private sources. Additionally, commercial spaceflight services are only possible now because of substantial public investment in past research. Therefore, the public has an important role in helping to shape the commercial interests of companies, and data that builds on initial public investments in spaceflight research should be treated as community resources. What we learn in the early years of commercial spaceflight will be critical for ensuring the safety of future missions, and research with cSFPs has the potential to improve human health not only in space but also on Earth (*8*). Thus, early cSFPs arguably have a heightened social responsibility to help advance research to build the evidence base.

Appealing to principles of social responsibility differs from preexisting ethical frameworks that give primacy to autonomy because it explicitly calls on those privileged to have the opportunity to travel into space to contribute to research activities that benefit society at large.

Scientific excellence

Poorly designed, duplicative, and low-priority studies beget poor-quality data. They cloud the evidence base, endanger participants, and waste resources. Bad science is also bad for business. It can misguide strategy, permit inefficiency, and expose organizations to liability. By adhering to standards of excellence, those who sponsor and conduct research in commercial spaceflight show by example how rigorous science drives successful business practice.

Proportionality

Spaceflight research, like all research that involves humans, is only permissible if it maximizes social value and minimizes the likelihood and severity of harms to participants, crew members, and other personnel. Spaceflight is a high-risk activity, and research procedures that pose minimal risks on Earth could pose substantially increased risk when performed in space. The add-on risks of research participation should therefore be evaluated against the baseline risks of spaceflight, minimized to the extent possible, and proportionately balanced in relation to the anticipated benefits to the individual cSFP and to society.

Global stewardship

The benefits of human space exploration and its resources should be enjoyed by all (*7*). Spaceflight research should therefore engage, and be conducted by, individuals and communities representative of humankind's diversity. We draw on stewardship principles and concepts advanced in space governance (*9*), the environmental sciences, and natural resource fields to inform how we might fairly distribute the knowledge benefits of commercial spaceflight research. We emphasize responsible use of time, data, and natural resources in ways that take full and balanced account of the interests of society, future generations, and other species, as well as of private interests to advance the science of safe human space exploration (*10*).

NEW APPLICATIONS OF EXISTING POLICIES AND PRACTICES

Free and informed consent

If we take seriously the principle of social responsibility, we might condition commercial spaceflight on informed research participation focused on improving human health or safety, at least in the early years. Although all astronauts are thoroughly briefed on research protocols and voluntarily consent to participate, many view their participation as an occupational responsibility to support longitudinal health surveillance that benefits future crew. Privately funded cSFPs may not be motivated by the same occupational responsibility but rather could be moved to participate in minimally invasive or minimal risk studies under the principle of social responsibility.

To compel cSFP participation in research as a condition of spaceflight in the commercial context could undermine

the business interests of privately funded companies, including their ability to attract future customers. It could also violate cSFP autonomy by providing an excessive benefit that challenges voluntariness. Travel to space can present an opportunity so compelling that cSFPs could opt in to risky research not customarily tolerated on Earth without appropriate safeguards. Furthermore, some cSFPs are employees of commercial space companies, and conditioning employment on research participation is generally impermissible.

All prospective cSFPs should be fully informed about the social value of any proposed research protocols and be encouraged to participate. Incentivizing participation may be justified, so long as the incentive is calibrated with the risks and does not create undue inducement (*11*). Commercial companies may give preference to those cSFPs willing to participate in research, but further ethical attention is needed to determine whether cSFPs should remain flight eligible even if they decline research participation.

Maximizing benefits to society

The social value of research increases proportionately to the usefulness of new knowledge gained. Well-annotated datasets—including information about the flight protocol, operational endpoints, and adverse events—should be of sufficient scientific quality to substantiate social value. Those who conduct research in space should share these data to ensure findability, accessibility, interoperability, and reusability for the scientific community and society well into the future. Indeed, private companies must commit to openly sharing scientific data if they are operating on behalf of a signatory to the 2020 Artemis Accords (*10*), which includes Australia, Canada, Italy, Japan, Luxembourg, the United Arab Emirates, the United Kingdom, and the United States.

Minimizing risks

Known physiological effects of spaceflight stem from research principally performed with government astronauts and other highly trained personnel who cleared stringent medical tests before flight. Prospective cSFPs may not undergo the same tests, and commercial companies indeed plan to fly cSFPs with preexisting health conditions (such as cancer) and physical disabilities (for example, the European Space Agency parastronaut program). The attendant risks of cSFP research participation are expected to compound as a result. This is particularly true for cSFPs with less experience managing adverse events that affect fellow crew or responding to operational emergencies during spaceflight. Missions that enable quick and safe return to Earth could thus be prioritized for crews composed mostly of cSFPs without prior spaceflight experience. Competent adults ought nevertheless to be able to assume risks for the advancement of knowledge and betterment of society.

cSFPs may participate in multiple studies, each with their own set of risks and safeguards against adverse events. Future planned studies are likely to reflect different types of research (ranging from noninvasive, to minimally invasive, to invasive), with a broad spectrum of risk potential. Companies, principal investigators, and ethics committees therefore need to consider the portfolio of risks for cSFPs individually, as well as in the aggregate (*3*). Different risk thresholds may be justifiable for different crew members. Companies may, for example, limit a crew medical officer or commander from participating in research that could lead to impairment or incapacitation because their role is essential to the safety and welfare of the entire crew.

To further substantiate spaceflight safety and enhance informed consent for prospective cSFPs, a formal system for reporting adverse events should be developed like what is required of pharmaceutical drug companies. Such a system should be focused on adverse events related to research involving cSFPs, separate from adverse events from operational failures or crew error.

Data protections and governance

Some instances of research data sharing can be in tension with the proprietary interests of commercial companies or their customers. The commercial spaceflight industry would benefit from direct engagement with regulators to develop and

Ongoing cSFP research related to spaceflight-associated neuro-ocular syndrome (SANS).

SANS is associated with long-duration spaceflight and is thought to be the result of increased intracranial pressure (ICP). Symptoms include optic disc edema, changes in near vision, and possible reductions in cognitive functions that could compromise mission-critical tasks (*15*). Nearly 70% of NASA astronauts develop some degree of SANS, underscoring the need to identify its pathophysiologic mechanisms and find effective countermeasures. Commercial companies have a vested interest in management and prevention of SANS and support cSFP participation in studies of the issue. The most accurate method for measuring ICP—inserting a probe directly into the brain or cerebral ventricles—is too risky for spaceflight. Investigators developed a less risky method: a catheter surgically implanted in the lumbar cerebral spinal fluid space and attached to a subcutaneous telemetric ICP sensor that would enable ICP readings before, during, and after flight. After NASA concluded that the risks of the modified implant on long-duration missions were also too high, this approach was pursued by the Translational Research Institute for Space Health and a competitively selected experienced research team in coordination with a commercial spaceflight company to include a healthy cSFP in this study (https://taskbook.nasaprs.com/tbp/index.cfm?action=public_query_taskbook_content&TASKID=15266).

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implement methods to share data for research purposes without compromising intellectual property. An industry-wide database should be created to securely store and manage controlled access to relevant study data for research purposes [for example, (*12*)]. Robust data governance mechanisms—including penalties or sanctions to hold users accountable for data misuse—should be developed simultaneously with data infrastructures and should reflect the interests of contributors as well as downstream users of the data.

Similar data types may be collected to monitor cSFPs' health and welfare while in space and later repurposed for space health research (*13*), with appropriate consent. Privacy and confidentiality of these data rely heavily on the ability to deidentify them. However, the small sample size per mission and extensive data linkages needed to support robust data analyses means that cSFP privacy could be compromised even for minimal risk studies (*14*). Limits to data privacy should be disclosed to cSFPs at the time of consent, and prospective cSFPs should demonstrate that they fully comprehend the realistic risks that research data could be attributed to individual cSFPs and other privacy-related consequences of participation.

EXTENSION OF EXISTING POLICIES AND PRACTICES

Setting research priorities

Research investigating the effects of spaceflight on cSFPs can be expensive, risky, and difficult to reproduce because opportunities are rare, and only a select few cSFPs can be accommodated on space vehicles. Such extreme resource constraints have both practical and ethical consequences for setting research priorities, which places a premium on prioritizing scientifically rigorous studies that add the most social value, address questions about which there is genuine uncertainty, and can only be carried out in space as opposed to an Earth analog.

There may also be competing priorities for commercial spaceflight companies and sponsors of research in terms of what scientific questions to ask and where to invest research dollars. Those who conduct commercial spaceflight research should develop a transparent research agenda that meaningfully incorporates input from diverse stakeholders, including the public, scientists, regulators, funding agencies, and other industry partners. To avoid redundancy and increase scientific impact, research sponsors should consolidate studies that ask similar scientific questions or call for participation from cSFPs with similar health and demographic profiles whenever possible. This will require collaboration within a competitive space and sharing data for the public good as gestures of responsible stewardship, while protecting trade secrets to stimulate commercial investment.

Scientific and ethics review

Independent ethics review of research involving humans in space is expected, as it is on Earth. Although federally funded research is legally required to obtain ethics review, research funded entirely by private organizations is not. Legal authorities can also be unclear for research that involves cSFPs funded through multinational space agency collaborations, in which each agency maintains their own requirements. Research that involves cSFPs should nevertheless undergo independent ethics review that is free of any real or perceived investigator conflict of interest even if not strictly required by law because it is a longstanding ethical obligation that predates many legal requirements.

Given the specialized research focus, many research ethics committees will not have the necessary expertise to conduct quality, comprehensive reviews of spaceflight research. A specialty body could be named, external experts could be consulted, or membership on ethics committees could be expanded to include human spaceflight experts.

Promoting diversity of cSFPs and researchers

cSFPs have not so far been representative of society in terms of gender, age, genetic ancestry, health, and socioeconomic status. Where such individual attributes are known or suspected to have physiological ramifications for spaceflight, findings from research with less diverse cSFPs may not be generalizable. This raises at least two justice concerns: inequity in knowledge gained for those living on Earth, and inequity in evidence collected to support safe spaceflight for more diverse cSFPs in the future.

Investigators should be encouraged to consider diversity when designing research protocols, but ultimately, sample diversity will be driven by the specific research questions. With proper oversight, commercial spaceflight research presents a historic opportunity to address prior underrepresentation and redefine who can safely experience the wonders of spaceflight. Companies that fly their own staff as well as prospective customers on research missions should therefore also invest in the training, recruitment, and retention of researchers and cSFPs from diverse backgrounds to sustain a thriving commercial spaceflight workforce (*2*) and participant pool.

CONCLUSION

To demonstrate trustworthiness and reduce their own risk and liability, companies should issue policies and develop best practices to ensure that sponsored research is performed in a socially responsible and ethical manner. To demonstrate their commitment to global cooperation and responsible stewardship of space resources, regulatory agencies will need to strategize how to effectively implement and ensure accountability for ethical research standards across public and private sectors. We believe that there is ample opportunity for collaboration on both fronts that is consistent with our proposed ethical framework. Future work should focus on identifying specific responsible actors and determining what level of policy is appropriate for ensuring implementation of the framework. ■

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Doarn et al.—Multinational Medical Support for ISS (2021)

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Overview: Describes cooperative medical support structures for ISS operations as a template for future exploration missions.

Ethically cleared to launch?

Vasiliki Rahimzadeh, Jennifer Fogarty, Timothy Caulfield, Serena Auñón-Chancellor, Pascal Borry, Jessica Candia, I. Glenn Cohen, Marisa Covington, Holly Fernandez Lynch, Henry T. Greely, Michelle Hanlon, James Hatt, Lucie Low, Jerry Menikoff, Eric M. Meslin, Steven Platts, Vardit Ravitsky, Tara Ruttley, Rachael D. Seidler, Jeremy Sugarman, Emmanuel Urquieta, Michael A. Williams, Paul Root Wolpe, Dorit Donoviel, and Amy L. McGuire

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A Framework for Multinational Medical Support for the International Space Station: A Model for Exploration

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INTRODUCTION: In the 1990s, Canada, member states of the European Space Agency, Japan, the Russian Federation, and the United States entered into an international agreement 'Concerning Cooperation on the Civil International Space Station'. Among the many unique infrastructure challenges, partners were to develop a comprehensive international medical system and related processes to enable crew medical certification and medical support for all phases of missions, in a framework to support a multilateral space program of unprecedented size, scope, and degree of integration. During the Shuttle/Mir Program, physicians and specialized experts from the United States and Russia studied prototype systems and developed and operated collaborative mechanisms. The 1998 NASA Memoranda of Understanding with each of the other four partners established the Multilateral Medial Policy Board, the Multilateral Space Medicine Board, and the Multilateral Medical Operations Panel as medical authority bodies to ensure International Space Station (ISS) crew health and performance. Since 1998, the medical system of the ISS Program has ensured health and excellent performance of the international crews—an essential prerequisite for the construction and operation of the ISS—and prevented mission-impacting medical events and adverse health outcomes. As the ISS is completing its second decade of crewed operation, it is prudent to appraise its established medical framework for its utility moving forward in new space exploration initiatives. Not only the ISS Program participants, but other nations and space agencies as well, concomitant with commercial endeavors in human spaceflight, can benefit from this evidence for future human exploration programs.

KEYWORDS: International Space Station, international medical system, exploration, multilateral, policy, spaceflight.

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Collaboration in human spaceflight among nations began in earnest in the 1960s. In early bilateral dialogue between U.S. President John F. Kennedy and USSR Premier Nikita Khrushchev, spacefaring nations discussed the possibilities of working together to achieve a common goal.[10–12] While not initially leading to joint missions, these discussions signaled the possibility for space program physicians, scientists, and engineers to collaborate. After the Moon landings, the U.S.-USSR Joint Working Group (JWG) on Space Biology and Medicine was created and held its first meeting in 1971.[5] With openness highly unusual for the times, both sides began sharing mission medical and research data; for example, medical summaries of Gemini 7 and Apollo 15 missions were presented by NASA experts while the Russian side shared knowledge on space station atmospheres.[16] The JWG also became a forum for coordination of experiments on the Bion and Cosmos satellites,[5] and ultimately served as the foundation for the Apollo-Soyuz Test Project (ASTP), which culminated in a July 15–24, 1975, joint flight (docking occurred on July 17, 1975).[12,13]

Once the political decision on a docking mission of the Apollo and Soyuz capsules was reached in 1972, the members

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of the JWG engaged with engineering specialists to solve the problem of differing atmospheric pressures and compositions in the two vehicles. The joint medical operations plan of ASTP was a major achievement; besides addressing the environment problems, it set the stage for a new level of international collaboration in space physiology and medicine.[6] Notwithstanding all the prior contacts between the U.S. and Soviet space medicine specialists, it was the ASTP that revealed and managed the many barriers to collaboration, such as differences in medical and engineering standards, culture, language, and operational philosophy.

Beginning in 1978, the Soviet Union provided citizens of other countries access to flights aboard Salyut 6, Salyut 7, and Mir space stations through its Interkosmos (Интеркосмос) program. In addition, during the period of 1983–2003, individuals from a variety of countries (Belgium, Canada, France, Germany, India, Israel, Italy, Japan, Spain, Russia, Saudi Arabia, Sweden, Switzerland, and Ukraine) flew on the U.S. Space Shuttles as spaceflight participants (payload specialists or mission specialists).

Shuttle/Mir—Phase 1 of the International Space Station Program

In 1984, President Ronald Reagan proposed that the United States partner with Western European countries, Japan, and Canada to build Space Station Freedom. During this same time period, the Mir Space Station Program continued to grow and involve international crewmembers. On June 17, 1992, U.S. President George H. W. Bush and the first President of the Russian Federation Boris Yeltsin concluded an agreement on 'Exploration and Use of Outer Space for Peaceful Purposes.' The William J. Clinton Administration invited Russia to join the development of an international space station; the invitation was accepted in 1993 and formalized in 1994 under the auspices of the 'U.S.-Russian Joint Commission on Economic and Technical Cooperation', co-chaired by U.S. Vice President Albert Gore and Prime Minister Viktor Chernomyrdin. The commission oversaw the establishment of the Shuttle/Mir program, known as Phase I, including the groundwork of its medical support.[9]

In the early 1990s, eight Russian cosmonauts participated in the Shuttle/Mir Program as Shuttle crewmembers, while seven U.S. astronauts completed long-duration tours on Mir (**Table I**). Each of these missions enriched the collective experience of the aerospace medicine community in the intricacies of international human spaceflight. Notably, Shuttle/Mir signified the progression from an intermittent host-visitor relationship toward a stable bilateral system of medical support, which was seen as the precursor of the International Space Station (ISS) multilateral medical organization.

Prior to commencement of Shuttle/Mir missions, medical experts from the United States and Russia, under the leadership of the JWG, worked together in the newly established Medical Operations Working Group to define the operational medical support system and prepare for crew exchanges in both Shuttle and Mir operations in Phase I.[8] The lessons learned from the interactions of U.S. and Russian specialists in nominal Phase 1 flights, and several serious off-nominal situations, were instrumental in the development of the medical and environmental requirements for ISS, which were officially approved in September 1998.[9]

Thus, Phase 1 medical operations served as the foundation for the development of the framework that the ISS uses today.[7] Following the Intergovernmental Agreement[15] among the partner states, the final memoranda of understanding (MOU) between NASA and the four cooperating agencies of the ISS Program (Canadian Space Agency, European Space Agency, the Science and Technology Agency of Japan, and the Russian Space Agency) were signed on January 29, 1998, to replace the three earlier MOUs from 1989,[14] i.e., before Russia's participation in the program was proposed and confirmed (1993).[4]

Article 11.4 of the new MOUs defined the framework for ISS multilateral medical operations. The medical leadership of all five partners was already proactively engaged in developing work on the ISS Medical Operations Requirements Document (MORD) and the common medical standards for selection of crewmembers for the ISS Program (**Fig. 1**).

Organizational Structure

The medical management structure of the ISS Program was created in accordance with Article 11.4 of the MOUs (**Fig. 2**), which provided the framework and the cardinal principles of multilateral authority and decision-making. Similar to other MOU clauses, Article 11.4 was neither intended nor written to address all aspects of the Multilateral Medical Policy Board (MMPB), the Multilateral Space Medicine Board (MSMB), or the Multilateral Medical Operations Panel (MMOP) function. Integration of Article 11.4 took place through programmatic documentation, such as the Station Program Implementation Plan (SPIP) and the charters of each medical board/panel. The principles of medical management in MOUs and SPIP were reflected in the 'ISS Medical Operations Requirements Document (ISS MORD)', which was generated by the MMOP. Specific roles and responsibilities, functionality, forums, and interfaces of the MMOP, the MSMB, and the MMPB were further discussed and coordinated using their charters as vehicles for negotiation among the five agencies and the ISS Program management.

Article 11.4 stipulated the development of medical standards and requirements as a function of the MMOP and specified an approval pathway through the MSMB. In addition to ISS medical operations design and implementation, the MMOP was further charged with ongoing functions to oversee joint medical operations and to maintain mission medical readiness assessment and reporting processes. In the nominal operational paradigm, the ISS Program defined a dual primary interface for the MMOP; medical policy matters would be communicated with the highest medical authority (the MMPB), while operational implementation and budgetary matters were to be approved by the highest-level operational authority [ISS Multilateral Mission Operations and Integration Board (MMIOCB)]. The latter reporting pathway enabled mission readiness and

Table I. Astronaut and Cosmonaut Participants of the Shuttle/Mir Program.

NAME	MISSION	DURATION	DATES
Sergei K. Krikalev (Russia)	STS-60 (no rendezvous with MIR)	8 d, 7 h	Feb. 3–11, 1994
Vladimir Titov (Russia)	STS-63 (rendezvous only)	8 d, 6 h	Feb. 3–11, 1995
Norman Thagard (USA)	↑Soyuz TM-21 / ↓STS-71 (Mir 18)	115 d, 8 h	March 14, 1995–July 7, 1995
Anatoly Solovyev (Russia)	STS-71	9 d, 19 h	June 27–July 7, 1995
Nikolai Budarin (Russia)	STS-71	9 d, 19 h	June 27–July 7, 1995
Gennadi Strekalov (Russia)	STS-71	9 d, 19 h	June 27–July 7, 1995
Vladimir N. Dezhurov (Russia)	STS-71	9 d, 19 h	June 27–July 7, 1995
Shannon Lucid (USA)	↑STS-76 / ↓STS-79 (Mir 21)	188 d, 4 h	March 22, 1996–Sept. 26, 1996
John Blaha (USA)	STS-79 / ↓STS-81 (Mir 22)	128 d, 6 h	Sept. 16, 1996–Jan. 22, 1997
Jerry Linenger (USA)	↑STS-81 / ↓STS-84 (Mir 22/23)	132 d, 4 h	Jan. 12, 1997–May 24, 1997
Yelena Kondakova (Russia)	STS-84	9 d, 4 h	May 15–24, 1997
C. Michael Foale (USA)	↑STS-84 / ↓STS-86 (Mir 23-24)	144 d, 13 h	May 15, 1997–Oct. 5, 1997
David Wolf (USA)	↑STS-86 / ↓STS-89 (Mir 24)	127 d, 19 h	Sept. 25, 1997–Jan. 31, 1998
Salizhan Sharipov (Russia)	STS-89	8 d, 19 h	Jan. 15–25, 1998
Andrew Thomas (USA)	↑STS-89 / ↓STS-91 (Mir 24-25)	140 d, 15 h	Jan. 22, 1998–June 12, 1998
Valery Ryumin (Russia)	STS-91	9 d, 19 h	June 2–12, 1998

STS = Space Transportation System; ↑ = launch; ↓ = return; d = days; h = hours.

mission status input, communication of operational concerns and requests, as well as cost, technical, and engineering decisions related to medical operations. In the final medical authority arrangement with the ISS Program, the MMOP was delegated control of the medical requirements and medical standards documentation, with concurrence of the MSMB and the MMPB for medical standards and with the MMIOCB approval of changes that entailed additional costs or affected nonmedical organizations or processes.

The MSMB functions as the medical board with final authority for crew medical certification. The MMPB serves for policy formulation and conflict resolution should the MSMB or the MMOP fail to reach consensus on matters within their respective responsibilities.

Governance

Article 11.4 of the MOUs delineates how the three entities (the MMPB, the MSMB, and the MMOP) are structured and where they interface with the ISS Program management. Each of these groups have established charters and structures that ensure their efficient operation. The MMPB and the MSMB have U.S. and Russian co-chairs. The MMOP chair rotates among the five partners on an annual basis, with the U.S. member otherwise serving as a co-chair to help coordinate functions and logistics. All members of the three multilateral bodies are physicians with significant experience in the discipline of space medicine (see **Fig. 3**).

The MMOP receives specialized expert input from its 12 chartered working groups across a range of disciplines and depends on their multilateral input for both standard-setting and ongoing management of medical operations. In addition, unique challenges have resulted in the creation of ad hoc "tiger teams" or permanent "sub-working groups" dedicated to specific areas of focus.

The MMOP also conducts a weekly virtual meeting as the ISS Space Medicine Operations Team to review all aspects of current medical operations, including ISS crewmember health status and concerns. As of February 2020, this forum had met 1000 times since the beginning of ISS habitation.

Multilateral documentation. As the Phase 1 Program was coming to an end and the ISS Program was ramping up, the framework laid out in Article 11.4 of the MOU began addressing significant issues related to multilateral foundations of crew selection, crew training, on-orbit medical operations, environmental monitoring capabilities, countermeasures, and extravehicular activities. Medical personnel, biomedical engineers, and life scientists were also participants in other system integration issues that were related to human health and performance.

In the early construction phase of the ISS, in parallel with the coordination of the MMPB, the MSMB, and the MMOP

Fig. 1. Medical representatives of the five ISS Agencies at the 3rd meeting of the ISS Multilateral Medical Operations Working Group [later renamed the Multilateral Medical Operations Panel (MMOP)], Houston, TX, USA, 1997. From left to right: Tadashi Murai, Michael Barratt (standing), Chiharu Sekiguchi, Ashot Sargsyan, Alexander Kulev, Charles Doarn, Alexander Kulev, James Collier, Valeri Morgun, Valeri Bogomolov, Gary Gray, Volker Damann, Roger Billica, and Yuri Kataev (courtesy of NASA).

11.4. NASA, ESA and the other partners will establish a Multilateral Medical Policy Board (MMPB) to provide coordination and oversight of crew health issues. NASA and ESA will each provide a single point of contact for medical support who will have full responsibility on behalf of its respective agency to resolve issues related to the development of a common system for medical support. The MMPB will be supported by a Multilateral Space Medicine Board (MSMB) and by a Multilateral Medical Operations Panel (MMOP), established by NASA and ESA with the other partners, which will be the primary working level groups for coordination of crew health matters including clinical care, medical standards, preventative medicine (including operational countermeasures) and environmental monitoring. The MMOP and the MSMB will operate on the principle of consensus. The MMOP will develop medical standards, certification criteria, pre-flight, in-flight, and post-flight medical care requirements, medical hardware responsibilities and operational procedures and recommend them to the MSMB for approval. The MSMB will present its decisions and findings to the MMPB and MCOP, as appropriate, for review and concurrence. NASA and ESA will be responsible for medical certification of their respective crew members in accordance with agreed standards, and will present the appropriate documentation to the MSMB for approval. The MSMB will have responsibility for final medical certification of crew and for oversight of the implementation of medical operations.

Fig 2. The text of Article 11.4 of the ISS Memorandum of Understanding (MOU) between NASA and ESA signed into force on January 29, 1998. There are three other MOUs, with the same contents, between NASA and three other partner agencies.

charters, two documents were developed to establish the high-level medical requirements of the program: ISS MORD and the three ISS Medical Evaluation Document (MED) volumes. The MMOP Working Groups were responsible for coordination of requirements in their respective areas of expertise, as well as for ongoing maintenance of those areas through recommendations to the MMOP.

The MORD was to define all aspects of medical operations in a high-level programmatic set of requirements, which would be adopted by the program as mandatory conditions for safe operation of a crewed station. Any requirements levied by the multilateral medical community, which the program would be unable to satisfy, were tracked as "unmet requirements", resulting in a waiver or awareness of added risk to health or performance. The MORD would also serve as a foundation for implementation documentation. As shown in **Table II**, ISS MORD continued to adapt to changing policies, new evidence, and programmatic revisions.

Despite the great difference in the size of the five partners' crew cohorts, all partners participated in the development of the second set of high-level medical requirements and medical standards, eventually called MED Volumes A, B, and C. These documents define crewmember testing routines for medical certification (part of Volume A) and in relation to flight (Volume B). Volume A also stipulates the process of medical certification, including the list of causes for rejection. Joint standards are essential for the operation of the certification process by the MSMB. All partners committed in a joint memorandum to full disclosure of medical information on each crewmember candidate and to decision-making by consensus. The MED Volume C is a set of relatively permissive selection standards developed for medical certification of individuals without operational responsibilities who would visit the ISS for a short period of time as "spaceflight participants" or "tourists".[2]

The framework also includes a wide variety of other documentation, all developed by multilateral medical leadership and subject matter experts. Table II lists the various types and levels of documentation that supports this framework.[15]

Challenges and Opportunities

As the ISS Program continues its service as a mature laboratory and a testbed for the future of human spaceflight, national and commercial space organizations continue to evolve and will likely build new partnerships to pursue even more ambitious goals, such as human missions to the Moon, Mars, and other destinations in the solar system.[3] A proven framework of the ISS collaboration represents a tremendous value to future partnerships. Any strong evidence from over three decades of the ISS collaboration should continue to be shared through scholarly forums for academic analysis to assure the best possible risk postures and health outcomes of future missions.

Fig 3. Multilateral Medical Policy Board (MMPB) Members in Moscow, Russia, in October 2018. Front row (L-R): Anatoly Grigoriev (Roscosmos), J. D. Polk (NASA), and Jean-Marc Comtois (CSA); back row (L-R): Guillaume Weerts (ESA), Charles Doarn (Executive Secretary, NASA), and Kazuhito Shimada (JAXA). (Courtesy of SC Roscosmos.)

Since the beginning of human spaceflight in the 1960s, the evidence base of space medicine has grown in parallel with the growth of medicine at large, in some areas positioning space medicine at the forefront of advanced technology utilization and medical innovation (e.g., telemedicine and ultrasonography of the eye). Another prominent success of space medicine is in its ability to create and operate a most sophisticated

Table II. Framework Documentation Development and Implementation Timeline.

DOCUMENTATION	TIME PERIOD	AUTHORITY	PROGRAM PHASE, NOTES
Intergovernmental Agreement	1993–1998	Nations	Shuttle / Mir - ISS
MOUs	1993–1998	Agencies	ISS
Charters (MMPB, MSMB, MMOP)	1998	Agencies and ISS Program	ISS
ISS MORD	Initial release: 1998	MMOP	ISS
MED Volume A	Initial release: 2005	MMOP	NASA document (AMERD) was used as an interim joint standard with agency-specific modifications
MED Volume B	Initial release: 2004	MMOP	
MED Volume C	Initial release: 2002	MMOP	ISS, specific to spaceflight participants
MMPB Policy Directives	2003, 2005, 2007, 2011	MMPB	ISS
ISS Generic Ground rules and Scheduling Constraints, medically relevant sections		MMOP	ISS
ISS Flight Rules, Aeromedical section	Updated as necessary	MMOP	ISS
MMPB Framework Document	Initial release: 2010	MMPB	ISS
ISS Joint Medical Operations Implementation Plan (JMOIP)	Initial release: 2015	MMOP	Includes Annexes: Flight Surgeon Training Document and Infectious Disease Prevention Document

MOU: Memorandum of Understanding; MMPB: Multilateral Medical Policy Board; MSMB: Multilateral Space Medicine Board; MMOP: Multilateral Medical Operations Panel; ISS: International Space Station; MORD: Medical Operations Requirements Document; MED: Medical Evaluation Document.
Med Volumes A, B, and C are updated as necessary to reflect growing and changing evidence in space medicine and terrestrial medicine at large.

international medical system, which has identified and tested solutions to numerous challenges (e.g., culture and medical practice, language, standardized protocols). It is widely believed by many mission planners and visionaries that a sustainable, long-term program of human space exploration should be international. With that presupposition, it will unquestionably mean the practice of space medicine in a functional multilateral medical system and the robust, time-tested medical organization of the ISS Program represents a validated precedent.

Characteristics of the ISS Multilateral Medical Policy

Pursuing a single goal to ensure the best possible health outcomes for the ISS crew, ISS medical policy foresees an 'integrated health support system operating on the best available evidence, with the best available resources, and to the highest ethical standards' as an essential system to the success of the ISS Program. Since the early 1990s, five international agencies, representing 26 nations, agreed to common standards and medical requirements that often differ from those used by each nation, individually. Principles that govern the selection and certification of crewmembers for flight, training, and certification of specialized aeromedical physicians (flight surgeons) to support ISS missions have been carefully developed and integrated across diverse medical cultures and national legislations.

The concept of consensus decision-making has served this program very successfully. The MMOP is the foundation for which this consensus is relegated. If the MMOP cannot come to a successful operational decision, the concern is escalated to the MMPB for resolution. In over 25 yr of ISS partnership, this process has rarely been invoked, demonstrating that the framework, established in the 1990s, has retained its effectiveness throughout decades of ISS operations. Also, over the course of 25 yr, policy statements promulgated by the MMPB in support of the MMOP's and the MSMB's functions have been exceptionally constructive in enabling and safeguarding a unique multilateral healthcare system.

As the ISS grew in size and complexity, the various specialized working groups, subgroups, and teams of the MMOP addressed a multitude of issues that were instrumental to construction and utilization of ISS. Some of these groups, highlighted below, continue to meet regularly while others interact less frequently based on need.

Working Group
- Biomedical Training
- Biomedical Operations
- Countermeasures
- Environmental Health
- Human Behavior and Performance
- Extravehicular Activity
- In-Flight Clinical Medicine
- Medical Informatics and Technology
- Medical Standards and Health Evaluation
- Nutrition
- Postflight and Rehabilitation
- Radiation Health

Subgroups
- Acoustics and Audiology
- Air Quality
- Fatigue Management
- Microbiology
- Spaceflight Associated Neuro-Ocular Syndrome
- Water Quality

Tiger Teams
- Crew Fatality
- Increment Duration

New 'tiger' teams are developed to address emerging operational concerns. Every group is staffed by at least one subject matter expert representing each International Partner.

A Model for Transition to New Initiatives in Exploration

It was the vision and leadership of a few individuals in the late 1960s and early 1970s that laid the foundation of the

international space medicine community through the JWG[6] and the ASTP.[1] The design of the joint ISS health system was heavily influenced by all preceding international activities that incrementally grew a body of enabling knowledge and operational solutions. As the ISS continues to benefit humanity in its 20th year of continuous human presence as of 2020, the United States and other ISS partner nations are rapidly forming plans for even more complex and daring missions. Many nations and commercial entities have expressed ambitions to join the community of human spaceflight and exploration. The drive for exploration, so natural for the human species, shows no signs of remitting. The experience of the joint ISS medical system will remain a powerful reference for constructive international collaboration in the post-ISS era of expansion of the human presence off the Earth.

The various multilateral groups, described above, worked hard to overcome the boundaries of time zones, language, culture, geopolitical interests, and geography. Through integrative and collaborative interactions, an international health system was developed to support all phases of human spaceflight on the ISS. The creation of authorities of medical policy (the MMPB), requirement setting and operational oversight (the MMOP), and certification (the MSMB) with consensus decision-making provided a single strong integrating mechanism. A collective trust among the five agencies had to be rapidly built, assured, and upheld for the long-term operation of the program. The MSMB, by virtue of its medical certification role, could only function on the basis of common criteria on the one hand, and full disclosure of medical information on the other. The potential collision of national medical standards and approaches at this level could not be prevented by full disclosure alone. Shared desire to achieve consensus through rigorous review of medical decisions played a hugely constructive role by upholding the quality of crewmember assessments and evidence-based considerations, thereby minimizing crewmember disqualifications due to the lack of consensus.

Overall, this tripartite medical management structure in a sterling manner has successfully executed its responsibilities over the course of the ISS Program and continues to do so. During that time, challenges and opportunities arose and were addressed. Beyond the life of the ISS, human spaceflight programs will include exploration initiatives and commercial spaceflight, which will heavily rely on the medical and administrative evidence of unprecedented value that the ISS Program created.

As nations and commercial providers ponder new programs for space travel, they would be at a great disadvantage if they did not consider the ISS framework that has been operational for several decades. New programs will bring new partners and new ideas and this framework provides an excellent platform with which all of us can continue to learn from and benefit from.

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POLICY CONSIDERATIONS FOR PRECISION MEDICINE IN HUMAN SPACEFLIGHT

Erik L. Antonsen & Rebekah D. Reed[1]

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INTRODUCTION

Over the 60-year history of human spaceflight, NASA has pushed the boundaries of human exploration, grappling with the challenge of understanding the risks faced by spacefaring crews and pushing the boundaries of technologies from many fields to help reduce those risks. After 20 years of constant human habitation in Low Earth Orbit ("LEO") aboard the International Space Station ("ISS"), NASA is poised to return to the Moon and eventually send humans to Mars. As NASA prepares to expand the reach of human exploration, it will benefit from leveraging advances in terrestrial health care to ensure that human explorers can travel longer and further than ever before, and safely return home to Earth.

Maintaining human health and performance in exploration missions is among NASA's most challenging technical problems.[2] This is due in part to the small number of people who have experienced those hazards. It is also a result of the daunting technical challenges of spaceflight itself, which have taken priority over understanding what long-term exposure to the spaceflight environment does to human explorers.[3] However, as NASA worked to solve the immense engineering challenges of exploration spaceflight, terrestrial advances in health care technology have changed the face of medicine. Clinical capabilities that seemed like science fiction 20 years ago—whole genome sequencing, tailored pharmaceutical and gene interventions for previously untreatable conditions, mail order genetic screenings, personalized medicine[4]—

2 INST. OF MED. ET AL., SAFE PASSAGE: ASTRONAUT CARE FOR EXPLORATION MISSIONS 3 (Wash., D.C.: The Nat'l Academies Press, 2001) [hereinafter SAFE PASSAGE] (Observing that "risks to human health of long-duration missions beyond Earth orbit, if not solved, represent the greatest challenge to human exploration of deep space. The development of solutions is complicated by lack of a full understanding of the nature of the risks and their fundamental causes.").

3 *Id.* at 18 ("Because of the engineering problems associated with early space endeavors, the historical approach to solving problems has been that of engineering. Long duration space travel will require a different approach, one requiring wider participation of those with expertise in divergent, emerging, and evolving fields.").

4 *See* NAT'L RESEARCH COUNCIL, TOWARD PRECISION MEDICINE: BUILDING A KNOWLEDGE NETWORK FOR BIOMEDICAL RESEARCH AND A NEW TAXONOMY OF DISEASE (Wash., D.C.: The Nat'l Academies Press 2011) [hereinafter TOWARD PRECISION MEDICINE]. The National Institute of Health (NIH) introduced the term "precision medicine" in this report. The NIH

are now becoming available to individual patients.[5] Advances in the fields of omics[6] and precision medicine provide an opportunity to gain a deeper understanding of the human body's response to space. However, the rate of technological change in medicine has outpaced the speed at which the federal government can develop appropriate policies and ethical frameworks to guide the adoption of new medical capabilities.[7] Faced with rapidly changing health care paradigms, NASA has the challenge of determining which advances are worthy of investment and investigation, and perhaps more critically, how to construct appropriate policy and ethical frameworks in advance that will allow the adoption of precision medicine technology as it becomes available. Exploring these issues may support NASA's work to mitigate the human health risks posed by exploration spaceflight.

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defines precision medicine as "an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person." Precision medicine allows the more accurate prediction of "which treatment and prevention strategies for a particular disease will work in which groups of people . . . in contrast to a one-size-fits-all approach, in which disease treatment and prevention strategies are development for the average person, with less consideration for the differences between individuals." GENETICS HOME REFERENCE, *What is precision medicine?,* U.S. NAT'L LIBRARY OF MED., NAT'L INST. OF HEALTH, lm.nih.gov/primer/precisionmedicine/definition (last visited Aug. 6, 2019).

5 *See* Geoffrey Ginsburg & Kathryn Phillips, *Precision Medicine: From Science to Value*, 37 HEALTH AFFAIRS 5 (May 2018), 694–701. *See also* Samuel Aronson & Heidi Rehm, *Building the Foundation for Genomics in Precision Medicine*, 526 NATURE 336 (Oct. 15, 2015).

6 "Omic" is a term intended to capture the information obtained in multiple domains including genomics, epigenomics, proteomics, metabolomics, and others. These include genetic information as well as the downstream effects of genetics within an individual.

7 *See e.g.*, Ginsburg & Phillips, *supra* note 5, at 3 ("Policy makers will need to address the return of results, privacy, confidentiality, and education while developing regulations and economic incentives that can align all stakeholders toward the same outcomes. Patients stand to benefit with optimized health outcomes in such a genomics and data enabled learning precision health system."); Benjamin Chin-Yee & Ian Chin-Yee, *Big Data, Precision Medicine, and Person-Centered Healthcare*, 6 EUR. J. FOR PERSON-CENTERED HEALTHCARE 513, 514 (2018) ("[T]he latest trend in precision medicine brings with it a focus on genomics, which has been criticized for downplaying the importance of other factors, such as social determinants of health. This is not to deny the importance of genes in human diseases, but simply to point out that if we understand disease solely in these terms we will inevitably constrain how we view problems and find solutions. As the common saying goes, if you only have a hammer, everything looks like a nail.").

Working with the Institute of Medicine ("IOM") (now known as the National Academy of Medicine)[8], NASA has spent several decades exploring the ethical and policy framework necessary to support human exploration and touched upon the need for an increased use of personalized medicine approaches. In its 2014 report, IOM observed that part of the ethics framework for exploration would include "identification of the astronauts health susceptibilities and personal risk factors (if known)" to inform decisions about mission participation.[9] The burgeoning field of precision medicine has the potential to help NASA develop this insight.

NASA has already made considerable strides to develop a policy framework that incorporates the IOM recommendations.[10] It has also begun building a framework for incorporating omics into NASA research.[11] For example, NASA's policy on genetic research was stimulated by work already being done in the NASA Twins Study.[12] This study was driven by the need ". . . to better understand the impact of prolonged spaceflight on human biology and health."[13] This study assessed longitudinal biomarkers including genomic, epigenomics, biochemical and physical changes that occurred during the one-year

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8 Throughout this paper, reference is made to the Institute of Medicine ("IOM"). In 2015, the IOM was renamed the National Academy of Medicine ("NAM"). Because this paper references studies published before the name change, the authors continue to reference the IOM.

9 INST. OF MED. ET AL., HEALTH STANDARDS FOR LONG DURATION AND EXPLORATION SPACEFLIGHT: ETHICS PRINCIPLES, RESPONSIBILITIES, & DECISION FRAMEWORK, 9 (Inst. of Med., National Academies Press, 2014) (hereinafter IOM HEALTH STANDARDS).

10 *See* IOM HEALTH STANDARDS, *supra* note 9. *See also* NAT'L AERONAUTICS & SPACE ADMIN., NASA PROCEDURAL REQUIREMENTS 8900.1B, NASA HEALTH AND MED. REQUIREMENTS FOR HUMAN SPACE EXPLORATION, APPENDIX F: ETHICAL PRINCIPLES AND RESPONSIBILITIES (Dec. 16, 2016), https://nodis3.gsfc.nasa.gov/npg_img/N_PR_8900_001B_/N_PR_8900_001B__Appendix F.pdf [hereinafter NPR 8900.1B APPENDIX F].

11 NAT'L AERONAUTICS & SPACE ADMIN., POLICY DIRECTIVE 7170.1, USE OF HUMAN RESEARCH GENETIC TESTING (Feb. 22, 2018), https://nodis3.gsfc.nasa.gov/npg_img/N_PD_7170_0001_/N_PD_7170_0001__main.pdf [hereinafter NPD 7170.1].

12 *See* NAT'L AERONAUTICS & SPACE ADMIN., FIREWORKS IN SPACE: NASA'S TWINS STUDY EXPLORES GENE EXPRESSION (Kelli Mars, ed., 2017), https://www.nasa.gov/feature/fireworks-in-space-nasa-s-twins-study-explores-gene-expression.

13 Francine E. Garrett-Bakelman et al., *The NASA Twins Study: A multidimensional analysis of a year-long human spaceflight*, 364 SCIENCE 6436 (2019).

mission over 24 months in an effort to ". . . provide critical metrics for astronaut health that could aid in assessment of increased risks and guide potential personalized interventions."[14] Studies like these help gain insight into high value data and metrics that can guide monitoring and countermeasures selection for exploration missions of the future. However, the access to and use of those types of data must be carefully considered to ensure both legal and ethical compliance and the current research policy does not extend to operational and clinical collection or use of data.

This paper explores how NASA might enable exploration spaceflight by anticipating developments in precision medicine, monitoring the field for advances that map to spaceflight-specific needs, and prospectively positioning policies for the appropriate collection and use of omic information. Ultimately, this paper recommends that NASA consider developing additional anticipatory policies that enable adoption and deployment of precision medicine as it becomes available while providing appropriate boundaries and guidance regarding ethical dilemmas before they are encountered.

I. HAZARDS AND RISK IN SPACE

To understand how precision medicine can help address the risks to human health, we must first explore the nature of those risks and the hazards that drive them. There are five recognized hazards in human spaceflight: radiation; microgravity; hostile closed environments; isolation and confinement; and distance from the Earth.[15] NASA has derived from these hazards 30 Risks to human health and performance in exploration spaceflight.[16] These 30 risks represent the most critical human health challenges human explorers

14 *Id.*

15 *See 5 Hazards of Human Spaceflight*, NAT'L AERONAUTICS & SPACE ADMIN. https://www.nasa.gov/hrp/5-hazards-of-human-spaceflight (last visited May 5, 2019).

16 *See* NAT'L AERONAUTICS & SPACE ADMIN., JCS-66705, JSC HEALTH AND MEDICAL TECHNICAL AUTHORITY, HUMAN SYS. RISK MGMT. PLAN (May 2014) (providing a detailed discussion of the human health risks in spaceflight). The current state of each risk and NASA's progress on understanding and mitigating it can be found at *Human Research Roadmap: Human Research Program Evidence*, NAT'L AERONAUTICS & SPACE ADMIN., https://humanresearch roadmap.nasa.gov/evidence/ (last visited Aug. 6, 2019).

will face as they travel to the Moon and Mars.[17] These include risks related to exposure to radiation, challenges in providing medical care, food and pharmaceutical degradation, mental health in long term isolation, human system integration and design, and many others.[18]

Each mission has different risks, based on its duration and distance from Earth. NASA has several Mars Design Reference Missions ("DRM"); they range in duration from just over a year to nearly three years, depending on how long the mission will stay on or near Mars.[19] It will take a minimum of six months in the most optimistic assessments to travel to Mars—one way.[20]

Mars missions, because of their length and distance from earth will be much more challenging for human crews than anything NASA has done before. As mission duration and distance from earth increase, an increasing number of system challenges can threaten the ability of crews to remain sufficiently healthy to perform the jobs they need to do. Compounding these challenges, Mars missions will not have access to resupply, real time communication with mission control, or emergency medical evacuation capability. Mass and volume will be severely constrained, limiting the medical supplies and capabilities that will be available on the missions.

As a result of these complex technical challenges, NASA does not plan to fly a mission to Mars until the 2030s. Between now and then, NASA plans to return to the Moon, using the experience in the lunar vicinity to research and validate technologies that need to be developed to enable a Mars mission.[21] Precision medicine is one of the many technologies that will need to be evolved for application on a Mars mission. Precision medicine has the potential to help NASA better predict and treat human health and performance issues on a

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17 *See Human Research Roadmap: Human Research*, *supra* note 16.

18 The list of current human system risks can be found at *Human Research Roadmap: Risks*, NAT'L AERONAUTICS & SPACE ADMIN., https://humanresearchroadmap.nasa.gov/Risks/ (last visited Aug. 6, 2019).

19 NAT'L AERONAUTICS & SPACE ADMIN., HUMAN EXPLORATION OF MARS DESIGN REFERENCE ARCHITECTURE 5.0 ADDENDUM 57 (2009), https://www.nasa.gov/pdf/373667main_NASA-SP-2009-566-ADD.pdf [hereinafter Design Reference 5.0 Addendum].

20 *Id.*

21 *See Moon to Mars Overview*, NAT'L AERONAUTICS & SPACE ADMIN., https://www.nasa.gov/topics/moon-to-mars/overview (last visited Feb. 2, 2019).

Mars mission, tailoring the countermeasures and medical capabilities to the individuals on board, and better preparing those individuals for the rigors of spaceflight. As a result, NASA may wish to begin exploring the policy needed to support the use of precision medicine techniques in the near future.

The need for policy guidance in this area is due in part because of the challenges already being encountered in fields like precision medicine and genomics. For example, NASA, like most other employers in the United States, is subject to the Genetic Information Nondiscrimination Act ("GINA"). As a result, NASA must refrain from using genetic information for employment decisions, including things like astronaut selection and flight assignment. These limitations must be borne in mind as NASA determines how best to use precision medicine in the clinical and operational setting. In 2017, NASA instituted a policy on capturing and using genetic information in human subject research.[22] However, there are currently no policies that address the clinical or operational use of genomic data. This clinical and operational use is where the transition from collection of omic data to precision medicine (clinical use of omic data) would occur.[23] Even without the GINA restrictions, precision medicine has a strong potential to contribute to mission risk reduction and it would be advisable for NASA to consider adopting policies that ensure the continued ethical use of that data.

II. ROLE OF PRECISION MEDICINE IN SPACEFLIGHT

Precision medicine is a relatively new field. Less than a decade old, precision medicine is an approach to medical care designed to optimize efficiency or therapeutic benefit for particular a patient or group of patients, including by using genetic or molecular profiling.[24]

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22 *See* NPD 7170.1, *supra* note 11.

23 *See* Erik L. Antonsen & Rebekah D. Reed, *Should NASA Collect Astronaut's Genetic Information for Occupational Surveillance and Research?*, *20* AMA J. ETHICS 9 E849–56 (2018).

24 TOWARD PRECISION MEDICINE, *supra* note 4, at 125 ("'Precision medicine' refers to the tailoring of medical treatment to the individual characteristics of each patient. It does not literally mean the creation of drugs or medical devices that are unique to a patient, but rather the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease, in the biology and/or prognosis of those diseases they may develop, or in their

In the past, genomics and precision medicine have been of limited value in the spaceflight arena for two reasons. First, the cost and maturity of technologies needed to characterize individual genomes and capture actionable information have not been sufficiently mature to seriously consider operational implementation. That is changing as advances in genomics have significantly reduced the costs and regulatory hurdles of gathering the relevant data. It has only been in the last two years that genomic testing has become affordable and widely available. In 2017, the cost of sequencing a single genome was just $1,000 (down from $100 million in 2001);[25] and, at the end of 2018, the FDA approved the first publicly available genomic testing technology targeting medication metabolism, ushering in a new era in direct-to-consumer testing.[26] Second, precision medicine has thus far been limited to discrete areas of medicine that were not immediately applicable to spaceflight, such as oncology.[27] The focus on oncology was in large part due to government initiatives that focused the short term work of NIH and other research institutions on cancer, leaving other areas for future investment.[28]

Despite these limitations, there is a general sense among those working in human spaceflight that genomics and precision medicine are likely to contribute significantly to our ability to understand and reduce the risks to individuals and crews involved in exploration missions. However, a general mapping of the risk-oriented needs to the areas in omics and precision medicine that are likely to yield benefits has not been done. As these fields mature, beneficial

response to a specific treatment. Preventive or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not.").

25 *See DNA Sequencing Costs: Data*, NAT'L HUMAN GENOME RESEARCH INST., https://www.genome.gov/sequencingcostsdata/ (last visited Feb. 2, 2018).

26 U.S. FOOD & DRUG ADMIN., *FDA Authorizes First Direct-to-Consumer Test for Detecting Genetic Variants that May be Associated with Medication Metabolism*, FDA NEWS RELEASE (Oct. 31, 2018), https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm 624753.

27 *See* Francis Collins and Harold Varmus, *Perspective: A New Initiative on Precision Medicine*, 372 N. ENG. J. MED. 793 (Feb. 26, 2015).

28 *Id.* at 793 ("The proposed initiative has two main components: a near-term focus on cancers and a longer-term aim to generate knowledge applicable to the whole range of health and disease. Both components are now within our reach because of advances in basic research, including molecular biology, genomics, and bioinformatics.").

crossovers come into sharper focus and illuminate areas where NASA may want to explore developing policies to ensure the appropriate collection, analysis, access, interpretation, and usage of data. This was the case with the NASA Twins Study and the subsequent policy on research use of genomic information.[29]

The danger of not anticipating policy needs is that the methods of a maturing scientific and medical practice may be brought to bear without guidance from the agency on appropriate usage. Failing to develop a supportive policy framework in advance could result in delayed implementation of important research and clinical capabilities that can drive down risk in human spaceflight. The section below explores some of the challenges that precision medicine could help to address.

A. The Challenge of the Small "n"

One of the main reasons that Genomics and precision medicine are potentially important to NASA is that the agency is responsible for developing the scientific evidence base needed to understand how humans adapt to and function in the unique environment of space. In all other medical fields, characterizing the state of the human system is accomplished through the study of a large number of individuals pooled together for both statistical and clinical significance to build a reliable evidence base. There is no analogous pool of subjects in human spaceflight because of the small number of individuals who have experienced the spaceflight environment and were sufficiently monitored to add useful information to our understanding of the human response in this environment. This what is referred to as the challenge of the small "*n*".[30]

The small *n* problem is not unique to spaceflight. Other distinct research communities, such as members of small isolated communities or persons diagnosed with a very rare disease, also have a small *n* problem. [31] Although NASA is not alone in struggling with the

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[29] Garrett-Bakelman, *supra* note 13, at 1. *See also* NPD 7170.1, *supra* note 11.

[30] Small "*n*" refers to an inability to reach sufficient statistical power for a variety of reasons including rareness of a condition being studies or limited exposure of subjects to the environment of interest as in human spaceflight.

[31] *See e.g.*, COMM. ON STRATEGIES FOR SMALL-NUMBER-PARTICIPANT CLINICAL RESEARCH TRIALS,

problem of a small *n*, the challenge is particularly acute and the small number of human subjects in space has real scientific consequences for understanding the effects of space on the human body.[32]

For comparison, FDA guidance suggests that phase 3 clinical trials of a new medication should have between 300–3,000 volunteer participants who are studied for 1–4 years each, in a closely controlled protocol and set of conditions.[33] In the recorded history of the human species, there have been 559 individuals who have ever flown in space.[34] Using the FDA guidelines as a benchmark, NASA would have had to expose over half of the participants in human spaceflight to date to the exact same conditions and duration in space and monitored the same parameters to even start to meet the basic scientific requirements for approaching validity in population-based research studies.

While NASA has flown several hundred crew, those crew were exposed for different exposure times, and their physiological data where not collected in a consistent manner over the last 50 years. Today, medical data is collected in a consistent and rigorous way. However, the data capture challenges and limitations NASA faced prior to the ISS program were recognized by IOM in 2001:

> An effective health care system is founded on data that are accumulated, analyzed, and used to continuously improve health care for astronauts on future space missions. Inherent in an appropriate health care system

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SMALL CLINICAL TRIALS: ISSUES AND CHALLENGES 3 (Charles H. Evans, Jr. & Suzanne T. Ildstad eds., 2001) [hereinafter SMALL CLINICAL TRIALS] ("[E]ven though the size of the available research population does not allow a randomized clinical trial with adequate statistical power to be conducted, there might still be a need to design and perform the research (e.g., because treatments are unavailable for a rare disorder or a unique patient population or because studies require the participation of patients with terminal or severely debilitating or incapacitating disorders). In addition, some distinctive research populations—such as astronauts or members of a small, isolated community—may consist of less than five individuals. This research situation, in which large numbers of study participants cannot be obtained, is defined as a "small *n* clinical trial," where *n* refers to the sample size.").

32 *Id.* at 3 ("The sample size in small clinical trials might be very small, for example, a group of astronauts during a space mission, or could range upward to more than 100 individuals. This is in contrast to the sample sizes of some large clinical trials, where the number of participants is in the thousands.").

33 *The Drug Development Process, Step 3: Clinical Research*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405622.htm (last visited Aug. 6, 2019).

34 Garrett-Bakelman, *supra* note 13, at 1.

> is a mechanism that can be used to gather and analyze data relevant to key variables. NASA could have collected and analyzed many more medical data had a comprehensive health care system focused on astronauts been in place and been given the priority and resources that it needed.[35]

While we have nearly twenty years of data on humans in LEO aboard the ISS, when missions beyond LEO are considered, our dearth of experience comes into even sharper focus. Only 12 people (all men) have walked on the surface of a celestial body other than the earth. No one has traveled beyond the Earth-Moon system.

NASA and the IOM both recognized the challenges posed by this small *n* problem. In 2001, at NASA's request, IOM reviewed NASA's approach to gathering and analyzing health information in preparation for exploration. The IOM observed that in addition to the challenge of having too few people to study, while clinical data was being collected that "data collection has not been done in a systematic way, nor have the data been fully analyzed."[36] This lack of health data was not the result of a failure on NASA's part to adequately plan or prepare, but a function of the engineering-centric approach to spaceflight that predominated in the pre-ISS era.[37] The IOM recognized that for NASA to successfully send humans on exploration missions beyond the Earth-Moon system, that approach would need adjustment.

While the small *n* problem has not been solved, NASA has been directed to use the International Space Station as a platform for biomedical research to understand the impacts of long duration missions.[38] Using this unique in-space platform, NASA has sought to

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35 SAFE PASSAGE, *supra* note 2, at 7.

36 *Id.* at 6.

37 *Id.* at 18 ("NASA, because of its mission and history, has tended to be an insular organization dominated by traditional engineering. Because of the engineering problems associated with early space endeavors, the historical approach to solving problems has been that of engineering. Long-duration space travel will require a different approach, one requiring wider participation of those with expertise in divergent, emerging, and evolving fields. NASA has only recently begun to recognize this insufficiency and to reach out to communities, both domestic and international, to gain expertise on how to remedy it.").

38 Nat'l Aeronautics & Space Admin. Authorization Act of 2005, Pub. L. 109-155 § 101(b)(2)(C), 119 Stat. 2895, 2898 ("Increasing knowledge of the impacts of long duration stays in space on the human body using the most appropriate facilities available, including the ISS.").

balance the challenges of small n research with the requirement that high quality and high value science be performed. One of the ways to address this challenge is by exploring the potential of omics research to improve longitudinal studies of individual crew to inform personalized risk profiles and countermeasures for exploration spaceflight.

B. Genetic Information and Research

Given the constraints on the number of humans we can fly in space, and the infeasibility of drawing on traditional clinical research approaches appropriate in a terrestrial setting, NASA should examine other ways to validly reduce risk.[39] Experts have recommended that NASA consider valid non-traditional approaches in the evaluation of research value where large-*n* studies are infeasible.[40] In the absence of traditional population-based studies, techniques for individual longitudinal studies called, *N*-of-1 studies, offer a promising pathway using precision medicine information.[41]

Omics is just one of many approaches to personalized medicine (as opposed to precision medicine which is focused on actionable, clinical data that is not omic-based). For example, Quantitative Computed Tomography ("QCT") has been researched to understand and model structural changes in bone that individual astronauts experience during spaceflight independent of omic information.[42]

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39 *See, e.g.* SMALL CLINICAL TRIALS, *supra* note 31, at 10 ("Studies of the use and effectiveness of various designs should be conducted and new methods should be developed. Evaluations of the utilities of individual and combined statistical analyses in a variety of small clinical trial designs will be necessary.").

40 Robert Ploutz-Snyder et al., *Justifying Small-*n *Research in Scientifically Amazing Settings: Challenging the Notion that only "Big-*n*" Studies are Worthwhile*, 116 J. APPL. PHYS. 1251, 1252 ("Such nontraditional approaches to communicating the value of small-*n* research are appropriate when large-*n* research is simply not feasible."). *See also*, SMALL CLINICAL TRIALS, *supra* note 31, at 10.

41 Nicholas J. Schork, *Time for One Person Trials*, 520 NATURE 609, 611 (2015) ("Key to making precision medicine mainstream is the ongoing shift in the relationship between patients and physicians. A major advantage of the *N*-of-1 approach over classical trials is that patients are no longer guinea pigs, whose involvement in a study may help only future generations. In *N*-of-1 trials, the effectiveness of different treatments are vetted for the actual participants.").

42 NAT'L AERONAUTICS & SPACE ADMIN., HUMAN RESEARCH PROGRAM, EVIDENCE REPORT: RISK OF EARLY ONSET OSTEOPOROSIS DUE TO SPACEFLIGHT 2 (2017), https://humanresearchroad

However, this is not predictive, but rather provides a post-flight measure of response. Empirical approaches such as ground testing have been used to personalize sleep medications for individual crew member use in spaceflight by testing for effectiveness and side-effects of different medications and doses prior to flight.[43] While effective, this method of ground testing is time consuming and expensive. However, as precision medicine advances in terrestrial applications, it is readily apparent that those same non-omic approaches used today could be correlated with omic information to identify relevant predictive biomarkers. Such an approach could eventually obviate the need for the more time-consuming and costly methods of assessing individual risk and response and yield more predictive information.[44]

Recognizing the potential value of omics in research, NASA implemented a genetic policy for research subjects in 2018;[45] however, the policy does not cover occupational surveillance of crews or applications of precision medicine to pre-flight and in-flight medical care and monitoring. In order to assess the utility of policies in operational and clinical care, it is important to understand the spaceflight specific challenges that may be approached through precision medical methods and the potential ethical difficulties that are likely to be encountered beyond the research domain.

map.nasa.gov/Evidence/reports/Osteo.pdf.

43 *See* David Dinges et al., *Effects of Zolpidem and Zaleplon on Cognitive Performance after Emergent Morning Awakenings at Tmax: A Randomized Placebo Controlled Trial*, 42 SLEEPJ, no. 3, 2019.

44 Schork, *supra* note 41, at 611 ("If done properly, claims about a person's response to an intervention could be just as well supported by a statistical analysis as by analyses designed to assess population-level responses on the basis of classical clinical trials.").

45 NPD 7170.1, *supra* note 11.

III. APPLYING PRECISION MEDICINE IN AN EXPLORATION CONTEXT

NASA and other Space Agencies have started to investigate the benefits of omics and precision medicine. The most notable human research so far was NASA's Human Research Program's Twins study in 2015.[46] The study compared astronaut Scott Kelly, who flew a one-year mission aboard the ISS, with his identical twin—also an astronaut—Mark Kelly being monitored on the ground. It was a unique opportunity to examine the changes that a year in space would cause to the human body. Twin Study researchers collected a Longitudinal Integrated Multi-omics analysis; biochemical profiles; immunologic assessments; cognitive assessments; and epigenetic and microbiome measurements in an effort to understand the changes induced by the spaceflight environment.[47]

NASA's GeneLab has been compiling omic data and metadata from experiments in space from 1995 on including Space Shuttle and ISS experiments.[48] More recently, the European Space Agency ("ESA") in 2015 published the results of a pharmacogenomics assessment of the ISS pharmaceutical formulary. The ESA study demonstrated that 30% of medications flown at that time may be metabolized differently by different individuals paving the way for pharmacogenomics matching for a spaceflight formulary.[49]

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46 For an overview of the Twins Study and the research released to date, *see NASA Twins Study Investigators to Release Integrated Paper in 2018*, NAT'L AERONAUTICS SPACE ADMIN. (Jan. 31, 2018), https://www.nasa.gov/feature/nasa-twins-study-investigators-to-release-integrated-paper-in-2018 (last visited Aug. 6, 2019). *See also* Christine Bear, *Twins in Space: How Space Travel Affects Gene Expression*, THE CONVERSATION (Jan. 19, 2019, 5:30 PM), http://theconversation.com/twins-in-space-how-space-travel-affects-gene-expression-107936. A complete description of the Twins study can be found at: *Human Research Program*, NAT'L AERONAUTICS & SPACE ADMIN., https://www.nasa.gov/twins-study (last visited Aug. 6, 2019).

47 Garrett-Bakelman, *supra* note 13, at 1.

48 *About Gene Lab*, NAT'L AERONAUTICS & SPACE ADMIN., GENELAB, https://genelab.nasa.gov/about (last visited Aug. 6, 2019) ("GeneLab's database is a collection of information from biological experiments that date as far back as 1995 through current studies conducted aboard the ISS and other platforms like the retired space shuttle program.").

49 Julia C. Stingl et al., *Where Failure is Not an Option – Personalized Medicine in Astronauts*, 10 PLOS ONE 10 (2015), https://journals.plos.org/plosone/article?id=10.1371/journal.

These studies suggest that clinical care informed by improved insight into genetic variability has the potential to significantly improve the safety and health of human space explorers in several areas. The potential gains that may be realized as the field matures fall into two overarching categories: (1) Improving NASA's ability to characterize the health risks faced by individual crew members and by extension mission risk due to performance decrements or Loss of Crew Life and (2) development of countermeasures to address those health and performance risks that are tailored to individual crew. This second part includes consideration of omic information to more precisely personalize countermeasures for individual crew members in a number of areas such as medication selection, food selection, sleep prescriptions, exercise prescriptions, and training modalities. Both the collection of the information needed to realize these benefits, and the real-world use of this information carries with it different legal and policy challenges. A short summary of potential mapping between precision medicine and possible application in spaceflight specific areas is reviewed in the following sections.

A. Radiation Hazard

For many years, the health effects of radiation during exploration missions have been regarded as one of the most challenging risks facing human explorers.[50] Radiation concerns historically have been broken up into two categories: in-flight concerns that radiation may affect a crew's ability to perform their mission and long-term health concerns for that radiation exposure during a mission would increase a crew member's lifetime risk of developing cancer and other diseases.

The in-flight issues can be broken into three major concerns for a long-duration exploration class mission:

1. Acute radiation sickness ("ARS") due to a large solar particle event;[51]

pone.0140764.

50 Jeffrey Chancellor et al., *Limitations in Predicting the Space Radiation Health Risk for Exploration Astronauts*, 4 NATURE PARTNER J.: MICROGRAVITY 1, 8 (2018).

51 *See* NAT'L AERONAUTICS & SPACE ADMIN., HUMAN RESEARCH PROGRAM, EVIDENCE REPORT: RISK OF ACUTE RADIATION SYNDROMES DUE TO SOLAR PARTICLE EVENTS, (2016), https://humanresearchroadmap.nasa.gov/Evidence/reports/Acute.pdf [hereinafter ARS EVIDENCE REPORT].

2. Subtle changes to central nervous system ("CNS") that may affect cognitive function and performance; and[52]
3. Degenerative effects on body tissues that will predispose to disease in mission.[53]

NASA has long been concerned that ARS would result if crews were exposed to large solar particle events ("SPEs").[54] ARS symptoms can have mission-ending consequences for the crew, including harm to the blood and circulatory system, the gastrointestinal system, skin, and neurovascular function. Crew performing EVAs during a SPE are also likely to experience severe symptoms within days after exposure, including nausea, vomiting, anorexia, skin injury, and fatigue.[55] Despite the potential seriousness of the ARS, the in-flight risk for ARS is now considered an "accepted" risk based on planned radiation shielding in exploration vehicles.[56]

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52 *See* NAT'L AERONAUTICS & SPACE ADMIN., HUMAN RESEARCH PROGRAM, EVIDENCE REPORT: RISK OF ACUTE AND LATE CENTRAL NERVOUS SYSTEM EFFECTS FROM RADIATION EXPOSURE (2016), https://humanresearchroadmap.nasa.gov/Evidence/reports/CNS.pdf [hereinafter CNS EVIDENT REPORT].

53 *See* NAT'L AERONAUTICS & SPACE ADMIN., HUMAN RESEARCH PROGRAM, EVIDENCE REPORT: RISK OF CARDIOVASCULAR DISEASE AND OTHER DEGENERATIVE TISSUE EFFECTS FROM RADIATION EXPOSURE (2016), https://humanresearchroadmap.nasa.gov/Evidence/reports/Degen.pdf [hereinafter DTE EVIDENCE REPORT].

54 *See generally* LYNDON B. JOHNSON SPACE CTR., NAT'L AERONAUTICS & SPACE ADMIN., HUMAN HEALTH AND PERFORMANCE RISKS OF SPACE EXPLORATION MISSIONS 171–190 (Jancy Mcphee & John Charles eds., 2009) (explaining in Chapter 5 ("Risk of Acute Radiation Syndromes Due to Solar Particle Events") the risk of acute radiation syndrome during the early human space program). *See also* NAT'L RESEARCH COUNCIL, RADIOBIOLOGICAL FACTORS IN MANNED SPACE FLIGHT 20–26 (Wash., D.C.: The Nat'l Academies Press, 1967); *What is Space Radiation?*, NAT'L AERONAUTICS & SPACE ADMIN. SPACE RADIATION ANALYSIS GROUP, https://srag.jsc.nasa.gov/SpaceRadiation/What/What.cfm (last visited Aug. 6, 2019) (describing space radiation and solar particle events).

55 *See* ARS EVIDENCE REPORT, *supra* note 51, at 4.

56 A full discussion of NASA's risk management process is beyond the scope of this paper. Under NASA's risk management guidelines, an "accepted" risk is one that has undergone the "formal process of justifying and documenting a decision not to mitigate a given risk associated with achieving given objectives or given performance requirements. Risk acceptance can take place when the consequences are tolerable should the risk occur, or when the risk cannot be reasonably mitigated with further action." NAT'L AERONAUTICS & SPACE ADMIN., DOCUMENT S3001: GUIDELINES FOR RISK MGMT. (Version G) 3 (Oct. 16, 2017), https://www.nasa.gov/sites/default/files/atoms/files/s3001_guidelines_for_risk_management_-_ver_g_-_10-25-2017.pdf.

The CNS and degenerative effects over long mission durations are less clear and in both cases NASA researchers see possible benefits to omic data for help in clarifying the clinical significance.[57,58]

The major long-term health concern from radiation exposure during an exploration mission is radiation carcinogenesis. This is most concerning for missions outside the Earth's magnetic sphere where crews are exposed to higher levels and different types of radiation than typically experienced on earth or in low earth orbit.[59] This is an area in which novel approaches using precision medicine are likely to play a larger role.

Currently NASA assesses individual risk for carcinogenesis base on a complicated algorithm that considers population-oriented statistics, but not individual response.[60] The current model incorporates sex and age at exposure to calculate excess risk from radiation induced cancers.[61] Susceptibility to radiation-induced cancer

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57 *See* CNS EVIDENCE REPORT, *supra* note 52, at 12 ("There are regional differences in tissues, and effects are sex-, age-, species-, and genetic background-dependent. Overall, the evidence points to persistent measureable [sic] changes in the functional status of the CNS similar to those seen during aging and in some neurological diseases, but we do not yet know if these changes rise to the level of operational or clinical significance in humans.").

58 *See* DTE EVIDENCE REPORT, *supra* note 53, at 29 ("[W]ith the recent advances in genomics research and "omics" data in general, it is likely that current and future research will provide an avenue to predict the risks of radiation based on genetic susceptibility.").

59 Chancellor, *supra* note 50, at 8 ("The health risks associated with exposures to space radiation will become more onerous as future manned spaceflight missions require extended transit outside of [low-Earth orbit] and beyond the protection of the Earth's magnetosphere.").

60 NAT'L AERONAUTICS & SPACE ADMIN., HUMAN RESEARCH PROGRAM, EVIDENCE REPORT: RISK OF RADIATION CARCINOGENESIS 12 (2016) [hereinafter CANCER EVIDENCE REPORT] ("as the models used currently at NASA to project space radiation risks are based on mortality data from population studies and do not include analysis of risk based on individual sensitivity, it is not currently recommended that genetic testing be performed on astronauts (NCRP 2010).").

61 *Id.* at 11 ("Because cancer is a genetic disease with important epigenetic factors, individual susceptibility issues are an important consideration for space radiation protection, and NASA's current cancer risk prediction model considers both sex dependence and how age at exposure effects the excess relative risks for radiation induced cancers (Cucinotta et al. 2013).").

is an area in which there is some level of known genetic variability.[62,63] Even very early studies of radiation victims showed evidence of individual susceptibility differences in radiation sickness and cancer.[64] As a result, individual genomic profiling may offer a more precise approach to defining individual health risks from radiation exposure than the current model which may over- or under-protect each individual crew member.[65]

When the National Council on Radiation Protection ("NCRP") approached this problem in 2010, precision medicine had not yet advanced to the point where there were identified genetic characteristics that could be linked to the "risk of radiation induced cancers or non-cancer health effects in humans."[66] Today, we are in a

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62 CANCER EVIDENCE REPORT, *supra* note 60, at 11 ("Genetic and environmental factors also impact risk of cancer from radiation exposure (NCRP 2010; Barcellos-Hoff et al. 2015). Studying the mechanisms of genetic sensitivity provides important insights into understanding the radiation risks to astronauts (Durante and Cucinotta 2008).").

63 *Id.* at 12 ("An important issue is how low penetrance genes impact sensitivity to radiation-induced cancer. A study on subjects exposed to high radiation doses… revealed a strong familial risk of radiation-induced meningioma (Flint-Ritcher and Sadetzki 2007), suggesting that radiation carcinogenesis might be an issue for a genetically predisposed subgroup of the general population, rather than a random event (Hall 2007; Sigurdson 2012). This is also supported by identification of genetic variants associated with increased occurrence of second cancers in survivors of childhood Hodgkin's lymphoma through the use of a genome wide association study (Best et al. 2011) and similarly, the identification of variants associated with radiation related papillary thyroid carcinoma in individuals exposed during the Chernobyl accident (Takahashi et al. 2010).").

64 *Id.* ("Studies of historical data sets such as the atomic-bomb survivors show that subsets of the exposed cohorts could have a higher than average radiation risk (Ponder 2001). A well-known example is *ataxia-telangiectasia* (AT) patients that dramatically demonstrated the importance of genetic susceptibility to radiation damage in cancer treatment. Other examples related to DNA repair genes include BRCA1&2, p53 (Ponder 2001), NBS (Pluth et al. 2008), Artemis (Wang et Risk of Radiation Carcinogenesis 12 al. 2005), and many other so-called high-penetrance genes involved in cancer susceptibility (Ponder 2001).").

65 *Id. ("*A predictive assay able to identify radiation hypersensitive, cancer-prone subjects could be useful in crew selection for long-term spaceflights. Alternatively, identifying resistant or reduced-risk individuals could substantially lower mission costs. However, as the models used currently at NASA to project space radiation risks are based on mortality data from population studies and do not include analysis of risk based on individual sensitivity, it is not currently recommended that genetic testing be performed on astronauts (NCRP 2010).").

66 NAT'L COUNCIL ON RADIATION PROTECTION, REPORT NO.167, POTENTIAL IMPACT OF INDIVIDUAL GENETIC SUSCEPTIBILITY AND PREVIOUS RADIATION EXPOSURE ON RADIATION RISK FOR ASTRONAUTS 4, 124 (Bethesda, Md., 2015).

different posture.[67] As mentioned above, genetic and environmental factors impact the risk of cancer from radiation exposure.[68] The Potomac Institute, in a recent report on a Projection of U.S. Cancer Mortality and Incidence Rates predicted that in the next several years, "[k]ey advancements in early detection and targeted treatment will allow cancer to be detected at its earliest and treated with precision, based on the unique genetic and epigenetic make-up of the individual and the cancer."[69] In 2017, the Human Research Program found that:

> Given the rapid advancement in genomics and personalized medicine, this type of assessment is likely scientifically achievable within the timeframe currently planned for a human deep space exploration mission. Ultimately, for a high risk and high cost endeavor such as a mission to Mars, screening astronauts for increased resistance to space radiation may be sought in order to reduce the costs of the missions or to support post mission disease surveillance.[70]

B. Ethical and Legal Implications

While GINA prevents NASA from using genetic information to make employment decisions, such as flight assignments, NASA can use genetic information to assess individual risk and to tailor countermeasures.[71] Of the four areas noted above, three (CNS, Degenerative Effects, and Cancer) appear to have the potential to use identification of individual sensitivities to radiation as a selection influencer. An example of this is the BRCA1 gene, which results in

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67 POTOMAC INST. FOR POLICY STUDIES, PROJECTION OF U.S. CANCER MORTALITY AND INCIDENCE RATES: FINAL REPORT 92 (2017) [hereinafter PIPS REPORT] (Noting that large advancements in DNA sequencing over the past decade has uncovered that more than 50% of human cancers conceal mutations in enzymes involved in chromatin organization. Cancerous tumor cells use epigenetic processes to ensure their survival. Thus, a growing field in cancer treatment research is the identification of drugs that target the epigenome.).

68 Cancer sensitivity in radiation therapy is an area where there are specific efforts to identify genomic markers for radiation sensitivity. Although spaceflight radiation is different, it is reasonable to assume there will be some crossover. *See* NCRP REPORT, *supra* note 65. *See also* Mary Barcellos-Hoff et al., *Concepts and Challenges in Cancer Risk Prediction for the Space Radiation Environment*, 6 LIFE SCIENCES IN SPACE RESEARCH 92 (2015); Brian Yard et al., *Radiotherapy in the Era of Precision Medicine*, 25 SEMINARS IN RADIATION ONCOLOGY 227 (2015).

69 PIPS REPORT, *supra* note 67, at 7.

70 CANCER EVIDENCE REPORT, *supra* note 60, 12–13.

71 *See* Antonsen & Reed, *supra* note 23.

increased likelihood of developing breast or ovarian cancer completely separate from radiation exposure. The incidence of breast cancer in individuals with the BRCA1 gene peaks in an age range of 41–50 years that is within the operational lifetime expected for career astronauts.[72] Cumulative estimates for breast cancer incidence in those with the BRCA1 gene is 40–87% by age 70; one study found that 72% of women with this genetic mutation developed breast cancer by age 80.[73] Additionally, this has implications for understanding whether individuals are at risk of increased incidence of cancer prior to their exposure to the spaceflight environment.

Genetic information may provide valuable insight into how the spaceflight environment, such as radiation, affects individuals and how to protect them. In 2010, NCRP noted that "it is generally not possible to predict an individual's inherent genetic susceptibility to the long-term risk of cancer or other diseases associated radiation."[74] Nearly 10 years later, it is worth revisiting that claim. Understanding an individual's predisposition for cancer or other illness is important not only to provide appropriate screening and countermeasures, but also to help guide determinations of the likelihood that a future incidence of disease is related to spaceflight, rather than just a part of normal aging. This will become increasingly important as NASA begins to implement the TREAT Astronauts Act. The TREAT Astronauts Act as written requires NASA to provide "monitoring, diagnosis, and treatment described in subsection (a) only for conditions the Administration considers unique to the training or exposure to the spaceflight environment"[75]

Beyond predicting the effects of radiation on an individual, precision medicine may help to inform countermeasures to counteract the effects of radiation. As above, three radiation considerations (ARS, CNS, and Degenerative Effects) may benefit from such personalized

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72 Karoline B. Kuchenbaeker et al., *Risks of Breast, Ovarian, & Contralateral Breast Cancer for BRCA1 and BRCA2 Mutation Carriers*, 317 JAMA 23, 2405 (2017) (observing that "[t]he peak [breast cancer] incidence[s] occurred in the 41- to 50-year age group (28.3 [95% CI, 23.1–34.7] per 1000 person-years").

73 *Id.* at 2403.

74 *See* NCRP REPORT, *supra* note 65, at iii.

75 To Research, Evaluate, Assess, and Treat Astronauts Act ("TREAT Astronauts Act"), Pub. L. No. 115-10, § 442, 131 Stat. 18, 44-45 (2017).

countermeasures for an exploration crew. Although ARS is an accepted risk, there is still the potential for symptoms such as nausea and vomiting to occur as a result of an acute radiation exposure event. Common medications to treat radiation-induced nausea and vomiting include Ondansetron and Granisetron, both of which are metabolized differently in the liver.[76] Precision medicine may allow personalization of the pharmacy for each individual crew member to ensure that effective medications are provided. Such personalization has the potential to improve health outcomes and reduce the volume of the formulary by ensuring the drugs included are optimized for the crew.

C. Medical Conditions Susceptibility

Beyond the medical impacts of radiation, there are many other medical conditions related to spaceflight that may be responsive to a precision medicine approach. NASA developed a list of 100 concerning conditions that may be encountered in exploration, known as the Exploration Medical Condition List.[77] Among these conditions there are some that are impacted by genetic predispositions. For example, a medical condition like Cardiac Arrest can have an increased risk of occurrence based on many genetic factors.[78] These can include structural heart disease, dysrhythmias, and blood clots

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76 Rebecca S. Blue et al., *Challenges in Clinical Management of Radiation-Induced Illnesses During Exploration Spaceflight*, 90 AEROSPACE MED. & HUMAN PERFORMANCE 966, 970 (2019) ("Recent research has demonstrated a pharmacogenetic component in the response to different 5HT3 antagonists. As these medications are metabolized by the cytochrome-P450 enzymes, genetic variation in enzyme metabolism can affect individual response to each medication. For example, ondansetron is metabolized by the CYP2D6 enzyme; ultra-rapid metabolizers of the CYP2D6 pathway have a higher frequency of vomiting within 24 h of radiotherapy when treated by ondansetron compared to those who metabolize at a slower rate. In contrast, granisetron is metabolized by CYP3A and is more effective than ondansetron for rapid metabolizers of the CYP2D6 pathway. This suggests that therapies could be tailored based on genetic predispositions and that medications selected for an exploration mission could potentially be adjusted for individual crewmembers.") (internal citations omitted).

77 *See* SPACE & CLINICAL OPERATIONS DIV., LYNDON B. JOHNSON SPACE CTR., NAT'L AERONAUTICS & SPACE ADMIN., DOC. NO. JSC-65722, EXPLORATION MEDICAL CONDITION LIST (June 2013) [hereinafter EXPLORATION MEDICAL CONDITION LIST, JSC-65722].

78 *See* Matthew T. Bennett et al., *Review: Assessment of Genetic Causes of Cardiac Arrest*, 29 CAN. J. CARDIOLOGY 100 (2013).

that can lead to pulmonary embolism.[79] Structural heart diseases are likely to be caught during medical exams and through EKG. However, some known genetic causes of dysrhythmias such as Long QT syndrome, Brugada Syndrome, and ARVD are often identified through reviewing family history. Similarly, genetic factors such as Factor V Leiden or Protein C or S deficiencies are the important predisposing factor for blood clots in people younger than 50 years old.[80] These can cause a pulmonary embolus that precipitates cardiac arrest. Genetic testing is recommended for relatives of carriers of the Factor V Leiden mutation, as even a heterozygous carrier has a 4–7x increased risk to develop blood clots.[81] In the interest of compliance with GINA, NASA does not currently consider family history in astronaut selection evaluation, and these genetic risk factors are not part of the clinical screening performed on astronauts.

While omic risk factors for specific medical conditions may have impact on the risk that individuals and a program will ultimately take on a given mission, it is also likely that omic information can help to tailor mitigations to those same risks. Two areas, Systematic Molecular Phenotyping and Pharmacogenomics, appear to be making promising progress in this arena. These are discussed throughout the following sections.

D. Precision Medicine and Immune Function

Immune function and dysfunction, are potentially significant issues in exploration spaceflight.[82] Advances in the precision medicine world are beginning to elucidate the linkages between infectious disease, immune function, and genetic markers that in the future will likely help predict disease susceptibility on an individual basis. Systematic Molecular Phenotyping is a set of analysis techniques that seek to use information from genomics, transcriptomics, proteomics, and metabolomics to individualize diagnosis and treatment decisions

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79 EXPLORATION MEDICAL CONDITION LIST, JSC-65722, *supra* note 77, at 10.

80 *See* Cristina Hotoleanu, *Genetic Risk Factors in Venous Thromboembolism*, ADV. EXP. MED. & BIOL. 1 (2016).

81 EXPLORATION MEDICAL CONDITIONS LIST, JSC-65722, *supra* note 77, at 6.

82 Brian Crucian et al., *Immune System Dysregulation During Spaceflight: Potential Countermeasures for Deep Space Exploration Missions*, 9 FRONTIERS IN IMMUNOL. 1437, 1439 (2018).

in clinical medicine.[83] Limakeng et al. (2016) noted that "[i]n some cases, such research has identified disease subtypes that may respond differentially to existing treatments."[84] An example of this is recent work in Group A strep throat where immune-genetic markers help explain why some children have recurrent strep throat infections leading to tonsillectomy and others do not.[85] Advances in genetic immune-profiling like this are currently in the research pathway for the NIH to map our genetic factors that drive immune variability in response to infectious disease.[86]

In space, immune system changes have been observed in the six-month mission timeframe. These changes have been mostly subclinical, that is they don't seem to predispose crew members to increased likelihood of clinical disease within the current mission timeframes.[87] As Crucian et al. (2018) noted, the "human immune system is fundamentally 'shaped' by environmental exposures impacted by lifestyle choices (*i.e.*, diet, exercise, social habits, etc.) leading to epigenetic changes in gene expression in determining specific individual responses to various environmental antigen challenges."[88]

Some experiments suggest that the microgravity environment itself can affect genetic transcription of the immune cells required to fight disease.[89] While these immune changes have not significantly impacted crews in general during 6 month missions, it is known that there is "…increased incidence of infectious disease as well as

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83 *See* Alexander T. Limkakeng, Jr. et al., *Systemic Molecular Phenotyping: A Path Towards Precision Emergency Medicine*, 23 ACAD. EMERGENCY MED. 1097, 1098–1101 (2016).

84 *Id.* at 1098.

85 *See* Jennifer M. Dan et al., *Recurrent Group A Streptococcus Tonsillitis is an Immunosusceptibility Disease Involving Antibody Deficiency and Aberrant TFH Cells*, 11 Sci. Translational Med. 478 (Feb. 6, 2019).

86 *Immunoprofiling*, IMMUNE MATTERS 5 (2018) (observing "[t]hey are mapping out the genetic factors that drive the immune system's variability and finding out which kinds of cells control infections and which ones fail.").

87 *See* NAT'L AERONAUTICS & SPACE CENTER, HUMAN RESEARCH PROGRAM, EVIDENCE REPORT: RISK OF CREW ADVERSE HEALTH EVENT DUE TO ALTERED IMMUNE RESPONSE 9 (2015) [hereinafter ALTERED IMMUNE EVIDENCE REPORT].

88 Crucian, *supra* note 82, at 7.

89 *See* ALTERED IMMUNE EVIDENCE REPORT, *supra* note 87, at 17.

increased allergic symptoms and persistent skin hypersensitivity reactions in some crewmembers during orbital flight" despite the fact that crews have been isolated from terrestrial pathogens in the pre-flight domain.[90] It is a concern that subclinical immune changes will manifest to a level that impacts human health and performance in much longer missions.[91] If genomic, epigenomics, or transcriptomic markers are identified that predict individual variability to the spaceflight environment or susceptibility to specific medical conditions, then they would be useful in assessing individual risk and potentially for tailoring countermeasures.

E. Pharmacogenomics

Pharmacogenomics is the study of how a person's genes affect their response to medications.[92] While this is not widely used across all areas of medicine, the advances in this domain and applicability to spaceflight warrant consideration for future potential. A 2014 study of the medications on the ISS showed that as many as 30% are known to be differentially metabolized by individuals with polymorphisms in Cytochrome p450 enzymes. This insight suggests there may be more variation in medication effectiveness among the astronaut population than previously suspected.[93]

In the terrestrial population, the Mayo RIGHT study recently found that 99% of over 1,000 people tested had at least one actionable pharmacogenomic polymorphism of five reviewed.[94] Three of these

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90 Crucian, *supra* note 82, at 2.

91 ALTERED IMMUNE EVIDENCE REPORT, *supra* note 87, at 5 ("The specific cause of immune system dysregulation during flight remains unknown but it's likely associated with one or more of the following: physiological stress, disrupted circadian rhythms, microgravity, isolation, altered environment, altered nutrition, and radiation.").

92 *See* GENETICS HOME REFERENCE, *What is pharmacogenomics?*, U.S. NAT'L LIBRARY OF MED., NAT'L INST. OF HEALTH, https://ghr.nlm.nih.gov/primer/genomicresearch/pharmacogenomics (last visited Aug. 6, 2019).

93 *See* Stingl, *supra* note 49.

94 Yuan Ji et al., *Preemptive Pharmacogenomic Testing for Precision Medicine: A Comprehensive Analysis of Five Actionable Pharmacogenomic Genes Using Next-Generational DNS Sequencing and a Customized CYP2D6 Genotypic Cascade*, 18 J. OF MOLECULAR DIAGNOSTICS 3, 443 (2016) ("Of the 1013 RIGHT patients, 99% carry at least one ACTIONABLE variant. Furthermore, 3% of participants carry actionable PGx variants in all of the five genes.").

same polymorphisms in the RIGHT study were also studied in Stingl's work. This suggests that it is both common for individuals to have some genetic predisposition to metabolizing medications differently and that a significant proportion of the medications that are already flown in space have the potential to be metabolized differently by different crew members in exploration missions.

It is not just possible—it is likely that genomics will impact the efficacy of treatment for medical conditions in exploration spaceflight. Of the 100 medical conditions that NASA lists in the Exploration Medical Conditions List,[95] 79 of them would indicate the use of at least one medication from the Stingl list known to have differential metabolizing properties in individuals. This list includes common medications for pain, fever, nausea, as well as some mediations that are definitive treatment for specific conditions such as phenytoin for seizures, and Bactrim for urinary tract infections.[96] Although these medications may not in every case be the terrestrial first-line medication, in an exploration mission where there is no possibility of resupply or adding new medications to a pharmacy, these medications would be drawn on heavily for treatment. The implication is that it may be common for individuals to have a variable response to the medications already flown in spaceflight as well as future medications likely to be considered for the formulary that are in part based on genetic indicators of metabolism. The deleterious effects of mismatched medications for a crew could be mitigated by one-time pharmacogenomics testing and personalizing pharmacies for exploration crews. Such a use of genetic information is consistent with GINA.[97]

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95 *See* NAT'L AERONAUTICS & SPACE CENTER, HUMAN RESEARCH PROGRAM, EVIDENCE REPORT: RISK OF ADVERSE HEALTH OUTCOMES AND DECREMENTS IN PERFORMANCE DUE TO IN-FLIGHT MEDICAL CONDITIONS (2017), https://humanresearchroadmap.nasa.gov/Evidence/reports/Medical.pdf. [hereinafter MEDICAL EVIDENCE REPORT]. *See also* EXPLORATION MEDICAL CONDITION LIST, JSC-65722.

96 *Id.*

97 *See* Antonsen & Reed, *supra* note 23.

F. Behavioral and Cognitive Factors

Personalized medicine may also improve Behavioral and Cognitive Health in exploration missions.[98] Current fitness for duty standards in Behavioral and Cognitive Health indicate that in-flight status shall be within clinically accepted values as judged by clinical psychological evaluation.[99] The maintenance of in-flight behavioral and cognitive function is expected to be more challenging in exploration missions than in low earth orbit. Increased distance from earth, time delays in communication, and extended isolation and confinement in smaller spaces are all expected to contribute to an increase in Behavioral Health and Cognitive needs.[100] NASA has already funded omic research that can inform Systematic Molecular Phenotyping approaches for Behavioral and Cognitive needs:

> NASA-funded research is currently assessing the predictive value of specific biomarkers, including catecholamines (such as dopamine), as potential biomarkers for sensitivity to central nervous system effects resulting from radiation exposure (Goel et al. 2015; St. Hilare et al. 2015);

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98 NAT'L AERONAUTICS & SPACE CENTER, HUMAN RESEARCH PROGRAM, EVIDENCE REPORT: RISK OF ADVERSE COGNITIVE AND BEHAVIORAL CONDITIONS AND PSYCHIATRIC DISORDERS 10 (2016), https://humanresearchroadmap.nasa.gov/Evidence/reports/BMed.pdf [hereinafter BMED EVIDENCE REPORT] ("The goal of the behavioral health component of the astronaut selection system is to identify individuals who, at the time of application, have diagnoses that are incompatible with the demands of space flight, and also to identify those who are believed to be best suited psychologically to be astronauts. Current BHP research efforts involving biomarkers may serve to inform the selection process for future exploration missions, as well as further enable a personalized approach to flight medicine.").

99 NAT'L AERONAUTICS & SPACE ADMIN., NASA-STD-3001 VOL. 1, REVISION 1 W/CHANGE 1, NASA SPACE FLIGHT HUMAN-SYSTEM STANDARD, VOL. 1 REV. A: CREW HEALTH 19 (Feb. 12, 2015), https://standards.nasa.gov/standard/nasa/nasa-std-3001-vol-1.

100 BMED EVIDENCE REPORT, *supra* note 98, at 11–12 (observing that "Not only might the missions be longer, but given their unprecedented distance from earth, there will also be other stressors not experienced on the Station. For example, depending upon the specific destination, exploration missions will be characterized by confinement in decreased habitable volume, decreased privacy, an inability to see Earth, a lack of resupply and care packages, anticipated periods of increased monotony and routine, limited medical care, no evacuation options, less social, physical, and sensory stimulation, danger from radiation exposure, and a delay in communication of up to 20 minutes one-way. These in turn are anticipated to affect both mission operations and crewmembers' perceptions of isolation and their limited ability to stay in touch with mission control and family and friends on the ground. Further, exploration missions will be marked with greater uncertainty as we move away from the known (the ISS) toward the unknown . . . .").

> metabolomics, as potential biomarkers of an increased stress response (see e.g., Cooksey et al. 2009) and epigenetic and genetic markers (e.g., Rokutan et al. 2005), such as single nucleotide polymorphisms of certain clock genes (e.g. PER3), as biomarkers for vulnerabilities to sleep loss (Goel 2015; Goel and Dinges 2011).[101]

Genomic markers of susceptibility to depression or anxiety might help to ensure the deployment of appropriate medications for in-flight countermeasures.[102] Genomic information would also help to ensure that the formulary for behavioral health and cognition are appropriate to the crew. As noted in the Stingl paper cited above, multiple medications relevant to behavioral health, cognitive performance, and sleep known to have variable metabolizing profiles based on the Cytochrome p450 system have already been flown in spaceflight.[103]

Sleep is an excellent example of a behavioral clinical issue with wide-ranging consequences that may be improved through genomics and precision medicine. Sleep interacts with many other health risks in spaceflight. For instance, animal studies have suggested that chronic moderate sleep restriction blunt the beneficial effects of exercise on immune function and carcinogenesis.[104] Crucian et al. (2018) note that "there is an established relationship between the immune system and psychological stress, circadian rhythms, and sleep."[105] Sleep issues in spaceflight are common, and a broad array of mitigation efforts have been brought to bear. Dinges and Goel note that there are genetic polymorphisms related to a variety of sleep parameters that impact individual variations observed in sleep that can impact performance as well as provide pathways for tailored countermeasures.[106]

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101 *Id.* at 10.

102 *Id.* at 60 ("An important consideration is future research on potential genetic biomarkers that will "personalize" the approach to help predict antidepressant and anxiety disorder treatment responses since both have effects on the serotonergic neurotransmitter system . . . .").

103 *See* Stingl, *supra* note 49.

104 Maria Moreno-Villanueva & Honglu Wu, *Radiation and Microgravity – Associated Stress Factors and Carcinogenesis*, 13 REACH: REVIEWS IN HUMAN SPACE EXPLORATION 9 (2019).

105 Crucian, *supra* note 82, at 12.

106 Namni Goel & David F. Dinges, *Predicting Risk in Space: Genetic Markers for Differential Vulnerability to Sleep Restriction*, 77 ACTA ASTRONAUTICA 207 (2012) ("In summary, a number

Approaches used to tailor countermeasures for sleep in spaceflight to date have been mostly empiric with little focus on genetic predispositions or pharmacogenomics impacts to countermeasures. These include scheduling accommodation, light spectral changes to affect circadian rhythm, and pharmaceuticals to help manage sleep and fatigue.[107,108] NASA currently employs individualized drug tolerance testing to manage challenges with sleep that are well known to occur in spaceflight.[109] This individualized drug tolerance testing requires overnight testing for individuals to try various medications at varying doses and measure parameters like sleep quality as well as post-sleep alertness. This is a time consuming and costly way to assess individual response to specific medications that likely have a genomic dependence for metabolism. Of the medications tested, Zolpidem is known to have a dependence on CYP3A polymorphisms[110] while Zalepon does not.[111] Pharmacogenomic testing may offer a simpler and cheaper way of reaching the same end goal of tailoring medication and dose to a crew member in order to optimize their performance while in-mission. By engaging in individual testing, NASA has already determined that the costs of doing this for crews on an empirical basis are worth the benefits realized in human performance in flight.

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of common genetic polymorphisms involved in circadian, sleepwake, and cognitive regulation appear to underlie inter-individual differences in basal (fully-rested) sleep parameters and homeostatic regulation of sleep in response to sleep loss (both chronic restriction and acute total sleep deprivation) in healthy adults.").

107 *See* George C. Brainard et al., *The Development of Lighting Countermeasures for Sleep Disruption and Circadian Misalignment During Spaceflight*, 22 CURRENT OPINION IN PULMONARY MED. 535 (2016).

108 *See* Erin Flynn-Evans et al., *Circadian Misalignment Affects Sleep and Medication Use Before and During Spaceflight*, 2 NATURE PARTNER J.: MICROGRAVITY 1 (2016).

109 MEDICAL EVIDENCE REPORT, *supra* note 95, at 27 ("In both the Space Shuttle and ISS Programs, NASA used personalized medicine, in the form of individualized drug tolerance testing, to personalize sleep and alertness interventions for crew . . . .").

110 Lisa L. von Moltke et al., *Zolpidem Metabolism* In Vitro*: Responsible Cytochromes, Chemical Inhibitors, and* In Vivo *Correlations*, 48 J. CLINICAL PHARMACOLOGY 89 (1999).

111 Stingl, *supra* note 49, at 6.

G. Bone Loss and Biologic Variability

A well-known example of concern in human spaceflight is bone loss associated with a prolonged exposure to the microgravity environment. A study of data from 45 long-duration astronauts and cosmonauts who were exposed to the spaceflight environment from 4–6 months in duration showed average bone mineral losses between 2–9% over a variety of bone sites recorded. The worst losses occurred in the hip bone (trochanter) and averaged around 7.8% with recovery times back to their pre-flight baseline estimated to take almost 3 years. This is remarkable because it suggests bone loss for the mostly white male cohort observed (there were 3 females included) averaging 43 years old responds to the spaceflight environment more like "*elderly*, post-menopausal white females."[112]

This only tells part of the story. Other studies that look at the internal structure of bone found significant losses beyond bone mineral density as well as significant individual variation. Research using different methods of looking at bone structure in 8 astronauts found average losses of 14% of hip bone trabecular bone mineral density lost; at least one individual showed much more rapid bone loss returning with a 24% decrease. [113]

The level of bone resorption and post-mission recovery varies dramatically among individuals. It is possible that genetic factors play a significant role in this variability for both loss and recovery of bone.[114] It is also thought that both psychological and physical stress

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112 Jean Sibonga et al., *Recovery of Spaceflight-induced Bone Loss: Bone Mineral Density after Long-Duration Missions as Fitted with an Exponential Function*, 41 BONE 973, 976 (2007).

113 Carpenter et al., *Long-term Changes in the Density and Structure of the Human Hip and Spine After Long-duration Spaceflight*, 67 ACTA ASTRONAUTICA 71, 79 (2010) ("In our study, crew members lost 14% of their femoral neck tBMD [Trabecular Bone Mineral Density] on average, or nearly 1/3 of the total expected lifetime loss, in only 4 to 6 months. One subject lost 24% of his femoral neck tBMD, or over 1/2 of the expected lifetime loss, in just over five months aboard the ISS. These results suggest that rapid changes in bone mineral distribution occur during spaceflight, and these changes affect bone structure for at least 4.5 years after returning to Earth.").

114 Sibonga, *supra* note 112, at 976 ("It is important, however, to note that skeletal recovery is highly variable among crew members . . . some crew members recover within the first year after return while others do not recover until much later. Factors that contribute to this variability in recovery are likely to include nutrition, skeletal muscle reconditioning, and genetics." (citations omitted)).

contribute to both immune function changes as well as changes in bone microarchitecture.[115] Other research has suggested that genetics accounts for as much as 60%–80% of bone remodeling in response to environmental loading and but that it may be the cumulative effects of many genes.[116] Researchers in this area have noted the potential benefit to understanding how genomic information affects bone metabolism.[117] In the case of bone loss, terrestrial research has long implicated genetic processes.[118] At least 24 genes and loci have identified genome-wide significant evidence for association with bone mineral density.[119]

If genetic or epigenetic markers are identified that can predict an individual astronauts' bone loss response to the spaceflight environment as well as likely metabolism rate of the medications under consideration, then that information could be used to provide improved individualized countermeasures to address bone loss. This offers potential in mission benefits including better characterization of the risk of fracture as the first crews plan to work on the surface of Mars as well as ways to personalize mitigation of the long-term health effects of multi-year missions in reduced gravity environments.

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115 Crucian, *supra* note 82, at 10.

116 Stefan Judex et al., *Genetic Loci that Control the Loss and Regain of Trabecular Bone During Unloading and Reambulation*, 28 J. BONE & MINERAL RESEARCH 1537, 1537–38 (2013) ("In spite of clear evidence that genetic variations influence bone's response to altered mechanical environments, little is known about the identity of the genes that harbor the responsible polymorphisms. For the acquisition of *peak bone mass*, it is assumed that 60% to 80% of the observed variability is due to genetic variables and that this trait is polygenic, with small cumulative effects of many genes.").

117 Sibonga, *supra* note 112, at 977 ("Collectively, future studies will not only need to evaluate how bone *metabolism* responds to changes in mechanical loading (at the molecular, cellular and tissue level) but how changes in skeletal mass and structure correlate with changes in muscle forces, with expression of skeletally relevant genes and with nutrient uptake in this crew member population.").

118 Stuart Ralston & Andr. . . Uitterlinden, *Genetics of Osteoporosis,* 31 ENDOCRINE REVIEWS 629, 630 ("Many factors influence the risk of osteoporosis, including diet, physical activity, medication use, and coexisting diseases, but one of the most important clinical risk factors is a positive family history, emphasizing the importance of genetics in the pathogenesis of the disease . . . .").

119 *See id*. at 641 (Table 4).

IV. POTENTIAL ETHICAL ISSUES IN PRECISION MEDICINE

While precision medicine has important applications to exploration, it introduces a number of ethical challenges. The challenges include balancing allowable uses of genetic information with mission risk and how to address incidental findings. Neither of these ethical challenges are unique to spaceflight. However, in the context of NASA's mixed role as both clinical care provider and employer, they take on particular significance.

A. Individual Variation and Mission Risk

In each of the examples discussed above—radiation risk, medical and immune response, behavioral and cognitive performance, and bone loss in space—there is reason to suspect that omic information about an individual crew member may help give insight into the risks that that individual will experience as well as the proportion of risk that they may bring to the larger mission. It may also inform and enable more effective countermeasures that are personalized for crew members, resulting ultimately in decreased individual and mission risks as exploration missions are undertaken.

Understanding the individual risk profile of crew members will also inform the risk profile for any mission that is undertaken. Using that information appropriately will require attention to the GINA restrictions. As an example, consider the Factor V Leiden mutation discussed above. Under GINA, it would be inappropriate to use that information in a flight assignment decision. However, there are appropriate and beneficial uses of that information that do not run afoul of GINA. While it is known that any individuals with a heterozygous mutation have a 4–7 fold increase in risk for blot clots, when oral contraceptives for control of menstruation are used by these individuals, the risk of blood clot increases 34 fold.[120] Female astronauts have long used oral contraceptive medications to suppress their menstrual cycle in spaceflight.[121] Flight surgeons could use this information to select personalized approaches that reduce risks to

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120 Hotoleanu, *supra* note 80, at 2.

121 Varsha Jain & Virginia Wotring, *Medically Induced Amenorrhea in Female Astronauts*, 2 NATURE PARTNER J.: MICROGRAVITY 1, 3 (2016).

individual crew members as well as the mission overall and remain in compliance with GINA. Such personalized approaches might include different methods of menstrual suppression or operational changes to account for avoiding suppressive therapy.

In cases where a crew member's individual risk predisposition increases mission risk overall without clear mitigation options, it becomes more challenging to use this information and continue to remain in compliance with GINA. Returning to the Cardiac Arrest example from above, Long QT syndrome is an important cause of sudden cardiac in young, previously healthy individuals including athletes.[122] It is estimated to be responsible for 7–23% of unexplained cardiac arrest, and up to half of the people who have this disorder have a normal resting EKG.[123] This acute risk is different from the lifetime risk of developing cancer as it may affect the safety and health of a crew while in space. To remain compliant with GINA, NASA policies would need to define how or whether this information is being collected and used. This presents an ethical dilemma in that not screening for it may be inconsistent with the responsibility that NASA has to "[f]ully inform astronauts about the risks of long-duration and exploration space flights and make certain that the informed decision-making process is adequate and appropriate."[124]

While this presents a dilemma, it also presents a possible path forward. NASA may wish to explore how to develop policies that balance the need to protect genetic information from misuse under GINA and the need to both inform astronauts of their own risk and appropriately manage overall mission risk.

Planning for precision medicine does not require a change in policy as much as it suggests the needs for additional policies that fills in areas in clinical and occupational use of information to establish appropriate use and boundaries. This would allow NASA to meet the ethical obligations for both understanding risk and mitigating risks it to the fullest extent possible. However, the benefits of precision medicine approaches must be balanced by considering the potential legal and ethical pitfalls.

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122 Bennett, *supra* note 78, at 101.

123 *Id.* at 102.

124 NPR 8900.1B APPENDIX F, *supra* note 10.

B. Incidental Findings

One of the most persistently perplexing challenges in genomics is the issue of incidental findings. An incidental finding is information that is unintentionally obtained in the course of research on or treatment for an unrelated condition.[125] In terrestrial medicine, incidental findings are a well understood ethical dilemma. As Berg et al. (2013) noted, "[a] central tension in the return of genomic IFs [Incidental Findings] is between the ethical principles of 'duty to warn' and 'do no harm' on the part of physicians" balanced against "the various choices of patients, some of whom wish to 'know everything' in their genome and others who will undoubtedly wish to exercise their preference 'not to know' certain findings."[126]

The sensitivities in this field are well illustrated by a real-life example. Dr. James Watson is notable for having received the Nobel Prize for his contribution to the discovery of the structure of DNA in 1963. In 2008, his full genome was sequenced and published with the exception of a single gene. That gene, ApoE, has been associated with an elevated risk of Late Onset Alzheimer's Disease. This disease, which is incurable, claimed one of his grandmothers.[127] Dr. Watson's ApoE results might have had implications for not only him, but his family, since it is heritable. Incidental findings may also reveal unwanted information about parentage, likelihood of developing disease, and other issues.

The problem of incidental findings is exacerbated by the disparity between what we can identify and what we can treat. Over 5,000 diseases can be identified through genetic testing, but only about 60 are considered actionable and therefore reportable from research results.[128] When the original recommendations for reporting

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125 *See* Shiri Shkedi-Rafid et al., *Defining and Managing Incidental Findings in Genetic and Genomic Practice*, 51 J. OF MED. GENETICS 715 (2014) (examining the challenge of incidental findings in genomic and genetics in several settings, including clinical care and research).

126 Jonathan S. Berg et al., *Processes and Preliminary Outputs for Identification of Actionable Genes as Incidental Findings in Genomic Sequence Data in the Clinical Sequencing Exploratory Research Consortium*, 15 GENETIC MED. 860, 861 (2013).

127 *See On Jim Watson's* APOE *Status: Genetic Information is Hard to Hide*, 17 EUROPEAN J. HUMAN GENETICS 147 (2009).

128 Sarah S. Kalia et al., *Recommendations for Reporting of Secondary Findings in Clinical Exome and*

incidental findings were released by the American College of Medical Genetics in 2012, there was community resistance based on the wording that suggested for any whole genome or whole exome testing 56 genes should be targeted and results provided to physicians to discuss with patients. [129] There was also a push to provide patients the opportunity to "opt out" of receiving information.[130] All of these issues are further complicated by the large uncertainty that still surrounds genomics: ". . . for most of the genes, we lack evidence about the predictive value of testing, genotype penetrance, spectrum of phenotypes, and efficacy of interventions in unselected populations."[131] These examples give credence to the need for a well-thought out policy approaches that anticipate issues before they arise in the clinic.

The potential for incidental findings creates an ethical challenge that NASA should consider addressing as it begins to collect genetic and genomic data. The recent Policy Governing Use of Human Research Genetic Testing[132] addresses these issues by making participation voluntary, restricting access to and use of data, requiring a separate database from the Electronic Medical Record, offering genetic counseling to all participants, and requiring monitoring for incidental findings such that the agency is aware of how often incidental findings occur.[133]

Beyond individual choice to know or not know about incidental findings, NASA may have an interest in clinically-significant findings. NASA's policy for the clinical and operational use of genetic information should engage with these difficult questions. Incidental findings could help NASA to characterize potential risks to mission success and the need for individualized countermeasures. Genetic

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Genome Sequencing, 2016 Update (ACMG SF v2.0): A Policy Statement of The American College of Medical Genetics and Genomics, 19 GENETICS IN MED. 249, 249 (2017).

129 Myra Roche & Jonathan Berg, *Incidental Findings with Genomic Testing: Implications for Genetic Counseling Practice*, 3 CURRENT GENETIC MED. REPORTS 166, 168 (2015).

130 *Id.* at 168.

131 Wylie Burke, *Recommendations for Returning Genomic Incidental Findings? We Need to Talk!* 15 GENETIC MED. 854, 854 (Nov. 2013).

132 NPD 7170.1, *supra* note 11.

133 *Id.*

markers for increased risk of heart disease or cancer could potentially alter mission risk profiles and call for enhanced screening and treatment capabilities during a mission. For instance, an incidental finding of a BRCA1 gene in a crew member would increase the likelihood of both breast and ovarian cancer. However, it is unknown if or when the disease might manifest and how it might progress. For a mission to Mars in which the training flow is at minimum two years and the mission itself three years, NASA policy would likely need to balance the interests of the astronaut with the interests of the crew and mission. Anticipating these issues will ensure a transparent and equitable process for addressing them.

Despite the GINA prohibitions on the use of genetic information for employment decisions, the IOM recommended that NASA consider doing just that as part of a larger strategy of risk reduction for Exploration Spaceflight:

The committee recommends that, wherever possible, NASA use actuarial data … as well as additional sources such a genomic data, where available to estimate and/or model the likelihood of intrinsic health alterations for crew who will be part of the Mars mission. Utilization of this information as part of the selection criteria for astronauts should be considered. After intrinsic health risks are estimated, NASA should then estimate and/or model the contribution of the space environment and life support system malfunction to increased risk.[134]

While it is unclear if there is a right answer in how to deal with these challenges, it is clear that the likelihood is increasing that NASA will have to deal with issues like this as genomic testing becomes more available, and potential application to characterizing and mitigating individual and mission risks matures.

CONCLUSION

NASA has adopted the ethical framework for Exploration set forward in the IOM report in 2014 and written it into agency policy.

134 INST. OF MED. ET AL., A RISK REDUCTION STRATEGY FOR HUMAN EXPLORATION OF SPACE: A REVIEW OF NASA'S BIOASTRONAUTICS ROADMAP 50 (Wash., D.C.: The Nat'l Academies Press, 2006).

This includes responsibilities to (1) create an adequate and appropriate risk informed decision-making process for exploration spaceflight; (2) adhere to a continuous learning strategy that draws from all relevant sources; and (3) provide comprehensive health care to protect their health, improve mission safety, and reduce risks for current and future astronauts.[135] Precision medicine as a field is making rapid advances that warrant the attention of NASA as it seeks to fulfill each of these responsibilities. On the timeframe for exploration missions to Mars, these fields are likely to have significant advances that will drive a desire for inclusion of these developing capabilities in clinical and operational areas such as astronaut selection, crew flight assignment, individual and mission risk assessment, fielded medical and pharmacologic capabilities in-mission, and health-care for crews post-mission.

By taking advantage of expected gains in these fields in the clinical and operational domains, NASA can position itself well through proactive development of enabling and bounding policies. Policies which enable the rapid application of advances in precision medicine as they mature will allow NASA to reduce the health risks inherent in human spaceflight in a number of ways. It will allow NASA to identify crew members at increased risk for medical conditions that may manifest during spaceflight and then support the development of tailored countermeasures to reduce the incidence and severity of those conditions. Systematic Molecular Phenotyping may allow improved understanding of crew responses to the spaceflight environment or medical conditions in-mission. Pharmacogenomic profiling may help to build personalized formularies for exploration, tailored to the unique metabolic profiles of a particular crew, minimizing waste and required mass and volume and improving outcomes. Increased insight into the Omic components of health risks associated with spaceflight are likely to aid NASA in assessing the long-term health consequences of exposure to the exploration environment.

The policies already put in place for Human Research on Genomic Information[136] can serve as a strong starting point for additional policy in the clinical and operational domain before NASA employees start

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135 NPR 8900.1B APPENDIX F, *supra* note 10.

136 NPD 7170.1, *supra* note 11.

grappling with the ethical questions that will inevitably arise. Identifying and addressing issues like incidental findings, operational use of precision medicine information, and appropriate use of genetic information in the operational context will help to ensure that policy does not lag too far behind technological advances.

NASA has an opportunity now, given the foreseeable trends in precision medicine and the potential benefits in human spaceflight, to enact anticipatory policies addressing clinical and operational challenges before they arise. This may include things such as appropriate collection of genomic information, how such data is stored and accessed, incidental findings, use of genetic information for occupational surveillance, development of personalized countermeasures, and the use of genomic information for individual and mission risk characterization. Policies that guide beneficial aspects of these fields into new standards and that help flight surgeons and others working in human spaceflight to deal with anticipated ethical challenges in the application of precision medicine and genomics will substantially improve our risk posture as we seek to explore outward into the solar system.

Doarn—Evolution of NASA Medical Policy (2011)

Doarn, Charles R. *Medical Policy Development for Human Spaceflight at NASA: An Evolution.* Aviation, Space, and Environmental Medicine, 2011, 82:1073–1077.

Overview: Reviews the development and modernization of NASA's medical policy structures over time.

Medical Policy Development for Human Spaceflight at NASA: An Evolution

Charles R. Doarn

Doarn CR. ***Medical policy development for human spaceflight at NASA: an evolution.*** **Aviat Space Environ Med 2011; 82:1073–7.**

Codification of medical policy for the National Aeronautics and Space Administration (NASA) did not occur until 1977. Policy development was based on NASA's human spaceflight efforts from 1958, and the need to support the operational aspects of the upcoming Space Shuttle Program as well as other future activities. In 1958, the Space Task Group (STG), a part of the National Advisory Committee on Aeronautics (NACA), became the focal point for astronaut selection, medical support, and instrumentation development in support of Project Mercury. NACA transitioned into NASA in 1958. The STG moved to Houston, TX, in 1961 and became the Manned Spacecraft Center. During these early years, medical support for astronaut selection and healthcare was provided through arrangements with the U.S. military, specifically the United States Air Force, which had the largest group of subject matter experts in aerospace medicine. Through most of the 1960s, the military worked very closely with NASA in developing the foundations of bioastronautics and space medicine. This work was complemented by select individuals from outside the government. From 1958 to 1977, there was no standard approach to medical policy formulation within NASA. During this time, it was individualized and subjected to political pressures. This manuscript documents the evolution of medical policy in the NASA, and provides a historical account of the individuals, processes, and needs to develop policy.

Keywords: Spaceflight, medical policy, history, space medicine.

FROM 1915 – 1958, the National Advisory Committee on Aeronautics (NACA) was the organization in the United States that focused on aviation and, eventually, on space. On July 29, 1958, President Eisenhower signed the National Aeronautics and Space Act, which established the National Aeronautics and Space Administration (NASA). On October 1, 1958, NASA assumed all of NACA's activities and its 8000 employees (4,10). The Space Task Group (STG) was established on November 5, 1958 under the direction of Robert Gilruth. Within months, NASA moved forward with Project Mercury (10), including selection of the first American astronauts.

At this time, NASA did not have a program for selecting individuals to be astronauts or developing and monitoring astronaut health. NASA did not adopt or institutionalize a medical policy development process, including standards for medical selection and retention of astronauts, until the late 1970s. Instead, NASA relied on the U.S. Air Force (USAF), which had significant aerospace medicine experience. An agreement between NASA and the Department of Defense to develop a Bioastronautics Program was established to support the new space agency's efforts (10,13). Military aerospace medicine experts were assigned to the STG, initially part of NACA and then with NASA. This collection of experts included representatives from the U.S. Air Force (Dr. Stanley White), the U.S. Army (Dr. William Augerson), and the U.S. Navy (Dr. Robert Voas).

This group began to conduct extensive medical evaluations in preparation for selection and eventually flight. These evaluations were conducted at military installations such as Wright-Patterson Air Force Base in Dayton, OH, and the Lovelace Foundation for Medical Research and Education in Albuquerque, NM. Prior to this effort, testing and evaluation throughout the 1950s had been done on mice, dogs, and monkeys (11).

Medical standards for crew selection were guided by the U.S. military with input from the research community, pioneering subject matter experts, and leaders in aerospace medicine like Dr. Randolph Lovelace (10,12). In addition, selection procedures were mostly experimental for the first several groups of astronauts from the U.S. Air Force, U.S. Army, and U.S. Navy (3). These standards and guidelines were used to support selection for Projects Mercury, Gemini, Apollo, Skylab, and Apollo-Soyuz. The medical support during this time period was primarily focused on getting the astronauts ready for flight and developing an understanding of how spaceflight affected them during flight and postflight.

NASA's Foundation of Space Medicine Approach

In the early 1960s, NASA created a Space Medicine function at NASA Headquarters under the direction of USAF General Charles H. Roadman. Standards for aeromedical practice were adopted to support the development of medical testing and medical kits for incorporation into the Mercury, Gemini, and Apollo spacecraft through the STG (15). Early work was supported by subject matter experts from panels such as the Life Sciences Panel and the Ad Hoc Working Group on Bioinstrumentation.

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A Bioastronautics Agreement with the USAF helped solidify the pooling of resources to help NASA build its fledgling space medicine function (9,10,12). In 1961, the STG was relocated from Langley, VA, to Houston, TX, and became known as the Manned Spacecraft Center (MSC) (now Lyndon B. Johnson Space Center, JSC). Here the expertise of Drs. W. Randolph Lovelace, Stanley White, William Douglas, Robert Voas, William Augerson, Charles Berry, and others, all on loan from the U.S. military, helped push the foundation of space medicine forward for NASA and for the discipline of space medicine itself.

The disciplines of Aerospace Medicine and Life Sciences shared a common stage at the beginning of the human spaceflight program at NASA. There was often conflict between NASA's extramural community, i.e., the Kety Committee* and the Special Committee on Life Sciences, and different NASA field centers. Furthermore, there was an ongoing conflict between NASA and the USAF and Congress with regard to expertise and duplications of effort.

NASA's extramural community and the USAF were critical of NASA management and the organization of its Life Sciences and Space Medicine functions. In 1964, NASA Deputy Administrator Robert C. Seamans, Jr. sought to alleviate the some of the challenges by establishing the Life Sciences Director's Group (9,10). This was to provide an advisory role for Life Sciences within NASA and to appease the external advisory committee's observation that Life Sciences and Aerospace Medicine functions were not coalesced under one program office. It functioned from 1964–1968 with little authority. Life Sciences functions at the NASA MSC and Ames Research Center (ARC) were conducted with limited interaction from the NASA Headquarters Life Science management. In 1968, NASA Associate Administrator Homer Newell replaced this Group with the NASA Space Biology and Aerospace Medicine Board. During this decade (1960–1970), NASA ARC and the NASA MSC were on different tracks and were often seen as autonomous—a trait carried over from the NACA STG days, and which in some ways still exists today.

Policy Development

Space medicine in the 1960s and 1970s was successful in identifying and validating, through limited research, the medical challenges of human spaceflight and the mission of getting to the Moon. The knowledge gained with each successive mission provided valuable insight (5,6). Medical support in the early missions was primarily to support operational medicine. Due to space constraints and limitations in the space capsules, very little was done in the way of research during flight. As the cabin became larger, in-flight research opportunities increased. Nevertheless, significant knowledge was gained from pre- and postflight research.

Many issues related to crew selection and the lack of sufficient evidence in decision making regarding crew health had been observed. While the cadre of astronauts selected to date had been subjected to a wide variety of testing, there was no consistent approach or standard protocols, and there were often adversarial relationships. Medical decisions were based on understanding of each individual astronaut and not on a standardized approach using evidence-based medicine. The selection criteria which NASA used were based on those used for military pilots (11). Research protocols developed by the Lovelace Foundation and the Mayo Clinic were utilized, although these were largely untested.

In 1977, NASA began to finalize plans for the Space Shuttle Program. There was a need to develop selection standards based on a new kind of astronaut; one who was not categorized as a military pilot, but one who would conduct research tasks during spaceflight operations. These types of astronaut came to be known as Mission Specialists and Payload Specialists. In addition, medical evaluation, certification, and decision making had not been standardized. There was a need to develop an approach that eliminated inconsistencies and establish "standard" procedures and processes.

At JSC, Dr. Arnauld Nicogossian began to develop the concept of a medical policy board to ensure that there would be a practical way to address crew health and performance on a clinical and scientific basis. He also began to draft new selection standards. In 1977, Dr. Nicogossian joined Dr. Rufus Hessberg and the Life Sciences effort at NASA Headquarters under the direction of Dr. David Winter. The medical standards and policy boards were coordinated by Dr. Nicogossian at NASA Headquarters in cooperation with the Office of Personnel Management and the Office of Management and Budget to ensure that an occupational health model was followed and that the proper federal process was adhered to. Dr. Hessberg, the NASA Headquarters Chief of the Space Medicine Division, oversaw and assisted with the process (Nicogossian A. Personal communication; March 14, 2011). To evaluate the efficacy of these standards, a full simulation was conducted on 20 subjects. Each individual completed the selection process with no issues and the new guidelines were approved for use (Pool SL. Personal communication; Feb. 1, 2011).

In addition to selection standards, there was a need for a governing board. The NASA Space Medicine Board (SMB) was created to function as the entity that would review medically related issues and crew selection and then decide on a course of action. The NASA Space Medicine Policy Board (SPMB) was created as a higher level authority board that would develop and maintain Agency-wide medical policy. The philosophy of NASA senior medical personnel at this time was influenced by

*An ad hoc Bioscience Advisory Committee to study the capability in space-oriented life-science research and development to outline the scope of current and future problem areas in the space bioscience field, and to recommend the future role of NASA in a bioscience program. Composed of leading scientists, this committee was under the chairmanship of Dr. Seymour S. Kety, Director of the Clinical Science Laboratory of the National Institutes of Health, and known as the Kety Committee.

the Space Shuttle Program and the experiences of the past two decades of human spaceflight activities.

Two specific issues helped shape the need for a formal medical policy board. The first issue was intermittent atrial fibrillation affecting astronaut Deke Slayton and his eventual flight assignment to the Apollo Soyuz Test Program. The other was that throughout human spaceflight there has been disagreement regarding physical exercise and the overall impact of in-flight exercise on the musculoskeletal system. Different protocols and timelines for annual crew certifications were employed. Crewmembers assigned to Apollo or Skylab missions performed exercise in-flight based on research needs (5,6,14). Crews not assigned to flight opportunities participated in exercise that was clinically driven. This paradigm did not permit adequate comparison of data and, therefore, a standardized in-flight countermeasure prescription could not be written (Nicogossian A. Personal communication; March 14, 2011). Operational (flight) medicine and researchers were often in disagreement as to how best measure it and what the appropriate standards were.

Development of Selection Standards and NASA Medical Policy Structure

As indicated above, the early selection standards for Mercury, Gemini, Apollo, Skylab, and Apollo-Soyuz were based on those used by the military (11). Slight changes occurred with each astronaut selection. It was the development of the Space Shuttle Program that laid the foundation and established the need for NASA to develop and certify selection standards to meet this new era of human spaceflight. These same standards were reviewed and updated as necessary to support the Shuttle/Mir program and the International Space Station (ISS). Beginning with the Space Shuttle Program, approval of these standards was the responsibility of the SMPB.

Tempered by need and experience, Space Medicine and Life Sciences personnel at NASA Headquarters and JSC developed the appropriate documentation. This documentation was reviewed by a group of intramural and extramural aviation and space medicine experts (see **Table I**).

The outcome of this effort was a baseline NASA Management Instruction (NMI) document entitled NMI 1152.59 – Space Medicine Boards in Support of Space Crew Qualification for Space Flight. This NMI became effective on July 8, 1977. This document established two boards, the Headquarters-level SMPB and the JSC SMB. The document outlined the function of the boards to medically qualify astronauts for spaceflight. **Table II** lists the chronology of medical policy authority documents, which have been updated on a regular basis or as needed.

Codification

NASA Space Medicine, led by Dr. Nicogossian for more than 25 years under successive administrators, established and utilized a management structure complete with documentation that granted authority and responsibility for various functions. Documentation structure and nomenclature were modified and updated as NASA evolved. They evolved from NASA Management Issues to NASA Management Instructions (NMI) and eventually to NASA Policy Charters (NPCs), NASA Policy Directives (NPDs), and NASA Procedures and Guidelines. Although documentation nomenclature and process changed, the SPMB structure and function remained consistent and supported by all NASA administrators. All documents flow from the original and amended Space Act of 1958, 42 USC 2473 (c)(1), Section 203 (c)(1).

Astronaut healthcare is authorized through additional documentation, including NPD 8900.1A Operational Medical Responsibility for the Space Transportation System (now known as Astronaut Medical and Dental Observation Study and Care Program), which was initially approved in early 1981, prior to the first Space Shuttle launch. It has evolved and has been updated periodically, usually at a frequency of 4 – 5 years. These documents have laid out the responsibility, requirements, and systems for care of astronauts during all phases of human spaceflight.

Purpose of Medical Policy

The authority that provides responsibility for selecting astronauts and supporting medical care with all

TABLE I. MEMBERS OF THE INITIAL MEDICAL POLICY DEVELOPMENT WORKING GROUP.

Name	Title	Organization
Arnauld Nicogossian, M.D.	Manager, Aerospace Medicine	NASA HQ, Aerospace Medicine, Life Sciences Division (LSD), Office of Space Sciences and Applications (OSSA)
Rufus Hessberg, M.D.	Chief, Space Medicine	NASA HQ, Aerospace Medicine, LSD OSSA
Frank Austin, M.D.	Director of Environmental Life Science	Office, Under Secretary of Defense for Research and Engineering
Homer L. 'Rick' Reighard, M.D.	Federal Air Surgeon	Federal Aviation Administration (FAA)
George E. Schafer, M.D.	Surgeon General	USAF, Office of the Surgeon General
Robert Moser, M.D.	Advisor	American College of Physicians
Gerald Soffen, Ph.D.	Director, Life Sciences	NASA HQ, OSSA

LSD = Life Sciences Division; OSSA = Office of Space Sciences and Applications; USAF = United States Air Force; FAA = Federal Aviation Administration.

TABLE II. MEDICAL POLICY AUTHORITY DOCUMENTS (NASA HEADQUARTERS).

Year	Document Number	Document Name	Responsible HQ Office
Jun 24, 1965 Sep 14, 1966	NMI 1152 NMI 1152.18A	NASA Life Sciences Directors Group	OART/OMSF/OSS
July 8, 1977	NMI 1152.59	Space Medicine Boards in Support of Space Crew Qualification for Spaceflight	SB/Office of Life Sciences
Jan 18, 1980	NMI 1152.59A	Space Medicine Boards in Support of Space Crew Qualification for Spaceflight	SB/ Life Sciences Division
Apr 4, 1984	NMI 1152.59B	NASA Medical Boards in Support of Crew Qualifications for Spacecraft Operations	EB/Life Sciences Division
Oct 2, 1989	NMI 1152.59C	NASA Medical Boards in Support of Crew Qualifications for Spacecraft and Aircraft Operations	EB/Life Sciences Division
Dec 12, 1991	NMI 1152.59D	NASA Medical Boards in Support of Crew Qualifications for Spacecraft and Aircraft Operations	SB/Life Sciences Division
June 29, 1993	NMI 1152.59E	NASA Medical Boards in Support of Space Flight Operations	M/Office of Space Flight
Dec 4, 1998	NPC 1152.59F	NASA Medical Boards in Support of Space Flight Operations	M/Office of Space Flight
Jul 1998	NPC 1152.4	NASA Medical Policy Boards in Support of Space Flight Operations	Code U
May 20, 2003	NPD 8900.5	Review and Approval of Human Health Related Research Requirements and Biomedical Research Deliverables	Code AM - Office of the Chief Health and Medical Officer (OCHMO)
May 16, 2006	NPD 8900.5A	NASA Health and Medical Policy for Human Space Exploration	Code QA – OCHMO
Jul 25, 2007	NC 1000-12	NASA Medical Policy Board and ASM Board	Code QA – OCHMO
Dec 17, 2009	NC 1000-26	NASA Medical Policy Board and ASM Board	Code QA – OCHMO

NPC or NC = NASA Policy Charter; NMI = NASA Management Instruction; NPD = NASA Policy Directive.
Note: Each successive document replaced the previous.

phases of spaceflight is stated in NASA documentation. As outlined above, there is a long lineage of documentation that supports the overall mission of ensuring the health of the men and women who fly in space. The need for medical policy as outlined above was to support NASA's medical efforts during spaceflight activities. The intent was to create the necessary structure for reviewing all issues that pertained to crew healthcare at both an operational level (NASA JSC) and at an Agency level (NASA Headquarters).

The purpose of policy in any organization is to provide guidelines for determining how things are accomplished. The NASA SMPB function is to establish and set forth the policies necessary to establish the appropriate requirements, standards, and systems to ensure the selection of new astronauts, resolve medical disputes, and provide for astronaut healthcare in support of NASA missions.

The current NPD 8900.5A states that it is NASA policy to:

1. Provide a healthy and safe environment for crewmembers to enable successful human space exploration;
2. Provide health and medical care systems for crewmembers for all mission phases – preflight, flight and postflight (health is defined as encompassing physiological, psychological, and dental well-being. Medical refers to the treatment of illness and injury);
3. Update crewmember health and medical services based on best supporting evidence and current standards of medical practice, lessons learned, risk management, and expert recommendations;
4. Design initial and recurrent medical training for crewmembers, consistent with mission requirements, and commensurate with available resources and priorities; and
5. Establish spaceflight health and medical standards that address:
   a. Health and medical screening, evaluation, and certification (including selection and retention standards);
   b. Health and medical diagnosis, intervention, and care (including management and training);
   c. Health maintenance, preventive programs and countermeasures (including permissible exposure limits, permissible outcome limits, and fitness for duty standards);
   d. Habitability and environmental health guidelines and standards as appropriate (These standards are documented in NASA-STD-3001, Volume 1: NASA Space Flight Human System Standard - Crew Health and NASA-STD-3001 Volume 2: NASA Space Flight Human System Standard - Human Factors, Habitability, and Environmental Health); and
   e. Sponsor health and clinical research to enable human space exploration.

Evolution of the Boards and Their Functions

The SMPB became known as the MPB in 1989. This board was comprised of senior physicians from various NASA Centers (ARC, JSC, Kennedy Space Center, etc.), a physician member of the astronaut corps, and physicians from other federal agencies, including the Federal Aviation Administration and the National Institutes of Health. The chair of the MPB has been held by Dr. Nicogossian (1978–2002) and Dr. Richard S. Williams (2002–2011). An executive secretary coordinates the MPB meetings, including agendas, all correspondence, maintenance of the policies, and preparation of minutes from each meeting.

The MPB Chair works closely with the JSC SMB (now called the Aerospace Medicine Board [AMB]) to resolve any medical issues related to crew health or selection. The MPB Chair rarely intercedes on an AMB decision.

The process of medical policy can result from a number of inputs, such as mission definition, a medical event, new knowledge from research outcomes, or input

from an operational issue. An issue, challenge or opportunity is brought before the MPB for consideration. The MPB reviews the pertinent information and supporting documentation and develops a policy. Once this policy is approved by the MPB, it is adopted and communicated with the operational elements at JSC.

The MPB was a result of the post Apollo Program. It was fully functional prior the start of the Space Shuttle Program and has remained viable through each of NASA's human spaceflight programs since 1977. As NASA worked closely with its ISS partners, Dr. Nicogossian established a similar medical structure to support ISS operations. This included the Multilateral Space Medicine Board and the Multilateral Medical Policy Board. These boards and the MPB have been very successful in supporting crew selections for the Space Shuttle missions and the missions to the ISS (7,8).

Summary

During the first two decades, NASA's human spaceflight program was focused on getting into space and landing on the moon. While this was the major thrust, there was minimal time and resources to conduct a broadly-scoped research program on humans in space. Once the Space Shuttle Program started and the number of flight opportunities increased, there was a need to develop policies and selection criteria for new astronauts, and evaluate the longitudinal impact of spaceflight on those who have flown in space, all through evidence-based medicine (2). The future of human spaceflight required a medical policy function.

It is likely that the same structure would be in place to support whatever mission NASA is tasked with doing. Over the past decade or so, there has been discussion and plans to send humans back to the Moon, to Mars, or to an asteroid. Each of these missions will require unique medical capabilities, unique crew composition, and strong medical policy (1). The foundation of the MPB has resulted in processes that will serve human spaceflight into the future, whether it is unique to NASA or is multicultural in nature. The MPB will serve as a model for commercial spaceflight activities as well.

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Mautner—Life-Centered Ethics (2009)

Mautner, Michael N. *Life-Centered Ethics and the Human Future in Space.* Bioethics, 2009, 23(8):433–440.

Overview: Advocates for an ethical framework that supports expanding life into space as a moral imperative.

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ARTICLES

LIFE-CENTERED ETHICS, AND THE HUMAN FUTURE IN SPACE

MICHAEL N. MAUTNER

Keywords
bioethics,
life-centered ethics,
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ABSTRACT
In the future, human destiny may depend on our ethics. In particular, biotechnology and expansion in space can transform life, raising profound questions. Guidance may be found in Life-centered ethics, as biotic ethics that value the basic patterns of organic gene/protein life, and as panbiotic ethics that always seek to expand life. These life-centered principles can be based on scientific insights into the unique place of life in nature, and the biological unity of all life. Belonging to life then implies a human purpose: to safeguard and propagate life. Expansion in space will advance this purpose but will also raise basic questions. Should we expand all life or only intelligent life? Should we aim to create populations of trillions? Should we seed other solar systems? How far can we change but still preserve the human species, and life itself? The future of all life may be in our hands, and it can depend on our guiding ethics whether life will fulfil its full potentials. Given such profound powers, life-centered ethics can best secure future generations. Our descendants may then understand nature more deeply, and seek to extend life indefinitely. In that future, our human existence can find a cosmic purpose.

I. INTRODUCTION

Biotechnology can transform life extensively, especially in the new environments of space. These developments will raise profound questions in bioethics and space ethics. Life-centered (biocentric) principles can provide guidance. These ethics can be generalized as biotic ethics, which value organic gene/protein life itself, and as panbiotic ethics, which seek to expand our family of organic life in the universe.

Expansion in space may be in fact imperative for our future. In contrast to fragile and limited Life on Earth, multiple worlds in space can secure our survival, and provide rich resources.[1]

[1] N.A. Rynin. *K. E. Tsiolkovskii: Life, Writings, and Rockets*. Leningrad, 1971. (Vol. 3, No. 7 of Interplanetary Flight and Communication. Leningrad Academy of Sciences of the USSR. Translated by the Israel Program for Scientific Translations, Jerusalem). 'The Earth is the cradle of the human mind, but one cannot live in the cradle forever'. A. Starchild. 2000. *Science Fiction of Konstantin Tsiolkovsky*. New York, NY: International Specialized Books Services; F. Dyson. 1979. Time Without End: Physics and Biology in an Open Universe. *Rev. Modern*

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These visions are developing into concrete programs.[2] For example, large-scale space colonies,[3] and the terraforming of Mars,[4] are studied. Seeding new solar systems deeper in space with life was proposed,[5] motivated by life-expanding panbiotic ethics.[6] Adapting life to these new environments can affect the future of evolution.[7]

The potentials for life in space are supported by experimental astro-ecology.[8] Plant cultures on meteorite/asteroid materials suggest that the Solar System can support populations of trillions.[9] These resources can make territorial conflicts obsolete, assure human survival, and increase biological and cultural diversity.

Life in space opens ethical and philosophical questions that have been discussed starting with Tsiolkovski,[10] and addressed more recently in several books.[11] In parallel, biocentric ethics are also advancing. Life-centered principles have been established since antiquity, as in the edict 'choose life',[12] and in Buddhist principles,[13] and they are receiving new attention by environmental ethics.[14]

Space ethics and biocentric ethics are both at early stages. They are usually considered separately, although a connection was suggested for seeding other solar systems with life, motivated by life-centered principles.[15] This paper will propose further basic connections between life-centred ethics and space ethics.

Space adaptation through designed evolution may affect the future profoundly, especially when our designs become self-fulfilling. Our survival can then be secured only if it is pursued deliberately. In that future our guiding ethics can have far-reaching consequences.

This paper intends to contribute to a discourse on life-centered astroethics and on its effects on the future. In particular, it will postulate that expansion in space, combined with life-centered ethics, can best secure our long-term survival.

II. SCIENCE-BASED ARGUMENTS FOR BIOCENTRIC ETHICS

Before biocentric ethics are applied to space, these life-centred principles need to be justified rationally. Of course all ethics are subjective, but scientific insights can provide rational foundations.

Molecular biology shows that all organic cellular life share a common feature, self-reproduction through gene/

Phys. 1979; 51: 447–468; F. Dyson. 1988. *Infinite in All Directions*. New York, NY: Harper and Row.

[2] S. O'Keefe, NASA Administrator. *Pioneering the Future*. 'To improve life here, to extend life to there, to find life beyond'. April 12, 2002. Syracuse University. Similar programs were announced by the European Space Agency, India, China, and Japan.

[3] G.K. O'Neill. The Colonization of Space. *Physics Today* 1974; 27: 32–38; G.K. O'Neill. 1977. *The High Frontier*. New York, NY: William Morrow.

[4] M.J. Fogg. Terraforming: A Review for Environmentalists. *The Environmentalist* 1993; 13: 7–12.

[5] M.N. Mautner. 2000. *Seeding the Universe with Life: Securing Our Cosmological Future*. Washington, DC.: Legacy Books. (www.panspermia-society.com)

[6] M.N. Mautner & G.L. Matloff. Directed Panspermia: A Technical Evaluation of Seeding Nearby Solar Systems. *Bull. Astr. Soc.* 1977; 9; 501 and *J. British Interplanetary Soc.* 1979; 32: 419–424; M.N. Mautner. Directed Panspermia. 2. Technological Advances Toward Seeding Other Solar Systems, and the Foundations of Panbiotic Ethics. *J. British Interplanetary Soc.* 1995; 48: 435–440; Directed Panspermia. 3. Strategies and Motivations for Seeding Star-Forming Clouds. *J. British Interplanetary Soc.* 1997; 50: 93–98. www.panspermia-society.com

[7] A. Rosenfeld. 1975. *The Second Genesis: The Coming Control of Life*. New York, NY: Vintage Books: 281; A.C. Clark. 1984. *Profiles of the Future*. New York, NY: Warner Books; 210; M.H. Hart. 1985. Interstellar Migration, the Biological Revolution, and the Future of the Galaxy. In *Interstellar Migration and Human Experience*, B.R. Finney & E.M. Jones, eds. Berkeley, CA: University of California Press: 278–291. Ethical aspects of evolution in space are also discussed in M.A.G. Michaud. 2007. *Contatct with Alien Civilisations*. New York, NY: Copernicus Books.

[8] M. N. Mautner. Biological Potential of Extraterrestrial Materials. 1. Nutrients in Carbonaceous Meteorites, and Effects on Biological Growth. *Planetary and Space Science*. 1997; 45: 653–664; Planetary Resources and Astroecology. Planetary Microcosm Models of Asteroid and Meteorite Interiors. Implications for Space Populations and Panspermia. *Astrobiology* 2002; 2: 59–76; M.N. Mautner. Directed Panspermia, Astroethics, and our Cosmological Future. *Int. J. Astrobiology* 2004; Supplement 1: 116 (www.Astro-Ecology.com)

[9] M.N. Mautner. Life in the Cosmological Future: Resources, Biomass and Populations. *J. British Interplanetary Soc.* 2005; 58: 167–180.

[10] Tsiolkovski, *op. cit.* note 1.

[11] E.C. Hargrove, ed. 1986. *Beyond Spaceship Earth – Environment Ethics and the Solar System*. Sierra Club Books; P.C.W. Davies. 1995. *Are We Alone? Philosophical Implications of the Discovery of Extraterrestrial Life*. London: Basic Books; B.R. Finney. 1985. Voyagers Into Ocean Space. In *Interstellar Migration and Human Experience*. B. R. Finney & E. M. Jones, eds. Berkeley: CA: University of California Press: 164–180.

[12] Bible. Old Testament *Deuteronomy*: ch. 30 vv. 15, 19.

[13] A. Hunt-Badiner, ed. 1990. *Dharma Gaia: A Harvest of Essays in Buddhism and Ecology*. Berkeley, CA: Parallax; B. Gruzalski. Gandhi's Contribution to Environmental Thought and Action. *Environmental Ethics* 2002; 24: 227–242.

[14] A. Schweitzer. 1990. *Out of My Life and Thought*. New York, NY: Holt: 131. '(being good:) to preserve life, to promote life, to raise to its highest value life which is capable of development'; P.W. Taylor. 1986. *Respect for Nature: A Theory of Environmental Ethics*. Princeton, NJ: Princeton University Press: 45; J.R. Des Jardins. 1997. *Environmental Ethics: An Introduction to Environmental Philosophy*. Belmont: Wadsworth. G.E. Moore. 1988. *Principia Ethica*. NY: Prometheus Books. 'With regard to some rules. . . . where the instincts to preserve and propagate life were strong. . . .'

[15] Mautner, *op. cit.* note 5; Mautner & Matloff, *op. cit.* note 6.

protein cycles. Biotic ethics value these core patterns of biology themselves, and strive to perpetuate them. Expansion in space can broaden these principles into panbiotic ethics that value all organic cellular gene/protein life, present and future, and seek to maximize life in all accessible habitats.

Although these ethics value all cellular gene/protein life, from a human point of view life may best enjoy conscious existence, further motivating self-propagation.

Molecular self-replication and the definition of life

When seeking to define Life, we ask: What objects in Nature are we willing to accept as fellow living beings? In this sense, 'what is Life?' is a question of judgement, rather than of science. However, science can reveal common features that help define fellow life.

Most definitions of life recognize reproduction and evolution as essential features. Of all known phenomena, only organic biological life reproduces actively, and evolves. A plausible definition may then state: 'Life is a process whose outcome is the self-reproduction of complex molecular patterns'. Importantly, Life is then a *process* that requires a constant flow of information, matter and energy.

More specifically, biological matter is composed of genetic information contained in DNA sequences that code proteins, which in turn help reproducing the DNA sequences. All organic cellular life uses these self-reproducing gene/protein cycles.

The unique position of life in nature

Complexity assigns a unique position to life. Proteins, DNA and membranes are all made of complex molecules that are structured precisely for their functions. Complex enzymes catalyze specific reactions, and complex t-RNA molecules convert DNA codes to amino acids in proteins. Even the most simple cell possesses thousands of finely tuned complex molecules that act in coordination. This complexity is unique to life.

Biology also depends on the precise coincidence of seemingly independent physical laws.[16] The universe contains just enough matter and energy to avoid fast collapse or expansion, allowing liveable conditions for eons. Stars such as the Sun last for billions of years and host habitable planets, due to a coincidence of the laws of gravity, nuclear physics, gas convection, and magnetic fields. Biology is based on carbon, formed in stars due to coincidental nuclear resonances. Electromagnetism bonds molecules with just the right strength, allowing chemistry and biology to exist.

Life therefore depends on the laws of gravity, nuclear forces, chemistry, thermodynamics and cosmology. These laws are seemingly independent of each other, but they coincide precisely to allow life to exist. In this sense, the physical universe itself comes to a unique point in life.

The unity of life

We have a special feeling for other living beings, an empathy called 'biophilia'.[17] This special relation exists even among very different life-forms. For example, we readily recognize a cactus being closer to us than a rock. We also recognize microorganisms as fellow life, and astrobiology searches for microorganisms in space to ease our cosmic loneliness. We sense that all living beings are one family who share mutual affinity and dependence.

This sense of unity is supported by science. From microorganisms to humans, we all share common designs. Every living cell is surrounded by selective membranes; processes energy through biochemical cycles using enzymes and ATP; has a complex genome coded in DNA sequences; and uses a common code and mechanism for translating three-letter DNA codes to amino acids in proteins. Ultimately, the proteins help to reproduce the DNA code, completing the gene/protein cycle.[18]

Further, phylogenetic trees indicate that all terrestrial life can be traced to a common ancestor.[19] Organisms as different from us as yeasts share half; mice, over 90%, chimpanzees, over 95%, and different human individuals share over 99% of our genome.[20]

These scientific insights give a deeper meaning to the unity of all Life. Our complex molecular patterns are common to all organic gene/protein life and distinguish us from any other phenomena of nature.

[16] L.J. Henderson. 1970. *The Fitness of the Environment*. Glouster: Peter Smith: 312. J. Gribbin & M. Rees. 1989. *Cosmic Coincidences*. New York, NY: Bantam Books: 269; F. Hoyle. 1983. *The Intelligent Universe*. London: Michael Joseph: 218; P.C.W. Davies. 2007. *Cosmic Jackpot: Why Our Universe Is Just Right for Life*. New York, NY: Houghton Mifflin.

[17] E.O. Wilson & S. McVay, eds. 1993. *The Biophilia Hypothesis*. Washington, DC: Island Press.

[18] W.K. Purves et al. 2001. *Life*: *The Science of Biology*. Sunderland, MA: Worth Publishers, Inc.

[19] S.L. Baldauf, J.D. Palmer & W.F. Doolittle. The Root of the Universal Tree and the Origin of Eukaryotes Based on Elongation Factor Phylogeny. *Proc. Nat. Academy Sci. USA* 1996; 93: 7749–7754.

[20] A. Gibbons. Which of Our Genes Make Us Humans. *Science* 1998; 81: 1432–1434.

Observational equivalence, and life and purpose

Expanding life in space will require action with purpose. 'The purpose of life' has been pondered since antiquity, but today it can be examined with scientific insights. One useful principle is 'observational equivalence': If two phenomena are identical in all observables, then they are identical in fact. Examples are the relativistic equivalence of gravity and acceleration, and Turing's test of intelligence.[21]

Applied to behaviour, self-perpetuation is usually included in the definition of life. All organisms act for survival and propagation, *as if* they pursued these outcomes deliberately. This of course does not imply conscious planning. However, if the *observed* behavior of organisms appears to pursue survival and propagation, then the *equivalent effective observable purpose* of life is survival and propagation. Therefore life may be seen to have an intrinsic purpose, and since the universe contains life, it contains purpose. In brief, the purpose of life is to live.

We, as living beings, share this effective purpose. The shared drive for self-propagation can then define a human purpose: to safeguard and perpetuate life. To this effect, we can expand life and seek to advance it into a controlling force in nature. These objectives can give human existence a cosmic purpose.

From a subjective point of view as conscious humans, we may wish to maximize conscious life. In fact, the conscious enjoyment of life can further motivate self-continuation.

In summary, life is united by its unique complexity, by the physical laws that precisely allow life, and by self-reproduction through gene/protein cycles. Life also has a special value for us as living beings. Therefore both objective science and our subjective judgement can support life-centered ethics and its purpose to propagate life.

III. SPACE BIOETHICS: PROSPECTS AND QUESTIONS

Astro-ethics and survival in a controlled future

In space, life can access limitless resources through astronomical times, helped by designed evolution in new environments. With such mastery of nature, our objectives become self-fulfilling.

With biotechnology that adapts us to space we can also control our biological future. However, these powers also entail dangers. In particular, tests by survival will always apply, both in natural and in designed evolution. Fit life-forms will survive, while failed designs will perish. This logic of life has guided, and will continue to guide, evolution. These tests of survival must be taken into account when designing future life.

In a designed future, what we pursue, we shall accomplish. Therefore, to prevail, survival must be pursued deliberately. This pursuit can be secured by ethics that aim to propagate life. Therefore, life-centered ethics themselves must be always propagated to secure our continued survival.

Ultimately it may depend on our ethics whether life will realize its cosmic potentials.

Astro-ecology and space populations. Should we create populations of trillions?

Life-centered ethics suggest that we should use space to advance life, and panbiotic ethics suggest that we should use space to maximize life. Of course, the quality of future life also matters, and in particular, we may wish to maximize conscious life.

Quantitatively, we may wish to maximize life over specific, maybe astronomically long, times. We can define a possible measure of the amounts of life in terms of biomass summed over of the time that it exists (Biomass Integrated Over Times Available (BIOTA) measured in kg-years).[22]

The potential amount of life in the Solar System can be estimated based on the available resources, such as the carbonaceous asteroids and comets that contain water, organic carbon and mineral nutrients. These resources can support, at high standards, human populations of thousands of trillions, more than one hundred thousand times the Earth's present population.[23] Cometary resources can yield biomass a hundred times larger; and a

[21] S. Goldberg. 1984. *Understanding Relativity: Origin and Impact of a Scientific Revolution*. Cambridge, MA: Birkhauser; A. Turing. Computing Machinery and Intelligence. *Mind* 1950; 256: 433–460.

[22] In mathematical terms, the objective is to maximize the term BIOTA (Biomass Integrated Over Time Available), defined as the integral of B(t)dt, where B(t) is total biomass as a function of time and the integration is over the habitable lifetime of the universe. The ultimate maximum would be achieved by converting all matter to biomass and maximizing its longevity. (Mautner, *op. cit.* note 9)

[23] The 1e22 kg carbonaceous asteroids contain 2% carbon, 10% water, and phosphorus and nitrogen, the limiting element. This could yield a human biomass of 3e20 kg (exponential notation, 3e20 = 3 x 10^{20}) in a population of 6e18, a hundred million present Earth populations. Alternatively these resources can yield 6e20 kg general biomass, and if 100,000 kg biomass supports one human, the population in the Solar System would be 6e15 (six thousand trillion) humans, equal to about 100,000 present Earth populations.

population equal to that of one million Earths. Extended to the galaxy, if one in ten stars has habitable environments, the above immense amounts can be multiplied further by ten billion.

Should we aim to create such immense amounts of life in billions of solar systems? Panbiotic ethics that seek to maximize life support these objectives. Further, this expansion will allow new lines of evolution, rich biodiversity, and ever advancing civilizations.

The potential time-scales of future life are also astronomical. For example, the expected lifetime of the Solar System is five billion years, while star-bound civilizations may exist for hundreds of trillions of years.[24] With these data, we can calculate the immense amounts of time-integrated BIOTA that resources in the Solar System permit.[25]

These immense populations may be created relatively rapidly, but biological wastage could exhaust life in the Solar System in half a million years. On the other hand, smaller but still very large populations could last through five billion future years of the Sun.

Should we construct immense shorter-lived populations or smaller but longer-lived populations? It would seem preferable that life should exist as long as possible.

The ultimate prospects. Should we propagate life if the future is finite?

Considering the amounts of matter in the universe and its duration in time, we can estimate the ultimate amounts of possible life in the universe.

If all matter was converted to biomass, some of it would have to be then converted to energy to sustain biology. On this basis, we can calculate the ultimate extent of possible life in the galaxy and in the universe, in the form of populations of trillions that last trillions of eons.[26] This potential scope of life is indeed immense, but by current cosmology, still finite.

Is there a point to maximizing life if it is finite? Panbiotic ethics that seeks to maximize life would answer in the affirmative. The vast scope of future life will allow great biological diversity, and rich experiences for intelligent beings. These potentials can further encourage us to secure and expand life.

Is the duration of life in the universe really finite? Cosmology will be controlled by dark matter and dark energy, both of whose natures are unknown. We have evidence about the past fourteen billion years since the Big Bang, but this is fleetingly short compared with trillions of future eons. Our descendants may have to observe cosmology for many eons until they can predict, and maybe control, the ultimate future.

For now, we need to secure Life for future generations. They may then understand Nature more deeply, and seek to extend life indefinitely.

Seeding other solar systems with life

We can soon start expanding life by seeding other solar systems. Human travel to other stars has major obstacles,[27] but we can soon start directed panspermia, sending microorganisms to other solar systems to plant the essential patterns of gene/protein life. We can also include eukaryotic organisms, hardy plant spores and the cysts of microscopic animals to start higher evolution.[28]

Solar sails or seeded comets can launch microbial capsules to nearby stars, or to clusters of new stars in interstellar clouds where they can seed many new solar systems.[29] Some of this new life may evolve into civilizations that can promote Life further in the galaxy.

These directed panspermia missions will be launched easily from space colonies, even by individuals or small groups. Should we proceed?

At present there is no scientific evidence for extraterrestrial life. The complexity of even a single cell suggests that the origins of life may be highly improbable and that it may not have occurred elsewhere even on billions of planets. Life on Earth may be unique, and the fate of life is then in our hands.

Seeding other planetary systems could prevent the study of pristine space but seeding a few hundred new solar systems will secure and propagate life while leaving hundreds of billions of pristine stars for exploration.

[24] F. Adams & G. Laughlin. 1999. *The Five Ages of the Universe*. New York, NY: Touchstone.

[25] With 6e20 kg asteroid-based biomass, in the five billion future years of the Sun the time-integrated biomass (BIOTA) in the Solar System will be 3e30 kg-years. Cometary resources can yield a biomass still a hundred times larger. (Mautner, *op. cit.* note 9).

[26] The estimated 1e41 kg baryonic matter in the galaxy can be converted gradually to biomass and then to energy, sustaining a steady-state biomass of 3e11 kg, possibly as ten billion humans, comparable to the current world population. In this manner life would last for an incomprehensible 1e37 years until protons decay, yielding BIOTA of 3e48 kg-years. For life in the universe these numbers may be multiplied by one hundred billion galaxies, allowing a time-integrated biomass of 3e59 kg-years of biological life in the universe. (Mautner, *op. cit.* note 9)

[27] E.F. Mallove & G.L Matloff. 1989. *The Starflight Handbook: A Pioneer's Guide to Interstellar Travel*. New York, NY: Wiley; J.H. Mauldin. 1992. *Prospects for Interstellar Travel (Science and Technology, Vol 80)* San Diego, CA: Univelt.

[28] Mautner, *op. cit.* note 5; Mautner & Matloff, *op. cit.* note 6.

[29] Mautner & Matloff, *op. cit.* note 6.

Conclusive proofs of extraterrestrial life could be provided by interstellar probes, but at achievable velocities, this would require millions of years. In the absence of such proof, we need to seed other solar systems to assure that life will indeed exist elsewhere in the universe.

However, the technology to seed space and, eventually, life itself in this Solar System, have finite durations. Should we accept the certain end of our family of gene/protein life, in order to avoid a small chance of interfering with putative alien life elsewhere?

The chances of interfering with other life-forms can be minimized by targeting young solar systems where life, especially advanced life, would not have yet started. Even if our microbial missions encounter other life, they may merge with local life and generate new biology. In either case, life will benefit.

Biotic ethics concerns first our own family of gene/protein life. If this family of life is unique to Earth, its fate is our hands. Panbiotic ethics can then motivate us to seed other solar systems to secure life, with cosmic consequences.

Fundamental changes in biology. How far can we transform, but still preserve, life?

Biology will have to adapt to space. Authors from Tsiolkovsky to Freeman Dyson, and much science fiction, realized that we may need to design new human traits in space.[30]

Resistance to radiation may be achieved by adapting human cells with genes from *Deinococcus radiodurans* and other microorganisms. Humans in space may need photosynthetic organs to use solar energy directly. They will need to adapt to reduced gravity, possibly reduce body size, develop new limbs for solar sailing and use engineered mechanical organs. Controlling these organs may require modified brains interfaced with computers. Long-distance space travel may require longevity of millennia, and artificial reproduction.

These technologies are developing, but their products still remain gene/protein life. Current research, however, also addresses basic biology itself. Novel proteins incorporate new amino acids for mechanical strength and for extreme conditions.[31] Correspondingly, DNA may be expanded with new nucleic bases to code for new proteins.

These developments can transform the very core of gene/protein life. Is this permitted by ethics that aim to preserve life? They may be allowed if the modified biology retains gene/protein reproduction. For example, the new biochemical components may be related to the natural amino acids and to DNA bases, or propagate otherwise through gene/protein cycles. These fundamental changes still preserve essentially gene/protein life.

However, biological life would be eliminated if humans were replaced by robots.[32] Although robots can be useful, to preserve biology, control should remain with biological beings. Specifically, control should remain with biological brains that have vested interest to perpetuate organic gene/protein life.

Biocentric ethics aims to propagate life. What does this mean when we can transform life? What is the essence of life that we should propagate? How far can we change, and still preserve, life? Biotechnology can soon turn these questions into actionable, practical choices.

Human survival

Similar questions apply to human survival. If humans are altered, does humankind still survive? Do we aim to preserve the present human species, or help its evolutionary progress?

Even if humans are altered, we would not become extinct if our genes are preserved and extended in advanced post-humans. This is in fact the natural course of evolution.

Biotic ethics value gene/protein life itself, and panbiotic ethics would favor evolution that helps to secure life. Similarly, if advanced post-human species can better secure life, then biotic ethics would approve continued human evolution.

Biocentric ethics, moral and religious values, purpose and determinism

By biocentric ethics, actions that secure life are morally good, and actions that threaten life are evil. These principles are ancient: 'I put before you good and evil, life and death. . . . choose life'.[33] This text identifies life as the essential moral good, and death as evil. So do more recent sources such as Schweitzer,[34] and discussions of panbiotic ethics.[35]

[30] J.W. Valentine. 1985. The Origins of Evolutionary Novelty and Galactic Colonization. In *Interstellar Migration and Human Experience*. B.R. Finney & E.M. Jones, eds. Berkeley, CA: University of California Press: 266–276; Hart, *op. cit.* note 7.

[31] J.L. Cleland & C.S. Craik, eds. 1996. *Protein Engineering: Principles and Practice* Chichester: Wiley.

[32] I. Aleksander & P. Barnett. 1983. *Reinventing Man: The Robot Becomes Reality*. New York, NY: Penguin Books.

[33] Bible, *op. cit.* note 12.

[34] Schweitzer, *op. cit.* note 14.

[35] Mautner, *op. cit.* note 5; Mautner & Matloff, *op. cit.* note 6.

By life-centered ethics, self-extinction is the ultimate evil. By these principles, dangers that threaten all life constitute infinite risk. No finite cause can justify an infinite risk/benefit ratio. Therefore, biotic ethics cannot accept even a small danger to all Life.

Conversely, endeavors that secure Life, such as expansion in space, are morally imperative. This endeavor will involve large-scale human collaborations, which require justice, peace, compassion, and truth. Human curiosity, ambition, and intelligence are also needed. These values are, therefore, consistent with biotic ethics.

Life-centered ethics are consistent with both religious and secular principles. In religious terms, a Creator who formed life will also desire its propagation. For secular ethics, life-centered principles suggest a rationally based human purpose and related moral and social values.

Having defined a purpose, can we in fact realize it? Is the future open or pre- determined, and can we control it? We cannot test experimentally if Nature is deterministic, because we can only observe one path of events that unfolds in time and cannot see if alternative paths are possible. However, lacking scientific proof that we can affect the future, we still make plans and often realize them.

Although the future cannot be predicted in detail, we can formulate principles that can guide it. Ultimately, biology will define the possible forms and scope of life, and survival will shape its evolution. These laws made us into a force of life in the universe, and will continue to advance us in the future.

Relations between biocentric, biotic and panbiotic ethics

Biocentric ethics value living organisms, species, and ecosystems.[36] More generally, a biotic ethics can be defined that values the core pattern of Life itself, that is, self-propagation through gene/protein cycles. This can be broadened further to panbiotic ethics, which seek to maximize life in space and time, and to incorporate in Life all the accessible resources.[37]

All life-centered ethics aim to secure our family of gene/protein life. Traditional biocentric ethics favor the conservation of existing species. Biotic ethics favor the evolution of new life-forms that help to secure gene/protein life in space. Panbiotic ethics favor the perpetual expansion of life with the continuing divergence of new species.

SUMMARY

Adapting Life to space will require major biological changes, helped by designed evolution. Our designs will then become self-fulfilling, and we shall need to propagate life deliberately in order to secure our survival. Life-centered ethics can motivate this quest, secure the future, and shape it with far-reaching, even cosmic, consequences. Therefore life-centered ethics themselves need always to be propagated.

Indeed, judging by observed behavior, the effective purpose of life is self-propagation. Briefly, the self-contained purpose of life is to live. Being part of life then defines a human purpose, to safeguard and propagate life. This also defines moral values: Acts that support life are good and acts that destroy life are evil.

Life-centered ethics can be supported by scientific insights: the biological unity of all gene/protein life, and the special place of complex life in nature, which precisely permits biology to exist.

Life-centered ethics can be generalized as biotic ethics that value the basic patterns of organic gene/protein life, and as panbiotic ethics that seek to expand life in the universe. The panbiotic objectives can be quantified, to maximize the time-integrated biomass in living matter. To maximize life, we can soon start to settle our Solar System, and to seed with life new solar systems beyond.

The expansion of life will increase biological complexity, diversity and intelligence, leading to new species who can further propagate life in the universe. From the human viewpoint, future life may best enjoy conscious existence, further motivating self-propagation. Indeed, control must always remain with organic gene/protein life that has a vested interest to continue organic life.

Whether future evolution will be designed or natural, selection by survival will always apply: Species that seek to propagate life will survive and species that do not, will perish. Therefore, in a designed future we shall always need to seek survival deliberately, and these life-centered principles will always need to be propagated.

[36] Schweitzer, *op. cit.* note 14.

[37] Technically, panbiotic ethics aim to realize the full biotic potential of gene/protein life using the carrying capacity of the universe. (See these terms in J.M. Anderson. 1981. *Ecology for the Environmental Sciences: Biosphere, Ecosystems and Man*. London: Edward Arnold; M. Began, M. Mortimer & D.J. Thompson. 1996. *Population Ecology: a Unified Study of Animals and Plants*. Oxford: Blackwell Science.

Ultimately, biology will define the possible forms and scope of life, and survival will shape its evolution. These laws made us into a force of life in the universe, and will continue to advance life in the future.

Given the projections of cosmology, life can expect an immense future. With the powers of intelligence, this future is in our hands. For now, we need to establish ethics that will secure life for future generations. Our descendants may then understand nature more deeply and seek to extend life indefinitely. In that future, our human existence will find a cosmic purpose.

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Gibson—Human Performance Enhancement Ethics (2006)

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Overview: Explores ethical questions surrounding pharmaceutical and technological enhancement of astronauts.

CONTROVERSY

The bioethics of enhancing human performance for spaceflight

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There are many ways of enhancing human performance. For military aviation in general, and for spaceflight in particular, the most important tools are selection, training, equipment, pharmacology, and surgery. In the future, genetic manipulation may be feasible. For each of these tools, the specific modalities available range from the ethically acceptable to the ethically unacceptable. Even when someone consents to a particular procedure to enhance performance, the action may be ethically unacceptable to society as a whole and the burden of risk for the individual may be too great. In addition, there are several characteristics that define the quality and the acceptability of the consent. Each method of enhancing performance will be examined in the context of the principles of medical ethics in a western society: autonomy, non-maleficence, beneficence, and justice. The aim is to draw the attention of aeromedical practitioners to the complexities of ethical dilemmas such as this particular one in order to help them to develop a morally justifiable code of practice that balances society's needs against individual ambitions and corporate goals.

Ethics is that branch of philosophy concerned with human character and conduct.[1] The study of ethics has given rise to a system of morals or rules of behaviour, including those governing professional conduct. Scientific advances in the last century have demanded corresponding development in ethical analysis. This is as true for biological sciences as for other realms of science. Bioethics has had to evolve to cope with genetics and transplantation as well as with numerous issues relating to the beginning and end of life.

There are several possible methods of enhancing human performance in general, including selection, training, special equipment, pharmacology, surgery, and genetic manipulation. These techniques may be applied to almost any form of human endeavour, including flying and space travel. Each of them may embrace processes that involve different degrees of ethical acceptability. An analysis of the basic principles involved should help us to develop a morally defensible code of conduct for the enhancement of human performance for spaceflight. This article will examine each of the techniques for enhancing performance with the aim of defining what would be, and what would not be, ethically acceptable.

Beauchamp and Childress[2] define the principles of biomedical ethics as autonomy, beneficence, non-maleficence, and justice. Beneficence is the positive requirement to promote goodness and to do good; non-maleficence is the requirement to do no evil; and justice is the quality of impartiality and integrity. Arguably, the most important aspect of biomedical ethics for the present article is autonomy.

Autonomy comprises respect and action for an individual's right to determine his or her own destiny. The legal basis for this was expounded 90 years ago by Judge Cardozo in a case in New York:

> … every human being of adult years and a sound mind has a right to determine what should be done with his own body …[3]

Autonomy implies the concept of consent to either an action or, conversely, an inaction. Consent has two main preconditions. The first of these is competence. Individuals must have the capability of understanding the implications of actions to which they have consented. The second is that the decision must be voluntary for consent to be valid. An important aspect of the ability to make a decision is the information that is presented to the individual to allow the decision to be made. The information must be germane to the course of action and must be presented in such a way as to aid understanding of the subject. Moreover, for consent to be meaningful, a decision has to be made on the basis of that consent and there has to be authorisation of the actions flowing from that decision.

Consent should ideally be given without undue pressure being brought to bear on the individual. Persuasion, and even some pressure on occasion, may be acceptable. An example would be the need for medical personnel to be immunised against hepatitis B. If you wish to work in such a capacity, then you must consent to the immunisation. It is possible to refuse the course of injections but employment in direct patient care will no longer be sanctioned. In addition, the requirement for consent can be overridden in certain circumstances by competing moral considerations—for example, when there is a conflicting requirement for scarce resources, when there is a risk to public health, or when there is a danger to others. Thus it has been argued that the US Armed Forces' mandatory anthrax vaccination programme is morally justified.[4] At the other end of the spectrum, coercion or involuntary consent is never morally justified. It can be seen that autonomy, and the freedom to make a choice, may be in conflict with beneficence and non-maleficence, but it is generally accepted nowadays that there is no place for the "doctor knows best" type of paternalism.

Another aid in deciding whether or not a proposed course of action is ethically acceptable is the concept of risk. Risk is the probability of loss or injury and has two main components. The first is the magnitude of the possible harm arising from an action and the second is the probability of that harm actually happening. Thus an action involving the highest amount of risk is one that has a high degree of

Abbreviation: NBC, nuclear, biological, chemical

probability of a great deal of harm. A lower degree of risk would accrue in an activity that had a very low probability of causing serious harm (such as a crash when flying) or a high probability of causing a very small amount of harm (such as getting a blister when walking a long way). The lowest degree of risk therefore applies when there is a low probability of very minor harm. Against risk must be balanced the potential benefit of the activity. As risk rises and as the potential benefit falls, then any ethical test of whether or not that activity is acceptable becomes harder to satisfy.

Personnel in the armed forces give up some of their rights when they join the military. In some circumstances their autonomy can be legally and ethically overridden by the interests of their colleagues, commanding officer, or, ultimately, the state.[5] Spaceflight is one area of high risk that may possibly be combined with a potential for benefit.

ENHANCEMENT OF PERFORMANCE

Performance of various activities may be improved by selection of the right individual for the task, training for the role, the provision of equipment, the use of drugs or surgery, and, more recently, the potential use of genetic modification. This is as true for spaceflight as for any other activity.

Selection

The practice of selection for employment is well established. Selection on the grounds of ability is not an issue. Physical size may also be an acceptable selection criterion where payload is a significant factor. However, selection on the basis of the ability to perform a job should not include consideration of factors such as gender, ethnic origin, religion, or sexual orientation. Disability should also not be an issue except in two circumstances: first, where the core requirements of the job cannot be performed even with reasonable adjustments if necessary; and secondly, where employment would carry a particular health and safety risk to the individual or others. Selection for driving a car will be less prescriptive in terms of health, intelligence, and even size than for flight of any kind. Similarly, it would be reasonable to expect higher physical and intellectual standards for commercial pilots than for sport pilots, for military aviators compared with those in the civil sector, and for astronauts compared with military pilots. In addition, it would be acceptable to select astronauts from only one country if national security was an issue for a particular space mission.

Training

It is entirely appropriate to provide training for a job. Indeed, it may be unethical not to provide training. However, there may be ethical difficulty with different types of training. In driving, the use of driving instructors or skid pans is acceptable but deliberate experience of crashes would not be ethical because of the risk of injury. In military operations, the use of nuclear, biological, chemical (NBC) simulants, such as CS gas, in controlled conditions is acceptable but exposure to live agents (as practised in some Warsaw Pact countries during the Cold War when, presumably, the justification was that the demands of the state overrode the rights of the individual) is not. Exposure of pilots to simulated high altitude in a decompression chamber to see if they are susceptible to decompression sickness is acceptable because this is done in a controlled manner with ready access to emergency treatment and recompression. This is preferable to disabling symptoms being experienced for the first time in flight when treatment is not immediately accessible. Similarly, in training for spaceflight, activities that expose astronauts to unnecessary and uncontrolled risk, such as prolonged sensory deprivation (with the risk of developing psychological disorders) or bedrest (with the risks of bone resorption and deep vein thrombosis), would not be acceptable. In short, training must be sufficiently rigorous to be useful but any risk has to be managed and minimised. If the risk is judged to be too high, then an alternative method of training for that activity must be found.

Equipment

It has been claimed by aviation medicine specialists since the1930s that aircraft engineers believe that a person should be adapted to fit the aeroplane rather than the other way round.[6] It is entirely acceptable to provide equipment—such as oxygen equipment, pressure suits and anti-g suits—to enable an aviator to survive in a hostile environment. However, that equipment must not, of itself, increase the risk. In operations in the UK, the risk of unconsciousness in flight from not wearing an anti-g suit outweighs the disadvantage of the additional heat stress. In hotter climes, the use of additional layers of protective equipment dictates the provision of effective conditioning systems, which could be cabin or personal conditioning. Different balancing of the risks can give rise to nations adopting different philosophies regarding protective equipment. For example, in the 1970s the United States Air Force used a lightweight helmet that did not impede head movement—and hence look-out—at high gravitational loads but did not provide a high degree of head protection during ejection. Conversely, the British helmets protected better in accidents but, at over 1 kg heavier (and thus effectively 8 kg heavier at a gravitational force of $8g_z$, which is routine in air combat) they were more unwieldy in the cockpit. The use of NBC protective headgear during peacetime training may not be acceptable because of the restriction of effective visual fields. However, when gauged against the greater risk of exposure to live agents in wartime, peacetime training with the equipment, in order to build familiarity and confidence, may become ethically acceptable. An acceptable compromise is to fly while wearing the headgear but with a safety pilot who is not similarly encumbered.

One example of an unacceptable item of equipment is a prototype British full pressure suit from the 1950s, which required the pilot to be bolted to the aircraft, thus giving no means of escape (figure 1). That this option was even considered is reminiscent of the objection of the General Staff in the First World War to the provision of parachutes on the grounds that aviators may use them unnecessarily.[7] For spaceflight, the dilemma lies equally in the failure to provide available equipment, such as an escape capability, and in the provision of equipment that would impact on safety. Initial arguments centred around complexity, cost, and unnecessary payload. Further justification at the time was that, provided the astronauts understood the risks and judged the benefits of spaceflight to be sufficient, withholding this capability would be ethically acceptable. However, after the Challenger accident, which involved personnel other than professional astronauts, a basic escape facility was provided by NASA. What would be more debateable is whether or not, in such a life-threatening situation with no chance of rescue, it would be ethically acceptable to provide astronauts with a means of committing suicide in order to prevent a potentially lingering death.

Pharmacology

Military aircrew have used serial ''uppers'' and ''downers'' for over 50 years under medical supervision (initially the drugs used were barbiturates and amphetamine derivatives; more recent ''downers'' have been benzodiazepines), but there has been no suggestion that equivalent pharmaceutical assistance is acceptable to enhance the performance of car drivers or private pilots.[8] Although it could be argued that everyone has the right to decide what substances to take as long as there is not direct harm or risk to others, in reality laws and

Figure 1 Prototype British full pressure suit, 1950s. ©Crown copyright/MOD.

regulations are in place to control this because these activities carry a greater inherent risk to non-participating individuals than state-sponsored, military, operational flying. However, it would be acceptable for drivers to use therapeutic agents such as antibiotics whereas the condition requiring their use would ground aviators. In some conditions, such as epilepsy, even the use of therapeutic agents may not allow the activity to be performed ethically until the risk is considered sufficiently small. For commercial aircrew, particularly with many current intercontinental flights lasting such a long time, the balance has to be made between the risks of fatigue and subsequent accidents, the potential side effects of the use of artificial stimulants, and the operational justification. So far, operators have relied on carrying additional aircrew to allow rest in flight. On the other hand, for the air raid on Libya in 1986, the United States Air Force allowed the use of barbiturate sleeping pills so the aircrew could sleep through the day before the mission and the use of stimulants (benzedrine) to maintain alertness over the target and for in-flight refuelling on the return journey.[9] It could be argued that mind altering drugs to change the perception of time on long missions may not be ethical for astronauts because of the unknown risks of developing psychotic disorders, but drugs to stimulate hibernation may be. The administration of female hormones to male astronauts to obviate the need for shaving may not be considered to convey sufficient benefit to make it ethically acceptable. On the other hand, the use of the same drug to control aggression or to diminish sexual urges on long duration missions may involve sufficient benefit to make the procedure appropriate. The self-evident conclusion is that, for any particular pharmaceutical agent, a robust and defensible risk–benefit analysis should be made.

Surgery

Surgery to correct a pathological condition would be acceptable for drivers and, in certain circumstances, for aircrew and space crew. The British Antarctic Survey used to require its employees who were over-wintering in Antarctica to have a prophylactic appendicectomy before travel. This would also be acceptable before long duration spaceflight, for example a Mars mission, where the benefit outweighs the potential risk. Corneal remodelling, such as Lasik, is now generally acceptable for drivers and many types of aircrew. Provided that the risks remain manageable, this procedure may also be ethically acceptable for astronauts. However, mutilating operations to enhance performance would not be acceptable. One example would be amputation of the legs to enhance tolerance to gravitational forces.

In general terms, the implantation of devices to enhance performance would be ethically acceptable, provided that the operation was not mutilating and the benefits considerably outweighed the risks. The debate would be over the definition of the word ''considerably''. The use of surgery to create cyborgs would be more controversial. However, it has been argued that the procedure would be ethical provided that the risk–benefit analysis suggested a significant benefit, that fully informed consent was given, and that the basic humanity of the cyborg was respected and preserved.[10]

Genetics

In the same way as for surgery, genetic modification of an individual to cure a disease or to remove the risk of a serious condition developing would arguably be considered ethically acceptable for drivers, aircrew, and astronauts alike. However, genetic modification to transform the physiological or psychological characteristics of an individual may be unacceptable for all classes.

CONCLUSION

This analysis is summarised in figure 2, which gives a representation of conceptual limits for each technique of enhancing performance for a range of activities. It can be seen that, as the activity becomes more intrusive, the likelihood of it becoming ethically unacceptable increases. In addition, as the activity involves fewer individuals (for example there are many fewer private pilots than drivers and

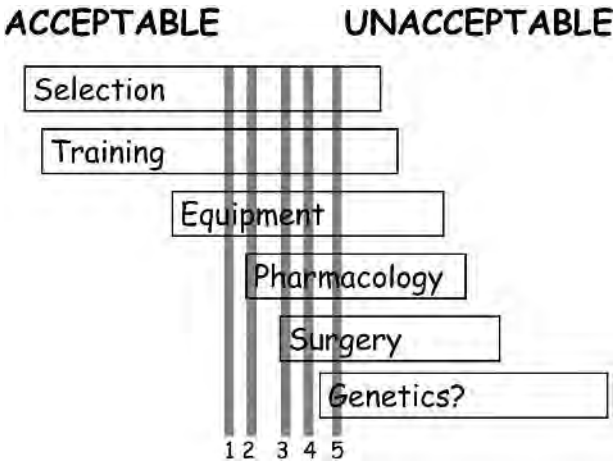

Figure 2 Suggested limits of ethical acceptability of techniques to enhance performance during different activities. 1 = driving; 2 = private flying; 3 = commercial flying; 4 = military flying; 5 = spaceflight.

considerably fewer astronauts) the ethical limit moves to the right, or is potentially eased. Alternatively, as the danger inherent in the activity intensifies, so the ethical limit is more likely to be relaxed provided that the benefit accruing is seen to be sufficiently great. However, what value can be put on a human life? Ackerman and Heinzerling suggest that, where the range of possible risks is large, one should assume that the worst will happen.[11] Despite this conservative approach, any form of enhancement of performance for human endeavour in space cannot be acceptable unless there is full, voluntary, and informed consent to the procedure. This applies just as much to physicians' willingness to carry out the procedures as to individuals' willingness to undergo them. In this respect, the aviation medicine practitioner has a key role to play to challenge the ambitions and aspirations of planners, politicians, engineers, and astronauts.

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Overview: Proposes foundational rights and protections for humans living and working in space.

Chapter 25

Foundations of a Space Bill of Rights

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25.1 Introduction

Human spaceflight has significantly advanced over the last century. The number of human beings who have traveled, lived, and worked in space has increased. Our understanding of how spaceflight impacts human physiology has likewise significantly advanced. It is now apparent that there is a substantially greater number of human beings who medically qualify for spaceflight. Space is no longer confined to carefully selected and trained astronauts, as has been the case in the past. Many civilians qualify for spaceflight. Although this can be highly dependent on mission-specific or vehicle-specific factors, realizing this fact should be considered a profound accomplishment of humankind. The prospect of sending classrooms of grade schoolers into space for a few orbits around the Earth and returning safely to attend class is another example of how spaceflight might one day enrich humanity.

The increase in the number of medically qualified human beings to go to space presents opportunities and challenges. Gradually making it possible for all humanity, in all its vast diversity, to travel and live in space requires thought and consideration of complex ethical and moral issues.

Human history, especially the last century, provides countless examples of our capacity to harm others and commit atrocities. Examples abound of religious and political persecution of entire populations and individuals (such as Socrates, Galileo, and countless others), including wars, slavery, democide, and torture. While some respect and regard our inherent human rights, others have and continue to actively exterminate individuals and whole populations in the name of religious, philosophical, political, or corporate ideologies.

It is clear, then, that as humanity fulfills its moral responsibility to advance human exploration and as technology continues to progress rapidly, intellectual and professional humility is an aspiration for the greater benefit of society and civilization. That is, we must recognize how little we know, and understand and proceed with the highest ideal of humanity in mind and adhere to methods of technological implementation that support that humanity. The multiuse nature of technological and medical innovations (including things such as the internet, AI, surveillance, neuroscience, and applied biology) requires moral and ethical scrutiny. And the technological advances from the progress of human spaceflight are not immune from such scrutiny either. Too often, we fail to consider the second- and third-order effects of our achievements. Among the many questions we can and should ask ourselves are "How can death, violence, and atrocities be prevented?," "How do we reduce and prevent harm, fear, and suffering?," and "How best can we preserve our shared humanity in the face of a changing world?"

Therefore, recognizing the empowering force of technology as well as its capacity for destruction and lethal harm, we are obligated to reaffirm and recommit our efforts to ensure justice and safety for all humankind. Thus, we believe that the ethical way forward is a recommitment to and reaffirmation of individual and universal human rights. It is on this basis that we can further legitimize continued human spaceflight and codify a Space Bill of Rights.

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25.2 Principles and assumptions

We believe it is common sense, and a simple reasonable reflection, to conclude that every human being is entitled to basic fundamental rights by virtue of being born a human. By extension, such rights are not bestowed upon us by governments.

Indeed, human beings have always been entitled to fundamental rights. It may be said that the history of humanity has been and is continuing a long process of discovery and of full realization of fundamental human rights. Only in the last 300 years or so have such fundamental rights been more explicitly formulated or articulated as we recognize them today in written thought and law. Tremendous work, effort, and sacrifice have been undertaken in the pursuit of vindicating these fundamental rights, with myriad achievements and triumphs in addition to the setbacks and failings encountered. Crucial, then, for the foundations of a Space Bill of Rights is to heed both the lessons from the past and presently existing human rights catalogs. Therefore, underlying any meaningful composition of a Space Bill of Rights must be an examination of important and fundamental human rights catalogs and theoretical works since the Enlightenment and the recent few centuries. They are permanent guides and monuments in helping us understand our just relationships with each other.[1]

25.2.1 The Magna Carta

Issued on June 15, 1215, the historic document entitled Magna Carta, a precursor to developmental social and government constitutions and treaties thereafter, was the founding document describing that the king (King John of England at Runnymede) and his government were subject to the Law in the same measure as their subordinates and citizens. It established that the Law was a power placing limits on royal authority.

Significantly within the context of the 13th century, the Magna Carta provided for a church free from the king's control, restated English law and concepts of justice, and defined guidelines for the personal behaviors of royal officials. Magna Carta was the first document of authoritative standing that encapsulated the notion that members of the king's domain could assert their own rights when oppressed by the ruling class. Included in this new idea was that the king's governmental power could be restricted, limiting overreach as a means of protecting the newly declared rights of individuals. While the Magna Carta still possessed many limitations, such as those concerning the rights of women, it represented an evolution in the concept of articulated rights for individuals.

In the broader development of constitutional principles, documents that expressed the emergent "will of the people," core concepts of the Magna Carta were drawn upon by the United States Founding Fathers when creating both the Declaration of Independence and the United States Constitution (1787).

25.2.2 The US Constitution and Bill of Rights

The Magna Carta and its preceding documents were originally of concern to the founding fathers of the United States specifically because they were *concessions, by kings, to the power of the people's lower-ranked representatives or leaders*. This document was, essentially, a promise by a powerful hereditary monarch that he would commit to not using his power to oppress citizens in specific ways. Several of the founding fathers did not wish to recognize another "monarchy" (in the emergent United States) that provided similar *concessions* via a bill of rights. There was also concern that a US Bill of Rights would have no practical power.

In 1803 the US Supreme Court assuaged these concerns by asserting the power to hold legislators accountable to the Constitution (including the Bill of Rights). In 1925, the US Supreme Court further ruled that the Bill of Rights (by way of the Fourteenth Amendment) applied to state law, too.

The US Declaration of Independence codified several derived principles of the laws of nature, which importantly included the concept that all people are endowed by the Creator with certain *unalienable* rights. By definition, *unalienable* means incapable of transfer. Thus an unalienable right cannot be given away nor taken away, especially by a civil government. Unalienable (or the contemporary, inalienable) means inherent or undeniable. Unalienable rights are incapable of being abolished or impaired. Unalienable rights are retained regardless of government edicts to the contrary because civil government does not grant them in the first place. These rights that are inherent to the individual are important tenets that have governed subsequent attempts to assert the rights of humans.

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1. See, for example, Declaration of Independence (July 4, 1776); Déclaration Des Droits De L'Homme En Société (Declaration of the Rights of Man in Society) (1789); Immanuel Kant, Grundlegung zur Metaphysik der Sitten (Groundwork of the Metaphysics of Morals) (1785); Statement of Essential Human Rights (1945); The Universal Declaration of Human Rights (1948); Charter of Fundamental Rights of the European Union; US Constitution, Amendments I-X, XIII, XIV, XV, XIX.

For a particularly notable example, the *Declaration of Independence* of July 4, 1776, provides an articulation of fundamental principles of perennial importance and relevance:

> *We hold these truths to be self-evident, that all men are created equal, that they are endowed by their Creator with certain unalienable Rights, that among these are Life, Liberty and the pursuit of Happiness. That to secure these rights, Governments are instituted among Men, deriving their just powers from the consent of the governed,—That whenever any Form of Government becomes destructive to these ends, it is the Right of the People to alter or to abolish it, and to institute new Government, laying its foundation on such principles and organizing its powers in such form, as to them shall seem most likely to effect their Safety and Happiness.*

These are revolutionary principles, the zeal and vigor of which manifest themselves by and through the Constitution of the United States and the Bill of Rights.

Also among the most notable human rights documents is the *Universal Declaration of Human Rights* of December 1948. It is one of the most profound achievements of humankind. This is especially so considering how recently in view are the horrors of colonialism and the World Wars. The Preamble and Article 1 are provided as follows:

> Whereas *recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family is the foundation of freedom, justice and peace in the world,*
>
> Whereas *disregard and contempt for human rights have resulted in barbarous acts which have outraged the conscience of mankind, and the advent of a world in which human beings shall enjoy freedom of speech and belief and freedom from fear and want has been proclaimed as the highest aspiration of the common people,*
>
> Whereas *it is essential, if man is not to be compelled to have recourse, as a last resort, to rebellion against tyranny and oppression, that human rights should be protected by the rule of law,*
>
> Whereas *it is essential to promote the development of friendly relations between nations,*
>
> Whereas *the peoples of the United Nations have in the Charter reaffirmed their faith in fundamental human rights, in the dignity and worth of the human person and in the equal rights of men and women and have determined to promote social progress and better standards of life in larger freedom,*
>
> Whereas *Member States have pledged themselves to achieve, in cooperation with the United Nations, the promotion of universal respect for and observance of human rights and fundamental freedoms,*
>
> Whereas *a common understanding of these rights and freedoms is of the greatest importance for the full realization of this pledge,*
>
> Now, therefore,
>
> The General Assembly,
>
> Proclaims *this Universal Declaration of Human Rights as a common standard of achievement for all peoples and all nations, to the end that every individual and every organ of society, keeping this Declaration constantly in mind, shall strive by teaching and education to promote respect for these rights and freedoms and by progressive measures, national and international, to secure their universal and effective recognition and observance, both among the peoples of Member States themselves and among the peoples of territories under their jurisdiction.*
>
> *Article 1: All human beings are born free and equal in dignity and rights. They are endowed with reason and conscience and should act towards one another in a spirit of brotherhood.*

Without even recalling the context of when this was formulated and promulgated, or the very recent catastrophe of the World Wars,[2] it is readily apparent that the truth-validity of many of these declarations transcend any immediate historical

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2. The trauma throughout the world after the World Wars and the widespread experience and understanding of the destructive capability of technology cannot be underemphasized. Another very important document worthy of review and study is the *Statement of Essential Human Rights* (1945), with notable excerpts included as follows: "the purpose of a successful international organization can be nothing less than a common aim for mankind. [. . .] The one objective that is big enough and specific enough to be common to all men is the welfare, the dignity, the inviolability of the individual human being. [. . .] a world society with so much power as ours must be organized to serve the dignity and welfare of the individual human being or it will destroy itself. [. . .] Only as the world organization fixes its eyes on the welfare of the individual and on the increase of his freedom and responsibility will it find the means and the popular support to carry it through the political, economic, and ideological storms ahead. [. . .] The first step is to define the indispensable human rights, if possible in terms that will be acceptable to men of good will in all nations. [. . .] One of the greatest dangers immediately ahead of us is that the groups concerned with security will lose sight of civil liberties and vice versa. [. . .] the ultimate purpose of international relations is to secure peace, freedom, food, and education for all."

context or stage of technological development. For example, that human beings have inherent dignity that deserves respect and equal rights worthy of protection; disregard and contempt for human rights leads to crimes and injustices; the collective conscience of humanity is outraged when we commit crimes and injustices against each other; all human beings are endowed with reason and conscience which make them worthy of respect; education and understanding are fundamentally important to develop friendly relations between nations and peoples; recognition of human dignity and equal rights is the foundation for liberty, justice, and peace. It is clear that this must inform any proposed Space Bill of Rights.

The Universal Declaration has been fundamental for enabling the world to refine and clarify the full scope and meaning of human rights, for nations, and for the international community.[3] It has also been fundamental for enabling the world to deliberate and address pressing global issues, such as defense and security,[4] atomic energy,[5] human health,[6] the environment,[7] global food supply,[8] Antarctica,[9] or outer space.[10] Other documents informed by the Universal Declaration such as those just cited are also valuable guides in helping create a Space Bill of Rights. They each remind us of humankind-responsibility and can help us address new and similar problems that have recurred over time in changing contexts with new generations.

For purposes of a Space Bill of Rights, particularly notable are the declarations, treaties, and agreements governing human activities related to spaceflight. For example, the foundational *Declaration of Legal Principles Governing the Activities of States in the Exploration and Use of Outer Space* (1963) declares nine principles that should guide States in the exploration and use of outer space: (1) the exploration and use of outer space shall be undertaken for the benefit and in the interests of all mankind; (2) outer space and celestial bodies are free for exploration and use by all States on the basis of equality and according to international law; (3) outer space and celestial bodies are not subject to national appropriation by claims of sovereignty; (4) the activities of States in outer space should be undertaken in accordance with international law, including the UN Charter, in the interest of maintaining international peace and security and promoting international cooperation and understanding; (5) States are responsible for their activities, whether by government or by nongovernment activities, and international organizations are also responsible for their activities and will be held accountable along with any States participating with them; (6) States shall be guided by the principles of cooperation and mutual assistance in the exploration and use of space; (7) States should maintain a registry of space objects and retain ownership of objects launched into space and upon their return; (8) States are internationally liable to other States and persons for damage or injury from outer space activities; and (9) astronauts are envoys of mankind in outer space and shall be rendered all possible assistance in events of accident, distress, or emergency landing. Any Space Bill of Rights, or spacefaring government, company, or other organization, cannot ignore such principles.

Subsequent formal and enforceable treaties and agreements incorporate these principles, guided by the notions of the progress of the exploration and use of outer space for peaceful purposes, for the benefit of all peoples, and in a spirit

3. *International Covenant on Civil and Political Rights* (1966, 1976); *International Covenant on Economic, Social and Cultural Rights* (1966, 1976); see also, *African Charter on Human and Peoples' Rights (Banjul Charter)* (1981, 1986); League of Arab States, *Arab Charter on Human Rights* (2004, 2008); Organization of American States, *American Convention on Human Rights* (1969); *Constitution of Japan* (1946) (Chapter III); *Constitution of the Republic of Korea* (1948) (1987) (Chapter II); http://www.constituteproject.org/constitutions (Accessed April 2024).

4. *The North Atlantic Treaty* ("The Parties to this Treaty reaffirm their faith in the purposes and principles of the Charter of the United Nations and their desire to live in peace with all peoples and all governments.").

5. *Statute of the International Atomic Energy Agency* (1989) ("The [International Atomic Energy Agency] shall seek to accelerate and enlarge the contribution of atomic energy to peace, health and prosperity throughout the world. It shall ensure, so far as it is able, that assistance provided by it or at its request or under its supervision or control is not used in such a way as to further any military purpose.").

6. *World Health Organization* (1948) ("The States Parties to this Constitution declare, in conformity with the Charter of the United Nations, that the following principles are basic to the happiness, harmonious relations and security of all peoples: Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition. The health of all peoples is fundamental to the attainment of peace and security and is dependent upon the fullest cooperation of individuals and States. [. . .]").

7. *Declaration of the United Nations Conference on the Human Environment* (1972) ("Man is both creature and molder of his environment, which gives him physical sustenance and affords him the opportunity for intellectual, moral, social and spiritual growth. In the long and tortuous evolution of the human race on this planet a stage has been reached when, through the rapid acceleration of science and technology, man has acquired the power to transform his environment in countless ways and on an unprecedented scale. Both aspects of man's environment, the natural and the man-made, are essential to his well-being and to the enjoyment of basic human rights and the right to life itself.").

8. The World Food Programme (1961).

9. *The Antarctic Treaty* (1959) ("[. . .] Convinced also that a treaty ensuring the use of Antarctica for peaceful purposes only and the continuance of international harmony in Antarctica will further the purposes and principles embodied in the Charter of the United Nations; Have agreed as follows [. . .]").

10. *The Artemis Accords* (2020).

of mutual international cooperation.[11] Among these, specific provisions are particularly relevant for human spaceflight. For example, Article V of *The Outer Space Treaty* of 1967 affirms that astronauts are envoys of mankind in outer space; that State Parties will assist them in their activities; and that phenomena discovered in outer space that are dangerous to the life or health of astronauts should be reported and the world informed of such phenomena. An Article like this helps provide substance to specific rights and helps legitimize the notion that any future spacefarers have a right to informed consent of the risks and dangers of spaceflight.

Similarly, *The Rescue Agreement* of 1968, *The Liability Convention* of 1972, and *The Registration Convention*, all help provide substance to specific rights of spacefarers, by clarifying the relation between government and nongovernment entities, establishing expectations of liability rights and obligations, or making clearer the risks of spaceflight activities.

Also notable is *The Moon Treaty* of 1979. For example, Article 10 provides for the safety, life, and health of persons on the Moon; Article 12 clarifies questions of jurisdiction and control over persons and equipment on the Moon; and Article 11 attempts to establish an international régime to govern natural resource exploitation on the Moon. Such provisions and others identify challenges and potential solutions to the risks involved from the increased human activity in outer space. Additionally helpful in thinking about this as well, besides referencing the *Artemis Accords* of 2020, is the *Antarctic Treaty* of 1959, which, among other things, addresses challenges of jurisdiction, scientific research coordination and cooperation, and dispute resolution. Furthermore, an emphasis that advancing scientific development and research, as well as coordination to that end, is particularly noteworthy when considering future advances and developments in outer space.

The *Artemis Accords* of 2020 reaffirm the importance of compliance with many of the treaties and agreements already mentioned or discussed. Among other things, these Accords seem to help lay the legal framework for commercial space resource extraction. Also noteworthy in this respect is Title 51 of the United States Code, Section 51303 (a portion of the *US Commercial Space Launch Competitiveness Act* of 2015), which grants property rights to private US citizens who collect or possess space resources. Provisions such as these help us understand how certain rights and obligations, liabilities, and property rights might be relevant for a Space Bill of Rights. The concepts of ownership, possession, and property seem intuitive but can be rather complicated. A central and crucial aim of the international human rights catalogs such as the Universal Declaration is to provide for increased global economic prosperity consistent with the preservation and protection of everyone's civil, political, and social rights.

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11. *The Outer Space Treaty* (1967) ("Article IV: [. . .] The Moon and other celestial bodies shall be used by all States Parties to the Treaty exclusively for peaceful purposes [. . .] Article IX: [. . .] guided by the principle of cooperation and mutual assistance [. . .] States Parties to the Treaty shall pursue studies of outer space, including the Moon and other celestial bodies, and conduct exploration of them so as to avoid their harmful contamination and also adverse changes in the environment of the Earth resulting from the introduction of extraterrestrial matter and, where necessary, shall adopt appropriate measures for this purpose. [. . .]"); *The Rescue and Return Agreement* (1968) (Calling "for the rendering of all possible assistance to astronauts in the event of accident, distress or emergency landing, the prompt and safe return of astronauts, and the return of objects launched into outer space [. . .] *Prompted* by sentiments of humanity. [. . .]"); *The Liability Convention* (1972) ("*Reaffirming* the importance of international cooperation in the field of the exploration and peaceful uses of outer space, including the Moon and other celestial bodies, and of promoting the law in this new field of human endeavor" [. . .] establishing rights and obligations pertaining to liability standards for outer space activities of States and entities); *The Registration Convention* (1975) (Establishing national registries and a central registry for space objects launched into outer space, and identification procedures); *The Moon Treaty* (1979) ("Article 3: [. . .] The moon shall be used by all States Parties exclusively for peaceful purposes. [. . .] Article 4: The exploration and use of the moon shall be the province of all mankind and shall be carried out for the beneft and in the interests of all countries, irrespective of their degree of economic or scientific development. [. . .] Article 10: States Parties shall adopt all practicable measures to safeguard the life and health of person on the moon. [. . .] Article 11: The moon and its natural resources are the common heritage of mankind [. . .]"); *The Principles Governing the Use by States of Artificial Earth Satellites for International Direct Television Broadcasting* (1982) ("Activities in the field of international direct television broadcasting by satellite [. . .] should promote the free dissemination and mutual exchange of information and knowledge in cultural and scientific fields, assist in educational, social and economic development, particularly in the developing countries, enhance the qualities of life of all peoples and provide recreation with due respect to the political and cultural integrity of States [. . .] [and] should accordingly be carried out in a manner compatible with the development of mutual understanding and the strengthening of friendly relations and cooperation among all States and peoples in the interest of maintaining international peace and security."); *The Remote Sensing Principles* (1986) ("Remote sensing activities shall be carried out for the benefit and in the interests of all countries, irrespective of their degree of economic, social or scientific and technological development, and taking into particular consideration the needs of the developing countries."); *The Nuclear Power Sources Principles* (1992) ("*Recognizing* further that the use of nuclear power sources in outer space should be based on a thorough safety assessment, including probabilistic risk analysis, with particular emphasis on reducing the risk of accidental exposure of the public to harmful radiation or radioactive material.") *The Declaration on International Cooperation in the Exploration and Use of Outer Space for the Benefit and in the Interest of All States, Taking into Particular Account the Needs of Developing Countries* (1996) ("*Desirous* of facilitating the application of the principle that the exploration and use of outer space, including the Moon and other celestial bodies, shall be carried out for the benefit and in the interest of all countries, irrespective of their degree of economic or scientific development, and shall be the province of all mankind [. . .]"); *The Intergovernmental Agreement on the Civil International Space Station* (1998); *Artemis Accords* (2020).

Especially worth consideration in attempting to formulate a Space Bill of Rights is the *Intergovernmental Agreement on the Civil International Space Station* of 1998 ("IGA"). The IGA also reaffirms the importance of compliance with many of the most important treaties and agreements already mentioned or discussed. Section 1 of Article 1 states as follows: "The object of this Agreement is to establish a long-term international cooperative framework among the Partners, on the basis of genuine partnership, for the detailed design, development, operation; and utilization of a permanently inhabited civil international Space Station for peaceful purposes; in accordance with international law. This civil international Space Station will enhance the scientific, technological, and commercial use of outer space." The IGA is comprehensive and surely will be a guide to implementing any future cooperative outer space projects. It provides for issues of jurisdiction and control (Article 5), ownership (Article 6), management (Article 7), use and operation (Articles 9 and 10), crew (Article 11), transportation (Article 12), evolution or changes in infrastructure (Article 14), communications (Article 13), data and goods exchange and transmission (Articles 19 and 20), intellectual property (Article 21), funding (Article 15), civil liability and criminal jurisdiction (Articles 16, 17, and 22), and signatory consultation and cooperation review (Articles 23 and 24). The provisions of the IGA such as these and others will help inform the construction of any Space Bill of Rights.

Particularly noteworthy is Article 11 which clarifies that a Code of Conduct for the Space Station crew is to be developed and approved by all the Partners to the IGA and that the crew members are to observe the Code of Conduct. The Code of Conduct established in the year 2000 is insightful (as are the 2013 and 2021 versions).[12] Particularly informative are Sections V and VI.

Sections V, Physical and Information Security Guidelines, provides that various data should be marked or identified as export controlled or proprietary, or otherwise protected. Importantly, included in these provisions is the protection of crewmember personal information from disclosure, including personal medical information, which must be transmitted privately and securely.[13]

Section VI, Protection of Human Research Subjects, provides requirements and qualifications for conducting research on crewmembers as human subjects, among which is informed consent and the right to withdraw or revoke such consent after research has begun. For example, no human research can be conducted that would jeopardize the life, health, physical integrity, or safety of the subject.[14]

These provisions are particularly insightful and important. Perhaps it is not a surprising realization that considering what rights spacefarers are entitled to is really another reflection of what rights all human beings are entitled to on Earth. In this light, Sections V and VI of The Code of Conduct are also worth thinking about in the context of the year of 2000 when the Code was promulgated and adopted. The context of the year 2000 is significant. At that time and since then, the commercial internet developed at a rapid pace without any similar parameters as those in the provisions cited earlier. Based predominantly on certain technical arrangements and highly questionable if not directly unlawful applications of contract-legal principles, the current commercial internet has developed into sometimes large and obscure networks of corporate and government entities.

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12. Code of Federal Regulations, Title 14, Part 1214 (December 21, 2000).

13. Full Text: "Sections V. Physical and Information Security Guidelines: Personal information about ISS crewmembers, including all medical information, private family conference, or other private information, whether from verbal, written, or electronic sources, shall not be used or disclosed by other ISS crewmembers for any purpose, without the consent of the affected ISS crewmember, except as required for the immediate safety of ISS crewmembers or the protection of ISS elements, equipment, or payloads. In particular, all personal medical information, whether derived from medical monitoring, investigations, or medical contingency events, shall be treated as private medical information and shall be transmitted in a private and secure fashion in accordance with procedures to be set forth by the MMOP. Medical data which must be handled in this fashion includes, for example, biomedical telemetry, private medical communications, and medical investigation data. Nothing in this paragraph shall be interpreted to limit an ISS crewmember's access to all medical resources aboard the ISS, to ground-based medical support services, or to his or her own medical data during preflight, on-orbit, and postflight activities."

14. Full Text: Section VI. Protection of Human Research Subjects: No research on human subjects shall be conducted which could, with reasonable foresight, be expected to jeopardize the life, health, physical integrity, or safety of the subject. No research procedures shall be undertaken with any ISS crewmember as a human subject without: (1) written approval by the Human Research Multilateral Review Board (HRMRB) and (2) the full written and informed consent of the human subject. Each such approval and consent shall be obtained prior to the initiation of such research, and shall fully comply with the requirements of the HRMRB. The HRMRB is responsible for procedures for initiation of new experiments on-orbit when all consent requirements have been met, but the signature of the human subject cannot be obtained; explicit consent of the human subject will nonetheless be required in all such cases. Subjects volunteering for human research protocols may at their own discretion, and without providing a rationale, withdraw their consent for participation at any time, without prejudice, and without incurring disciplinary action. In addition, approval or consent for any research may be revoked at any time, including after the commencement of the research, by: the HRMRB, the Crew Surgeon, the Flight Director, or the ISS Commander, as appropriate, if the research would endanger the ISS Crew Member or otherwise threaten the mission success. A decision to revoke consent by the human subject or approval by the other entities listed above will be final.

While those focused on human spaceflight in the spirit of benefiting all of humankind had protocols, procedures, and infrastructure considerations in place to protect personal communications and sensitive medical information, entire populations have basically become large-scale private experiments of manipulation and control, trapped within a seemingly inexplicable digital confinement, without just and proper recourse to vindicate their rights.[15] There is growing awareness of this situation, however. There is credible concern for society having turned into what is basically a patchwork of large-scale oligarchic entities funded and self-protected by vast digital surveillance architecture while touting commitment and vindication for human rights and representative government. A glimpse of where we have been, where we seem to be, and where we could be headed makes it easier to understand the lesson that actual contempt and disregard for human rights lead to barbarous crimes and moral outrages. Fortunately, many challenges to the legitimacy of the basis of such wealth and power are more openly declared and can actually be vindicated by proper legal and infrastructure reforms.[16] Likely, an entirely new computer and network architecture will be required.

Therefore, these Sections in the IGA Code of Conduct are helpful in thinking about the composition of any Space Bill of Rights because they depict considerations and safeguards to address issues on the relation of rights, medical ethics, and the use of particular technologies, such as networking and computing technologies.

A Space Bill of Rights must also be informed by medical ethics. With respect to medical ethics and human rights, foundational ethical doctrines and teachings within the tradition of the discipline of the study and practice of medicine are crucial guides. For ethical guidance for human research subjects, excellent examples are the *Belmont Report* of 1978 and the *Clinical Center Patients' Bill of Rights* from the National Institute of Health ("NIH").

The Belmont Report presents an analytical framework to help guide the resolution of ethical problems stemming from research involving human participants (the term participant is used herein, except for when the term subject is quoted by a source). Among other things, it was informed by the Nuremberg Code, which was drafted as a set of standards to judge physicians, psychologists, and scientists who had conducted biomedical experiments on concentration camp prisoners. In general terms, the Report specifies three basic ethical principles that should guide scientific research on human subjects: Respect for Persons, Beneficence, and Justice. Respect for persons means that individuals should be treated as autonomous agents, and persons with diminished autonomy are entitled to protection. The principle of Beneficence forms two general rules: do no harm, and maximize possible benefits and minimize possible harms. The principle of Justice requires fairness in the distribution of goods, on the principle that equals should be treated equally.

There are several formulations of just ways to distribute burdens and benefits: equal shares, according to individual need, according to individual effort, according to societal contribution, and according to merit. Showing that conceptions of justice are relevant for research involving human participants, the Report provides an example: "the selection of research subjects needs to be scrutinized in order to determine whether some classes (e.g., welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem beings studied."

Another important principle articulated by the Belmont report is that women must be included in research protocols because as a matter of justice, they have the same responsibility as men of direct participation in medical investigation. This was a reversal of the common conviction that women were (1) too unstable because of their endocrine fluctuations to be reliable clinical subjects and (2) with the exception of reproductive physiology, data obtained from males could be assumed to be identical to that of females without direct testing.

The Report then finds that a proper application of these ethical principles requires informed consent, an assessment of risks and benefits, and selection of subjects. Informed consent requires sufficient information, meaningful comprehension, and voluntariness or free choice. An assessment of the risks and benefits of research includes an analysis of whether the proposed research is properly designed and helps determine probabilities and magnitudes of possible harms and anticipated benefits. Such assessment can assist someone in deciding whether or not to participate in the research. The selection of participants should be based on fair procedures and outcomes.

In creating a Space Bill of Rights, attention also must clearly be given to the development and uses of certain technologies. Particularly relevant today, for example, are advances and new uses of the internet and artificial intelligence,

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15. See, for example, Konsinski, et. al., *Privacy in the age of Psychological Targeting* (2020); Knoop & Riedel, *Facebook—Can Ethics Scale in the Digital Age?*, Harvard Business School, 9−319−030 (July 29, 2021); Cherkoff, *Big Nanny is Watching You*, https://chiefexecutive.net/big-nanny-watching-data-security/4/ (Last Accessed April 2024); Zuboff, *The Age of Surveillance Capitalism* (2023); Tau, *Means of Control* (2024).

16. See, for example, *Federal Arbitration Act*, Section 10 (a) ("Where the award was procured by corruption, fraud, or undue means"); *U.S. Constitution, Amendment IX* ("The enumeration in the Constitution of certain rights shall not be construed to deny or disparage others retained by the people.").

as well as neurotechnologies, biotechnologies, and other medically related technologies (including pharmaceuticals). Generally speaking, the world is active and attentive to the implications that developments and use of new and existing technology can have for human rights. And certain fundamental rights remain true and valid for all time independent and transcendent of any particular historical context or technological development, while other rights have been defined and enumerated specifically to address technological innovations.[17] Technology must be in the service of human rights and must be informed by them, rather than threaten them. Efforts in this respect will likewise help inform the creation of a Space Bill of Rights.

In summary, the previous discussion helps clarify the principles and underlying assumptions that inform the creation of a Space Bill of Rights. A Space Bill of Rights must start with the common sense conclusion that every human being is entitled to basic fundamental rights by virtue of the fact of being human. An examination of fundamental human rights catalogs such as the United States Bill of Rights and the Universal Declaration is a necessary further step. Also, particularly notable for a Space Bill of Rights are the declarations, treaties, and agreements governing human activities related to spaceflight, such as *The Outer Space Treaty* of 1967, the IGA of 1998 and Crew Codes of Conduct, or *The Moon Treaty* and the *Artemis Accords*. It is also clear that medical ethics and ethics guiding scientific research must help shape a Space Bill of Rights. *The Belmont Report* of 1978 and the *Clinical Center Patients' Bill of Rights* from the NIH are especially informative in this regard. In creating a Space Bill of Rights, attention must clearly be given to the development and uses of certain technologies, such as neurotechnologies and artificial intelligence. Technology must be in the service of human rights and must be informed by them, rather than threaten them.

In light of these considerations, an attempt to formulate the founding principles of a Space Bill of Rights can now proceed. This Space Bill of Rights is deliberately written from the perspective of individual humans, though it is written with the goal that government and nongovernment entities will use them as their guide. It is the hope of the authors that some of these rights might inform any future bills of rights, or moral and ethical considerations for future human spaceflight projects, scientific research, or technology innovation. We also hope that some of these findings might help us understand how human rights can be better applied on Earth.

25.3 A Space Bill of Rights

Fundamental rights: human dignity and equality

1. All human beings are created free and equal in dignity and rights.
2. Human dignity is inviolable. It must be respected and protected for every person.
3. All human beings have the right to life, liberty, and the security of person.
4. All human beings have the right to recognition everywhere as a person before the law.
5. No person shall be held in slavery or involuntary servitude; slavery and the slave trade shall be prohibited in all their forms.
6. No person shall be subjected to torture or to cruel, unusual, inhuman, or degrading treatment or punishment.
7. All human beings have the right to respect for physical and mental integrity.

17. See, for example, *Charter of Fundamental Rights of the European Union* (2010) (Article 3 – Right to the integrity of the person (application to the fields of medicine and biology); Article 8 – Protection of personal data); *Dichiarazione dei Diritti in Internet* (Declaration of Internet Rights) (2015); *European Declaration on Digital Rights and Principles for the Digital Decade* (2022); *Constitution of the Republic of Chile*, Number 1 of Article 19, Law No. 21,383, Republic of Chile (Oct. 14, 2021) ("Scientific and technological development will be at the service of people and will be carried out with respect for life and physical and mental integrity. The law will regulate the requirements, conditions and restrictions for its use by people, and must especially protect brain activity, as well as the information from it."); *Colorado Privacy Act*, House Bill 24–1058, Concerning Protecting the Privacy of Individuals' Biological Data, and, in Connection Therewith, Protecting the Privacy of Neural Data and Expanding the Scope of the "Colorado Privacy Act" Accordingly (February 2024); *Constitution of the State of Georgia* (Article 1, Section 1, Paragraph 3—"Each person has the natural and inalienable right to worship God, each according to the dictates of that person's own conscience; and no human authority should, in any case, control or interfere with such right of conscience."); *Pavesich v. New England Life Insurance Company*, 122 Ga. 190 (1905); Genser, Damianos, & Yuste, *Safeguarding Brain Data: Assessing the Privacy Practices of Consumer Neurotechnology Companies*, Neurorights Foundation (April 2024) (key findings of a study of companies providing commercially available neurotechnology to consumers including that 29 of the 30 companies (96.67%) appear to have access to the consumer's neural data and provide no meaningful limitations to this access; consumers do not have adequate information about data practices, privacy, or their rights as users; consumers do not have adequate information about data practices, privacy, or their rights as users; data collection and storage practices are ambiguous; almost all of the companies can share data with third parties; the extent to which companies can or cannot sell data is unclear; user rights, such as withdrawing consent to data processing and requesting data deletion, are not uniformly extended; and the data safety and security provisions of consumer neurotechnology companies are generally ill-equipped to safeguard neural data.).

8. All human beings have the right to the protection of personal data and information concerning them, including but not limited to neurodata or brain activity. The information technology systems and devices of every person and the freedom and confidentiality of their electronic information and communications are inviolable.
9. No person shall be subjected to arbitrary interference with their privacy, family, home, or correspondence, nor to attacks upon their honor and reputation. Everyone has the right to the protection of the law against such interference or attacks.
10. All human beings have the right to be free from surveillance by military or police authority.
11. No person shall, in time of peace be required to quarter a soldier or law enforcement officer or any other individual in any dwelling, without the consent of the owner, nor in time of war, but in a manner to be prescribed by law.
12. All human beings have the right to self-defense against bodily harm by any means necessary

Liberty

13. All human beings have the right to freedom of thought, conscience, and religion; this right includes freedom to change their religion or belief, and freedom, either alone or with others and in public or private, to manifest their religion or belief in teaching, practice, worship, and observance.
14. Everyone has the right to freedom of opinion and expression; this right includes freedom to hold opinions without interference, to exercise conscientious objection, and to seek, receive, and impart information and ideas through any media and regardless of frontiers.
15. Everyone has the right to protection from slander or libel.
16. Freedom to form associations with others of an educational, political, economic, religious, social, cultural, or any other character for peaceful purposes is the right of every person.
17. The arts, scientific research, and academic freedom shall be respected and free of constraint.
18. All human beings have the right to freedom of movement and to establish residence.
19. No human being shall be considered to have waived or relinquished any of their rights without their informed, voluntary, and intelligent consent to do so.

Discrimination

20. All human beings are entitled to all the rights and freedoms without distinction of any kind, such as race, color, sex, gender, language, religion, political or other opinion, origin, property, national or jurisdictional identity, birth, or other status.
21. All human beings are equal before the law and are entitled without any discrimination to equal protection of the law.

Property

22. All human beings have the right to own property individually as well as in association with others.
23. All human beings have the right to own, use, dispose of, and bequeath their lawfully acquired property.
24. No person shall be arbitrarily deprived of their property.
25. Intellectual property shall be protected for every person.
26. All human beings have the right to freedom to conduct a business in accordance with law and fundamental rights.
27. All human beings have the right to ownership, control, recovery, retention, dissemination, and sale of any and all data stemming from their person, including but not limited to neurodata or brain activity, images, or likeness.

Civic participation and legitimate governance

28. For any government authority to be just and lawful, it must derive its powers from the consent of the governed.
29. All human beings have the right to take part in the government of his state, country, or jurisdiction, directly or through freely chosen representatives.
30. All human beings have the right to equal access to public service in their state, country, or jurisdiction.
31. The will of the people shall be the basis of the authority of government.
32. All human beings have a right of access to documents of the institutions, bodies, offices, and agencies of their government or jurisdiction, whatever their medium.
33. All human beings have the right to petition government or jurisdictional authority.
34. All human beings are entitled to a global and interstellar order in which the rights and freedoms of everyone can be fully realized.
35. It is a right and a duty of all human beings to throw off any authority, including government or corporate authority, whose object evinces a design to reduce them under absolute despotism.

Justice

36. No one shall be deprived of their rights without due process of law.
37. No one shall be subjected to arbitrary arrest, detention, or exile.

38. All human beings have the right to have their rights and criminal and civil liabilities determined by a fair public trial by an impartial jury of their peers, within the physical presence of a competent tribunal of proper jurisdiction before which such person has had opportunity for a full hearing and all guarantees necessary for an adequate and proper defense.
39. All human beings are entitled to adjudication of their rights or liabilities by human juries and tribunals and in proper jurisdictions; there shall be no adjudication of rights or liabilities by automated technology or other processes, including automated computing or artificial intelligence processes.
40. Everyone charged with a penal offense has the right to be presumed innocent; to be informed of the nature and cause of the accusation or indictment; to be confronted with the witnesses against them; to have a compulsory process for obtaining witnesses in their favor; and to have the assistance of counsel for their defense.
41. No one shall be held guilty of any penal offense on account of any act or omission which did not constitute a penal offense, under local, international, or interstellar law, at the time when it was committed. Nor shall a heavier penalty be imposed than the one that was applicable at the time the penal offense was committed.
42. No one shall be compelled in any adjudication of civil or criminal liabilities to be a witness against oneself.
43. Everyone has the right to seek and to enjoy in other jurisdictions asylum from persecution.
44. Everyone has the right to a national or jurisdictional identity.
45. No one shall be arbitrarily deprived of their national or jurisdictional identity, nor denied the right to change such national or jurisdictional identity.

Work and labor conditions

46. Everyone has the right to work.
47. Everyone has the right to reasonable conditions of work, including reasonable wages, hours, and other conditions of work that respect the health, safety, and dignity of the worker, including limitations and restrictions to worker monitoring and surveillance.
48. Everyone has the right to adequate food, oxygen, and habitation.
49. All human beings, as members of society and societies, have the right to social security and are entitled to realization, through personal, local, and national effort, and international and interstellar cooperation, and in accordance with the organization and resources of each jurisdiction, of the economic, social, and cultural rights indispensable for their dignity and the free development of their personality, and the maintenance of comprehensive arrangements for the promotion of health, for the prevention of sickness and accident, and for the provision of medical care and of compensation for loss of livelihood.

Medicine and human health

50. Everyone has the right of access to preventive health care and the right to benefit from medical treatment under the conditions established by national or jurisdictional laws and practices.
51. No human being shall be forced to undergo any medical treatment against their will.
52. No human being shall be forced to administer any medical treatment against their will.
53. Everyone has the right to live in a sustainable and balanced environment that provides conditions for quality health; each person has a duty to preserve and enhance the environment.
54. Personal information, including all medical information, private family conference, or other private information, whether from verbal, written, or electronic sources, shall not be used or disclosed by others for any purpose, without the consent of the affected person.
55. All personal medical information, whether derived from medical monitoring, investigations, or medical contingency events, shall be treated as private medical information and shall be transmitted in a private and secure fashion in accordance with procedures. Medical data that must be handled in this fashion includes, for example, biomedical telemetry, private medical communications, and medical investigation data.
56. No research on human participants shall be conducted without the informed, voluntary, and intelligent consent of the individual.
57. No research on human participants shall be conducted which could, with reasonable foresight, be expected to jeopardize the life, health, physical or mental integrity, or safety of the participant.
58. Human participants volunteering for human research protocols may at their own discretion, and without providing a rationale, withdraw their consent for participation at any time, without prejudice, and without incurring disciplinary action or sanction.
59. No human right shall be waived or relinquished merely by virtue of having a device, biologic, or any other form of medical technology applied to their person.

Rights specific to the context of spaceflight

60. No one shall be compelled to participate in any spaceflight without the informed, voluntary, and intelligent consent of the individual.

61. All human beings have the right to be sufficiently, comprehensively, and personally informed about how their fundamental rights will be or might be affected by participating in any spaceflight.

62. All human beings have the right before participating in any spaceflight to receive sufficient and comprehensive information about the scope, purpose, and risks of the spaceflight. Such information may include but is not limited to information regarding crew codes of conduct; spaceflight chain of command; spaceflight protocols or procedures; crew authority and responsibilities; training or preparation expectations for spaceflight participants; specifications and capabilities of spaceflight equipment and technical functions; medical risks; geopolitical and interstellar-political risks (treaties and agreements); physical risks; information regarding the unknowns and uncertainties of the spaceflight; and so forth.

63. The entity or entities responsible for providing the means for any spaceflight shall review each of the rights herein articulated with any prospective or committed spaceflight participant to ensure such participation is based on informed, voluntary, and intelligent consent.

Unenumerated rights retained

64. The enumeration herein of certain rights shall not be construed to deny or disparage other rights retained or not yet articulated or defined.

Limitations

65. No human right shall be surrendered as the result of a declaration of emergency without due process and without access to later redress, should the surrender of such rights lead to harm.

66. Nothing in this Bill of Rights may be interpreted as implying for any authority, group, or individual person any right to engage in any activity or to perform any act aimed at the destruction of any of the rights and freedoms set forth herein.

Johnston, Jones et al.—Lessons Learned Part II (Ch. 20, 2025)

Johnston, Smith L., Jeffrey A. Jones, and Smith T. Johnston. *Lessons Learned Part II: In-Flight Medical Equipment, Capabilities, and Countermeasures; and New Medical Paradigms for Future Flights.* In *Building a Space-Faring Civilization,* Elsevier, 2025, pp. 279–301.

Overview: Evaluates medical capabilities and countermeasures for in-flight healthcare and explores advanced care paradigms for deep space.

Chapter 20

Lessons learned part II: in-flight medical equipment, capabilities, and countermeasures; and new medical paradigms for the future flights to low earth orbit and beyond!

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20.1 Introduction: in-flight medical equipment and capabilities

In *Principles of Clinical Medicine for Space Flight*, many foundational principles are presented and are of such importance in helping provide understanding and insight that it is worth restating some passages at length [1].

For any crewed spacecraft, there are substantial challenges in designing the environmental systems, seat and cockpit configurations, medical systems, restraint systems, and extraction capabilities for the transport of crew members within a required anthropometry range. In addition to providing for the proper functioning of these systems within the mass, volume, thermal, pressure, and anthropometric constraints of nominal launch and reentry operations, human factors design considerations must account for the ability of crew members to function during off-nominal or contingency scenarios where risk trades between safety/redundancy and function become paramount [1].

The first consideration in design is the mission profile. Factors ranging from habitable volume, consumable stores, and distance/expected duration of free-flight operations will either be influenced by, or themselves drive, decisions on radiation shielding and whether pressure suits are required, among many others. For example, an Orion or Apollo mission profile in which the vehicle operates as the sole source of life support for the crew differs from the Soyuz and current or proposed Commercial Crew Vehicle profiles that are designed to dock with the International Space Station (ISS) for extended durations [1].

Long-duration missions aboard the ISS require planning for a variety of potential adverse medical events. These events include possible medical evacuations, both urgent and anticipated. Despite carefully selected, screened, and medically supported spaceflight crews, illness, accidents, life support system malfunctions, and logistic support problems may still occur. Though every effort is made to limit these risks, a medical event that exceeds onboard medical support capabilities should be anticipated with contingency plans developed to the greatest degree possible. Risk analysis is the first step in any medical contingency planning and is essential to justify the allocation of time and resources. Successful planning could determine the difference between serious in-flight morbidity or mortality and a favorable outcome with expedient and appropriate evacuation to Earth [1].

To help address these challenges and apply lessons learned from medical screening, selection, and incidents and events from Part I, Part II (Chapter 11) presents lessons learned from in-flight medical equipment and capabilities and in-flight countermeasures and then examines new medical paradigms particularly promising and useful for future human spaceflight missions.

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20.1.1 Current medical kits to address in-flight medical issues

Important for any probable risk assessment and for mission and spacecraft design is designing and accounting for medical equipment available for crew members during the mission. Medical kit contents and supply quantities are very important in helping treat ill crew members and reducing the risk of a health event developing into a mission-compromising situation. For example, the JSC Integrated Medical Model was developed to assist mission planners and medical teams in devising medical kit contents and supply quantities. A helpful review of medical kit contents and equipment can be organized by examples from short, intermediate, and long-duration missions (Fig. 20.1).

20.1.1.1 Short duration

Fig. 20.2 shows basic medical contents to manage minor skin trauma, GI upset, and low-grade pain. This is an example of a very small medical kit in a Soyuz survival bag.

In the first four missions (Mercury), the available drugs that could be delivered with autoinjectors (see Fig. 20.3) consisted of an antimotion sickness medication, a stimulant, and a vasoconstrictor for the treatment of shock. Later, the number of medications was reduced just to an antimotion sickness drug and an analgesic, both available in the suit and in the medical kit.

20.1.1.2 Intermediate duration

Fig. 20.4 shows the in-flight medical kits and medical equipment from the Apollo and Shuttle programs. The Shuttles Orbiter Medical System (SOMS) includes a medications and bandage kit (MBK) and an emergency medical kit (EMK), which can be used for both minor illnesses and injuries, and for stabilizing more severe conditions.

FIGURE 20.1 Joe Kerwin, MD examines crewmate Pete Conrad on Skylab 2 with components of the In-flight Medical Support System (INMSS).

FIGURE 20.2 **Soyuz medical kit.** Example of short-duration medical kit. This represents the evolution of medical kits over the development of the Russian space program.

FIGURE 20.3 Mercury autoinjectors. The drug delivery device was used during the first four missions.

FIGURE 20.4 Medical kits and equipment. These kit photos were part of crew medical officer crew training documents: (A) Apollo medical kit; (B) Apollo medical kit with contents displayed; (C) Shuttle medical kit; (D and E) medical accessory packs.

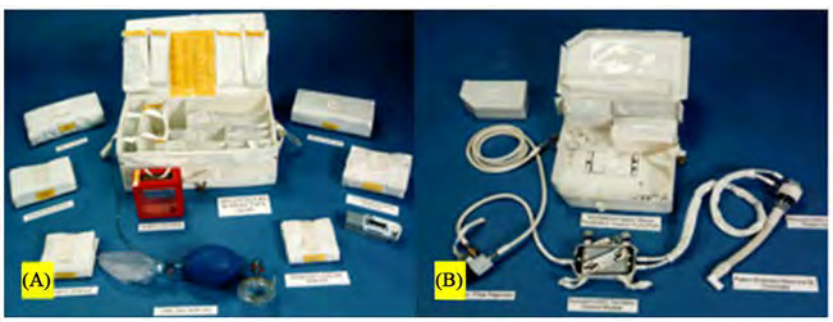

FIGURE 20.5 International Space Station support kits. (A) Photo of the ISS advanced life support pack (ALSP); (B) respiratory support pack (RSP).

20.1.1.3 Long duration

The ISS medical support kits (shown in Fig. 20.5) contain a range of medical supplies and equipment to help diagnose and treat medical conditions that may arise during space missions. The kits are designed to be lightweight and compact, yet still provide a comprehensive range of medical tools and supplies and include a variety of items such as medications, bandages, splints, and other medical equipment, such as a defibrillator, portable ultrasound, and an oto/ophthalmoscope (Fig. 20.6).

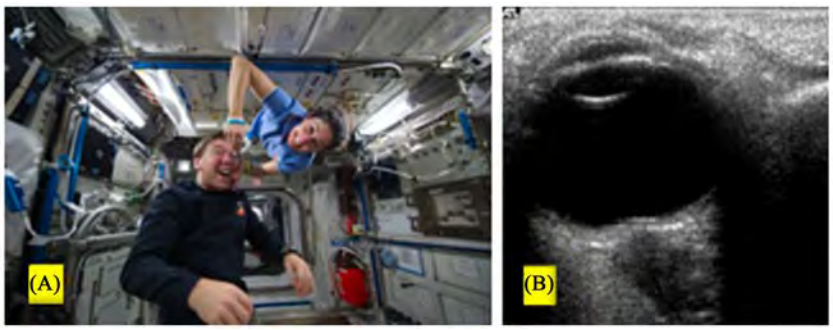

FIGURE 20.6 Mike Barratt undergoes ocular U/S assessment on ISS.

20.1.2 Medical system architecture and infrastructure

A significant amount of medical system architecture and infrastructure is required to maintain medical capabilities for any spaceflight mission and is indispensable for mission and spacecraft design considerations. This is usually associated with such things as electronic medical records, inventory monitoring/maintenance, medical stowage allocation (including pressurized or refrigerated volume), and so forth. Mass, volume, consumables, crew time, and effort are all relevant critical factors for mission planning. Table 20.1 provides an overview of expected life support capabilities for missions of various durations, as well as corresponding expected crew medical training and skill level. For additional context, Table 20.2 provides information on the required medical capabilities for the minimum standard of care on the ISS. Some further important considerations include the following:

- Electronic medical record with a searchable database and accessible online portal
- Medical equipment selected for ease of use
- Configuring environment for medical care (including privacy considerations)
- Obtaining and recording history of medical encounter
- Performing and recording the physical exam
- Assessing, recording, monitoring, and trending vital signs (including pulse oximetry and co-oximetry)
- Conducting ancillary tests as needed, including imaging, laboratory analyses, and electrocardiography
- Performing procedures
- Providing physical restraints for the patient, caregiver, and medical equipment
- Recording treatment plan
- Administering and managing medications (both oral and parenteral) and intravenous (IV) fluids
- Consumables
- Capability to treat decompression sickness
- Monitoring and altering work/rest schedule and balance
- Treating neurobehavioral disorders with medical devices and/or evidence-based asynchronous behavioral health treatment protocols available on electronic devices
- Private two-way audio and video communication with ground medical support, family, and crew-support system
- Private transmission of medical data (including imaging) to ground medical support
- Means of providing autonomous medical care and advanced life support
- Medical evacuation
- Palliative care

20.1.3 In-flight testing for health

In-flight medical testing of crew health is an important way to provide real-time health information to the crew and ground support teams. Medical equipment and instruments for testing and health data collection are in many respects crucial complements to the equipment and instruments used for treatment and prevention. For example, the medical kits currently onboard the ISS contain instruments (e.g., Point of Care testing "I-Stat Analyzer with cartridges") to test the crewmember's blood for the following: hemoglobin and hematocrit, an electrolyte panel (sodium, potassium, chloride, carbon dioxide), glucose, urea nitrogen, creatinine, and anion gap. Similarly, urinalysis involves a dipstick for pH, specific gravity, blood, ketones, bilirubin, leukocyte esterase, and nitrites.

TABLE 20.1 Projected medical capabilities [1].

Advanced life support capabilities	CMO training
Time to DMCF—24 h	
Low Earth orbit (ISS)	**Skill level**
– Specialized restraint systems – Intravenous/intramuscular medications – Oral and endotracheal airway/cricothyrotomy – Automated pneumatic ventilator – Blood pressure monitoring and pulse oximetry – BLS protocols	Emergency medical technician
– Informatics/telemedicine remote medical direction – Defibrillator with external cardiac pacing – ECG monitoring – IV fluids – Modified ACLS and ATLS protocols	Paramedic
– Hyperbaric treatment – Ultrasonography (abdominal, cardiac, thoracic)	Physician
Lunar missions/stable Lagrangian platforms	
Time to DMCF—days to weeks	
– Low Earth orbit/ISS capabilities with augmented supplies – Radiation Shelter	Physician and paramedic or paramedic and paramedic with advanced training
Mars and other expeditionary missions	
Time to DMCF 9–30 months	
– Lunar capabilities with augmented supplies – Stand-alone capabilities: • Limited surgical intervention • Banked or synthetic blood • Banked bone marrow • Informatics/expert systems/clinical decision-support tools • Radiographic/MRI diagnostic imaging • Recuperation and convalescence capabilities	Physician (with surgical training) and paramedic *or* physician and paramedic with advanced training

Note: This chart provides the anticipated medical capabilities, training, and skill levels for missions of varying complexity. DMCF, definitive medical care facility [on Earth]; CMO, crew medical officer; ISS, International Space Station; BLS, basic life support; ACLS, advanced cardiovascular life support; ATLS, advanced trauma life support; ECG, electrocardiogram; IV, intravenous.

20.1.4 In-flight testing for fitness

Common parameters to measure during spaceflight to assess the crewmember's fitness-level while they are exercising on in-flight exercise equipment include the following: electrocardiogram (ECG), blood pressure, pulse (heart rate), heart-rate variability (HRV), and VO_2-max. On the ISS, the Russians typically have performed this testing while the crewmember is running on the treadmill, turning a hand crank ergometer, or undergoing lower body negative pressure (LBNP); whereas, in the US program, the crewmember has these parameters measured while performing a cycle ergometry profile. Fig. 20.7 highlights some of this equipment.

20.2 Additional in-flight medical concerns and countermeasures

Besides what has been discussed earlier, the following list is a summary of particularly relevant medical concerns and countermeasures worth considering in the context of the in-flight stage of a human spaceflight mission:

- Optimization and periodic monitoring of nutrition intake—To include caloric density and macro/micronutrients (including antioxidants, flavonoids, lycopene, omega-3 fatty acids, lutein, sterols, and prebiotics), to support multiple physiological systems such as immune function, bone and muscle health, the effectiveness of radiation damage

TABLE 20.2 Required medical capabilities to meet the needed level of care [1].

Level of care	Minimum capabilities required
Basic	Basic CPR and first aid, including splinting and bandaging
Intermediate	Limited or modified ACLS and ATLS capabilities:
	• Crew medical restraint system (CMRS) • Intravenous and intramuscular therapeutics • Electrocardiography monitoring • Defibrillation • Airway management including medical suction • Mechanical ventilation
Augmented	Limited or modified hyperbaric treatment (using the combined pressure of cabin and EVA suit)
Advanced	24 h medical evacuation time to definitive medical care facility with hyperbaric chamber capability

Note: The table outlines the minimum capabilities required to meet the basic, intermediate, augmented, and advanced levels of care on the ISS. CPR, cardiopulmonary resuscitation; ACLS, advanced cardiovascular life support; ATLS, advanced trauma life support; EVA, extravehicular activity.

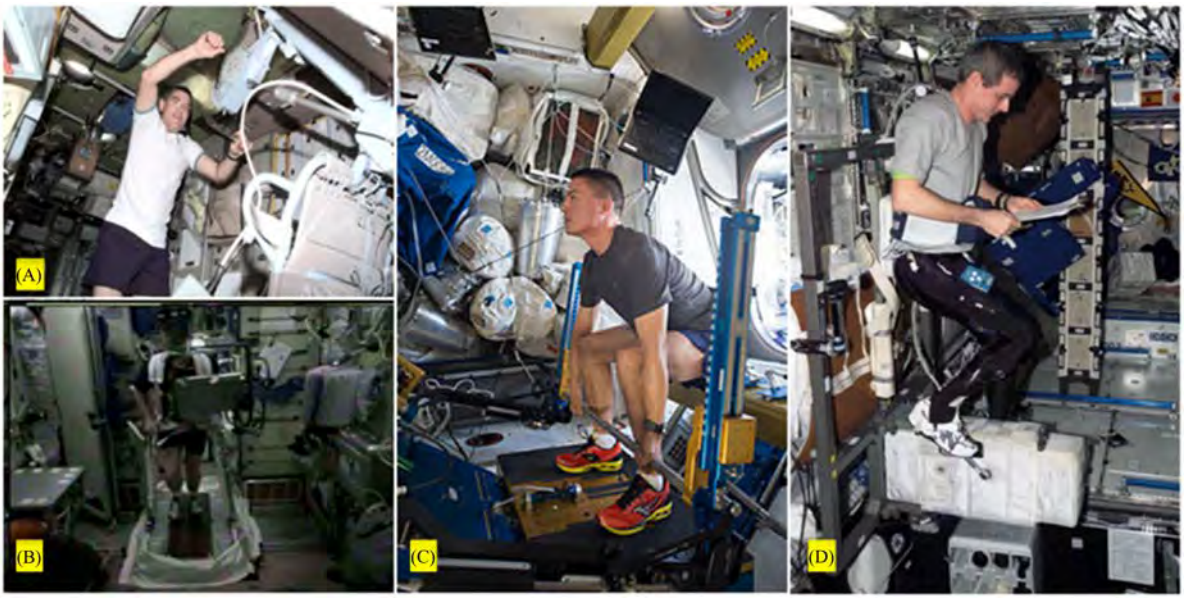

FIGURE 20.7 Equipment used to conduct in-flight fitness testing. (A) Jim Voss during MO-6 hand crank ergometry testing during ISS Expedition 2; (B) Bill Shepherd ISS CDR Exp 1 running on Treadmill with Vibration and Isolation System (TVIS); (C) Astronaut Kjell Lindgren exercises using the Advanced Resistive Exercise Device (ARED) on ISS in the Node; (D) ISS Expedition 12 CDR Bill McArthur reads a procedure while exercising on the Cycle Ergometer with Vibration Isolation System (CEVIS).

repair mechanisms, cognitive and mental well-being, and microbiome. Optimization of nutrition intake also includes such aspects as food palatability and food variety, to support psychological well-being and crew morale.

- Vitamin D supplementation (mandatory)—for bone and immune function.
- Vitamin and mineral supplements (voluntary).
- Maintenance and periodic monitoring of aerobic and strength physical fitness—for maintenance of muscle strength and aerobic capacity (essential for the performance of safety-critical physical tasks such as emergency vehicle egress), bone strength, immune system performance, sensorimotor function, stress relief, and reduction in renal stone formation.
- Maintenance and periodic monitoring of flexibility, agility, and balance—for sensorimotor function (essential for performance of safety-critical physical tasks such as emergency vehicle egress).
- Maintenance and monitoring of work/rest schedules and optimal sleep/circadian rhythm.

- Maintenance and monitoring of environmental parameters at optimal levels for crew health and performance, as outlined in other requirements.
- Prevention of decompression sickness by utilizing the appropriate prebreathe protocols.
- Hearing protection, including periodic monitoring.
- Optimization and periodic monitoring of psychosocial countermeasures for team cohesion, privacy, social isolation, and sensory deprivation.
- Preventive measures for orthostatic intolerance and neurovestibular challenges during *g*-transitions.
- Space Flight Associated Neuro-Ocular Syndrome (SANS) periodic monitoring and prevention with to-be-determined countermeasures (to be validated by research in the coming years).
- Periodic monitoring of vascular motility and patency of venous drainage pathways in the neck as well as the deep veins in the lower extremities.
- Optimization and periodic monitoring of immune function via implementation of a suite of multicomponent countermeasures.
- For missions that land on planetary bodies—training, capabilities, and resources for rehabilitation on the planetary surface, analogous to the functions of the post-Earth-landing recovery team, rehabilitation team, and flight surgeon team to enable surface mission success.
- Maintenance and monitoring of any future risks as they emerge.
- In-mission countermeasures to sustain hematological/immunological parameters within the normal range as determined by direct or indirect means.

More specifically, considerable attention has been given to the following in-flight medical concerns and countermeasures.

20.2.1 Spaceflight radiation exposure

It is important to minimize crew health risks due to radiation exposure by decreasing crew radiation exposure from all sources using the ALARA principle (as low as reasonably achievable). The ALARA principle is a fundamental guiding principle for radiation protection that requires programs to minimize radiation exposures below the limits/standards within the design constraints of the mission. Some examples of such considerations in the language of requirements include the following:

- All crew radiation exposures shall be minimized using the ALARA principle.
- An individual astronaut's total career effective radiation dose due to space flight radiation exposure shall be less than 600 mSv. This limit is universal for all ages and sexes but should be individualized in the future.
- Provisions shall be made to implement appropriate psychological support programs for the crew, key ground personnel, and crew families throughout the mission, utilizing the latest in holographic, haptic, and VR technologies.

Furthermore, lens limits are intended to prevent early (<5 years) severe cataracts, for example, from a solar particle event. An additional cataract risk exists at lower doses from cosmic rays for subclinical cataracts, which may progress to severe types after long latency (>5 years) and are not preventable by existing mitigation measures; however, they are deemed an acceptable risk to the program. New and more sensitive methods for the detection of radiation bioeffects may include such things as epigenomic markers; perhaps noninvasive (e.g., Raman spectroscopy of the retina—look at antioxidant levels).

20.2.2 Coronary artery disease risk mitigation strategies

The ASTRO-CHARM tool is the first integrated atherosclerotic cardiovascular disease risk calculator to incorporate risk factor and CAC data [2,3]. Utilizing AI to address cardiovascular risk and prevention will be important in the future and is a great example of the application of new paradigms to human spaceflight (see, e.g., Cleerly Heart Scans [4]). Also, cardiac MRI or PET scans may be utilized.

20.2.3 Crew-friendly countermeasures against musculoskeletal injuries

Clinical surveillance of mission-assigned astronauts to monitor astronaut health and performance, as well as countermeasure effectiveness, include the following:

Isokinetic skeletal muscle strength and endurance evaluations (pre- and postflight)
Functional fitness tests (pre- and postflight)

Cycle ergometer aerobic capacity VO_2-max test (pre-, in-, and postflight)
Dual-energy X-ray absorptiometry scan (pre- and postflight)

- Biomarker monitoring (pre- and postflight)
- *n*-Telopeptide monitoring (pre- and postflight)
- Vitamin D monitoring (pre-, in-, and postflight)
- On-orbit strength and conditioning monitoring (in-flight daily exercise logs)

Aviation and space medicine face many common musculoskeletal challenges that manifest in the crew of rotary-wing aircraft (RWA), high-performance jet aircraft (HPJA), and spacecraft. Furthermore, many astronauts are former pilots of RWA or HPJA. Flight crew are exposed to recurrent musculoskeletal risks relating to the extreme environments in which they operate, including high-gravitational force equivalents (*g*-forces), altered gravitational vectors, vibratory loading, and interaction with equipment. Several countermeasures have been implemented or are currently under development to reduce the magnitude and frequency of these injuries. Cervical and lumbar spine, as well as extremity injuries, are common to aviators and astronauts and occur in training and operational environments. Stress on the spinal column secondary to gravitational loading and unloading, as well as vibration, are implicated in the development of pain syndromes and intervertebral disk pathology.

While necessary for operation in extreme environments, crew-support equipment can contribute to musculoskeletal strain or trauma. Crew-focused injury prevention measures such as stretching, exercise, and conditioning programs have demonstrated the potential to prevent preflight, in-flight, and postflight injuries. Equipment countermeasures, especially those addressing helmet mass, center of gravity, and spacesuit ergonomics, are also key in injury prevention. Furthermore, behavioral and training interventions are required to ensure that crew is prepared to safely operate when faced with these exposures. The common operational exposures and risk factors between RWA, HPJA, and space vehicle pilots and astronauts lend themselves to collaborative studies to develop and improve countermeasures.

Countermeasures require time and resources, and careful consideration is warranted to ensure that the crew has access to the equipment and expertise necessary to implement them. Further investigation is required to demonstrate the long-term success of these interventions and inform flight surgeons' decision-making about individualized treatment. Lessons learned from each population must be applied to the others to mitigate adverse effects on crew health and well-being and mission readiness.

Some examples of such considerations in the language of requirements include the following:

- Countermeasures shall maintain in-mission skeletal muscle strength at or above 80% of baseline values.
- Countermeasures shall maintain the bone mass of the hip and spine at or above 95% of premission values and at or above 90% for the femoral neck.

Also noteworthy is that countermeasures, including an Advanced Resistive Exercise Device (ARED), cycle ergometer device, and treadmill, have resulted in the majority of crew members losing $<10\%$ bone mineral density in the femoral neck and $<5\%$ in total hip or spine during 6-month ISS missions. Additional countermeasures may also include pharmacological antiresorptive (bisphosphonate) therapy that has been tested in research space studies and decreased the bone loss further ($\sim 0\%$ loss) when used in combination with exercise countermeasures.

20.2.4 NASA nutritional guidelines

Inferring from available knowledge related to musculoskeletal health on Earth, NASA has developed a minimal set of nutritional guidelines and is currently testing nutritional guidelines for the health and performance of astronauts on long-duration space missions. Specific guidelines include the following:

- Maintain energy intake, body mass
- 2−3 servings fish/week (N-6:N-3 ratio <3.4)
- 6 servings fruits and vegetables/day
- 5 servings lycopene-rich foods/week
- 2 flavonoid-rich foods/day
- Maintain protein intake at 1.2−2.0 g/kg body weight
- Maintain potassium intake at >2600 mg/day in women, and >3400 mg/day in men
- Maintain calcium intake at 1000−1200 mg/day
- Sodium intake near or below 2300 mg/day
- Iron intake close to 10 mg/day or lower
- Vitamin D3 intake >800 IU/day

These guidelines are based on the National Academy of Medicine's Dietary Reference Intakes for North Americans, the position of the Academy of Nutrition and Dietetics, Dietitians of Canada, and the American College of Sports Medicine for nutrition and athletic performance, and other ground-based literature. These guidelines highlight the importance of balanced energy intake and the critical need for nutritionally stable processed food sources [2,5].

Some examples of such considerations in the language of requirements include the following:

- In-mission nutrient intake shall be no less than 90% of the calculated nutrient requirements, based on an individual's age, sex, body mass (kg), height (m), and an activity factor of 1.25.
- In-mission nutritional status shall be assessed and recommendations/countermeasures applied for any decrements below predetermined values.

20.2.5 Ultrasound technology mitigating nephrolithiasis

Space medicine depends on ultrasound imaging more than most other clinical disciplines because of the absence of other diagnostic imaging modalities, the operational nature of the setting with limited resources, and the very limited ability to safely and quickly evacuate the ill or injured crewmember. Depending on the clinical and operational circumstances, a focused diagnostic examination in space with a single binary clinical question (emergency medicine model) can evolve into a broader, comprehensive, and specific imaging application (radiology model). Therefore space medicine experts have a great interest in established and emerging ultrasound applications, monitoring the accelerating adoption of bedside ultrasound techniques in terrestrial medicine, novel devices, telemedicine solutions, and advances in ultrasound skill management and machine learning [2].

20.2.6 Dynamic lighting systems to mitigate circadian desynchrony

Over two decades of research support the efficacy of light as a countermeasure to promote alertness during spaceflight, and some findings have already been translated into Earth-based spin-offs for shift workers, patients with sleep disorders, travelers, athletes, and the military [2].

20.2.7 Fatigue risk management service

This service provides crew members with a structured implementation plan for fatigue risk management training and personalized guidance on the use of circadian shift schedules, which include advice on light exposure, light avoidance, melatonin, caffeine, and other pharmacologic hypnotic and alertness countermeasures to optimize the pre-, in-, and postflight sleep opportunities [2]. An example of such considerations includes the principle that the planned number of hours for completion of critical tasks and events, workday, and planned sleep period shall have established limits.

20.2.8 Behavioral health surveillance and countermeasures

Greater range/duration of orbital space travel will increase stressors while simultaneously requiring crew members to maintain mental stability and engage in crew-related duties essential for safety and mission success. Current ISS Behavioral Health Surveillance and Countermeasures have included the following:

- Private psychological conferences (PPCs) biweekly—private medical conferences (PMCs) weekly—spaceflight cognitive assessments (WinSCAT) monthly—unscheduled access to psychological support staff—private family conferences (PFCs) video/voice calls
- *Commercial SFPs will not have same scope/scale of mitigation

20.2.9 Countermeasures based on mission duration

The medical risks and countermeasures of a spaceflight mission in many respects depend on mission duration. Besides relevant information regarding this that has already been cited and/or discussed earlier, a helpful conception of the relationship between medical risks, countermeasures, and varying mission duration can be found in Table 20.3.

TABLE 20.3 Countermeasures for common risks based on mission duration [6].

Mission duration	Risks	Countermeasures
<3 days	Space motion sickness	Education, analog training, in-flight medication
	Sinus congestion	Medication
	Decreased GI motility	Hydration and/or medication
	Urinary retention	Auditory aids (sounds or running water), urinary catheters
5–7 days	Postflight orthostatic intolerance	Isotonic fluid loading, anti-G suit or counter pressure garment (Kentavr)
	Postflight disequilibrium	Restrict driving
	Circadian rhythm disruption	Scheduling mechanical sleep aids (light), medication
> 30 days	- Bone and muscle loss - Cardiovascular deconditioning	In-flight exercise
	Nephrolithiasis	Screening, maintain hydration, medication
	Psychiatric	Education and training, private family conferences, time off from duties
	Decreased immune function	Hygiene, clean, and cover breaks in skin

Note: This table lists countermeasures for common risks associated with missions less than 3 days, between 5 and 7 days, and greater than 30 days. It provides protocols for mitigating risks and ensuring crew safety for missions with varying mission durations.

20.2.10 Return to Earth under nominal conditions

For nominal postflight, several important issues must be considered to prepare for and effectively implement crew return and reconditioning to safely adjust to living back on Earth:

- Physiological changes occurring as a result of prolonged launch body posture.
- Space flight physiology.
- Injuries resulting from launch and landing contingencies (such as trauma, burns, hypoxia, and hypothermia).
- Hazards of exposure to space vehicle-associated toxic chemicals such as propellant, fuels, oxidizers, thermal control fluids, off-gassed products, and their unique treatments and responses.

Specifically, on landing day, or R + 0 or "return day 0," the crew is examined by their flight surgeons and undergo a variety of health assessments and often research study-related measurements to assess the effects of spaceflight on their physiology and to determine the optimal plan for their postflight rehabilitation, including any restrictions on their activities, such as driving and flying.

Upon return, the crew is subject to a rehabilitation or reconditioning period. For short-duration flights, the amount of time and planned modalities may be significantly abbreviated. The crew is typically restricted for at least a week from potentially dangerous activities, such as flying and driving, until the neurovestibular system has recovered; they are also usually restricted from heavy weight-lifting that could put the crew at risk of herniated nucleus pulposus. The crew returning from long-duration flights often require at least 90 days to fully rehabilitate all systems and even then, there may not be complete recovery. For example, with bone mineral loss in key regions such as the femoral trochanter, losses are still measurable in the crew based in DEXA, or QCT, 2–3 years after completion of the mission.

Some primary examples of postflight considerations in the language of requirements include the following:

- Crew members returning from spaceflight shall be monitored longitudinally for health and well-being parameters in a standardized manner. Data derived from standardized testing procedures, used in a pooled, nonattributable fashion, are essential to characterize the short- and (in particular) the long-term effects of space flight on human health (occupational surveillance).
- The postmission reconditioning shall be aimed at achieving a VO_2-max at or above the crewmember's premission values.
- Premission sensorimotor functioning shall be assessed and must be within normal clinical values for age and sex of the astronaut population.

- Postmission reconditioning shall be monitored and aimed at returning to baseline sensorimotor function.
- End-of-mission assessment and treatment for crewmember cognitive state shall include cognitive assessment, monitoring, and as needed, transitioning the crewmember back to premission values.
- End-of-mission assessment and treatment for the behavioral health of the crewmember shall include behavioral health and psychosocial assessment, monitoring, and as needed, transitioning the crewmember back into terrestrial work, family, and society.
- Postmission reconditioning shall be aimed at returning to baseline muscle strength.
- Postmission reconditioning shall be aimed at returning bone mineral density to premission baseline.

20.3 New medical paradigms for future flights to LEO and beyond!

The complexities and challenges of missions beyond low earth orbit (LEO) will be significant. From a medical perspective, however, many of the basic principles remain the same. Medical testing for spaceflight is geared to the three objectives of (1) detection of overt disease; (2) identifying asymptomatic disease; and (3) screening for the likelihood of development of a mission-impact disease process over a significant period of time, such as over an individual's mission and/or career.

For high-risk, Class-III type, and even some Class-II type, medical events, as articulated for ISS in Table 12, Table 13 of Chapter 10, potential medical transport and evacuation scenarios turn even more complex in considering a mission beyond LEO. Compared to a transport time of several hours from LEO, evacuation from a lunar base or a space station at one of five Earth−Moon fixed Lagrangian points would require several days at best. For a Mars mission, the one-way communication time may be up to 20 minutes duration, and there may be no evacuation capability. Clearly, injuries and illnesses that would be potentially treatable in LEO will carry more threatening implications if they occur in remote space. For many reasons including medical concerns, missions beyond LEO will require levels of spacecraft and crew autonomy and self-sufficiency beyond what is currently realized. Just as the fault-tolerant design of vehicle components and systems will be enhanced, crew members will be more highly cross-trained. The crew of a Mars or other deep space mission will likely have to anticipate how to complete their objectives despite the possible incapacitation or loss of a crewmember. Additional onboard capability to manage a disabling medical condition over the relatively long time frame of several months to years may be required, as well as means to deal with a pregnancy or a deceased crewmember. The expansion into the solar system will be in a staged fashion, with decreasing capabilities expected at increasingly remote sites. Medical evacuation from a deep space mission could one day be to a fallback position on Mars where a greater level of care is available, rather than by default back to a very distant Earth. Such staged medical evacuations have a long lineage of terrestrial precedent to draw upon, from military MEDEVACs to patient movements out of remote Antarctic field camps. Exploratory missions truly mark a change in potential risks to both the mission and individuals. Issues such as crew selection criteria, age at mission start, optimization of physical and mental conditions, informed consent of mission risks, notification of family of medical events, and mission-consequence long-term health effects are just some of the concerns attending medical operations planning for the future [1].

More immediately, the communication of health and safety risks from NASA and the aerospace medical communities to the engineering, operations, and design communities has been a perennial challenge, as experts in each field draw on different backgrounds with different conceptions of risk. These communities can find a common vocabulary in the use of (probabilistic risk assessment modeling) to communicate scenario-specific medical risk in quantifiable terms [1]. Probabilistic risk assessment has identified that interplanetary missions will have to grapple with (the following) challenges [2]:

1. Significantly reduced mass and volume for medical resources
2. Potential power and data bandwidth restrictions
3. More limited resupply capabilities driven by increasing distance from Earth
4. Increased need for autonomous medical capacity due to changes in operational paradigms expected with communication time delays
5. Increased evacuation times or no evacuation capability for ill or injured crew

Succinctly stated, "probabilistic risk assessment (PRA) provides a quantitative framework that can help prioritize medical capabilities in a process that respects mass and volume limitations to help guide systems engineering processes. The total risk that a planetary mission faces can be described as a balance between medical and nonmedical risk. In short-duration missions, the medical risk impact to total risk is generally small because of the selection of healthy individuals and limited exposure to spaceflight hazards that have a degrading effect over time. As mission duration and distance from Earth increase, the proportion of risk carried by the human system increases, and the need for

mission-appropriate medical support is likely to increase" [2]. This will continue to be an important insight for future mission design and medical care support.

New medical paradigms for state-of-the-strategies from advanced medical technology and methods, precision medicine, and the like will enhance the overall technical and mission design and procurement process, as well as mission-operational proficiency, by reducing medical risks identified (and not identified) that inform such PRA models. Some examples of such new paradigms include and can be summarized as follows:

- Whole body genomic sequencing to analyze individual genetic strengths, weaknesses, and mitigation strategies
- In-house (on the spacecraft and or on the surface stations) advanced imaging capabilities with AI-enhanced interpretations of full-body portable MRI, vascular CTA, OCT/retinal scanning imaging, ultrasound, and near-and-far infrared and laser analyses
- AI programs that have been trained to diagnose diseases from an asymptomatic patient's genetics, epigenetics, and biomarkers (e.g., proteomic evaluations for asymptomatic early disease predictions and mitigations)
- Bone density and body composition measurements (bioimaging, messaging, and epigenetics)
- Banking of stem cells for future individualized treatments (e.g., to counteract real-time solar flare exposures)
- Individualized protocols of exercise, diet, sleep, and pharma/nutraceuticals
- Use of laser, focused ultrasound, and near-and-far infrared light therapies for musculoskeletal injuries and other disease therapies
- Environmental monitoring of biofilm, atmospheric moisture (one of the many causes of adverse skin reactions, which is one of the most registered in-flight complaints in US Astronaut populations to date), along with monitoring toxic air exposures for CO_2, VOCs, and adverse particulate exposures (heavy metals and micro/nanoplastics such as polyfluoroalkyl substances (PFAS), phthalates, bisphosphonates) and their management (plasma donation or plasma therapeutic exchange—TPE)
- Individualized circadian lighting, melatonin, and ground-tested medication scheduling for proper entrainment and fatigue management performance protocols, inclusive of sleep enhancement and in cases of emergent awakening
- Ionizing radiation shelters, with enhanced warning and protections inclusive of pharmaceutical, nutritional (e.g., ketones, proteins), and genetic manipulation interventions
- Minimally invasive and noninvasive emergency medical, dental, ophthalmologic, obstetric and gynecologic, urologic, neurologic, and surgical capabilities (e.g., focused ultrasound, and laser technologies)
- Artificial gravity (short and long arm) exposures for gravitational transition training and possible emergent EVA acclimatization procedures on a space station with a long-arm centrifuge
- Hyperbaric oxygen therapies (HBOT) for decompression sickness (DCS) and vascular, musculoskeletal, and antiinflammatory/antiaging vascular endothelial wall (EGX) mitigations
- Passive osteopenia and sarcopenia mitigating garments utilizing mild compression and light therapy during sleep or sedentary operations (e.g., sleep)
- Individualized behavioral health programs with comprehensive as-needed evaluations via telemedicine utilizing 3D VR holoportation technologies for medical, family support, entertainment, and artistic expression (e.g., music), and mindfulness training [7]

More specifically, the following new paradigms of medical advances, considerations, and treatments appear quite promising for pre-, in-, and postflight/mission evaluations and therapeutic interventions.

20.3.1 Space as an accelerated aging paradigm: selecting clinical targets and countermeasures

Aging is characterized by a gradual loss of physiological integrity resulting in impaired biological function and increased vulnerability to disease and death. Human and animal data inform us that during and after extended space travel and gravitational transitions from 1G Earth to the microgravity of LEO, to the one-sixth gravity of the Moon and in the future the one-third gravity of Mars, there will be acute and chronic vestibular/motion sickness, neurological disorders, cardiovascular/fluid shift issues, increased risk for upper body blood hypercoagulation/stasis issues, SANS (space adaptation neuro-sensory problems) and increased risks of cancer, muscle atrophy (sarcopenia), and bone loss (osteopenia). Table 20.4 describes some of the deleterious effects of the space environment on the human organ systems, which amplifies the aging process compared to terrestrial standards.

The hallmarks of aging are biochemical changes that occur in all organisms that experience biological aging and lead to a progressive loss of physiological integrity, impaired function, and, eventually, death. They include the following terrestrially examples of aging but are further amplified by the closed loop and hostile environments of outer space

TABLE 20.4 Effects of spaceflight on human health [8].

Organ system	Effects
Neurology	– Space motion sickness – Urinary retention – Microgravity-induced brain changes – Space headache – Gray matter volume losses – SANS
Immunology	– Inflammatory cytokines – Elevated stress hormone levels – Reductions in monocyte, neutrophil, NK cell function – B-cell and T-cell apoptosis – Autoimmune diseases – Reactivation of latent viruses (e.g., EBV, VZV) – Radiation-induced cancer
Gastroenterology	– Space motion sickness – Space diarrhea – Alteration of gut microbiome – NAFLD – Obstruction of the gallbladder – Obstruction of the appendix
Cardiovascular	– Arterial stiffness – Accelerated atherosclerosis – Increased DNA oxidation – Myocardial fibrosis – Decreased circulatory blood volume – Reduced cardiac contractility – Orthostatic intolerance – Unload the cardiovascular system
Mental health	– Anxiety – Depression – Sleep deprivation
Dermatology	– Contact dermatitis – Psoriasis – Space dermatoses – Basal cell carcinomas – Squamous cell carcinomas
Pulmonology	– Pulmonary blood vessel structure – Extraterrestrial dust – Reductions in VC, FRC, ERV, RV – Ventilation/perfusion mismatch
Musculoskeleton	– Muscle atrophy – Osteoporosis – Changes to the elasticity of the ligaments and tendons – Disk herniation – Lower back pain – Bone and soft tissue tumor

Note: This table displays common adverse physiological effects due to the accelerated aging environment characteristic of space.

vehicles, stations, and bases (Moon, Mars, or an Asteroid) and will be denoted with examples in each category: (1) genetic instability (e.g., radiation damage), (2) epigenetic alteration (environmental toxins from air and food), (3) loss of proteostasis (inability to continue optimal individualized protein synthesis), (4) mitochondrial dysfunction (cellular level ATP production dysfunction), (5) altered intercellular communication (decreased intracellular communication integrity), (6) cellular senescence (lack of cellular apoptosis or cellular death recognition and clearance), (7) stem cell

exhaustion (lack of stem cell function and DNA/tissue regeneration), (8) deregulated nutrient sensing (impaired ability for the body to sense the need for key ingredients for key protein groups of IGF-1, mTOR, sirtuins, and AMPK), (9) telomere attrition (DNA loss of protection and methylation—degradation), (10) decline in autophagy (lack of diseased cell clearance), (11) chronic inflammation (DNA and cellular destruction), (12) gut microbiome dysbiosis (lack of gut biome balance), (13) extracellular matrix stiffening (organ infrastructure dysfunction), (14) immuno-senescence (lack of immune system function), (15) cellular exhaustion (increased cellular turnover), (16) disruption of circadian rhythms (sleep quantity and quality disruption especially with travel and or time-zone shifting), and (17) cell membrane dysfunction (cellular wall dysfunction—e.g., endothelial glycocalyx [EGX]) [8–11].

20.3.1.1 Mitochondrial dysfunction

Aging is accompanied by progressive loss of cellular function and systemic deterioration of multiple tissues, leading to impaired function and increased vulnerability to death. Of special note is mitochondrial dysfunction that underlies most chronic diseases. Mitochondria have become recognized not merely as being energy suppliers but also as having an essential role in the development of diseases associated with aging, such as neurodegenerative and cardiovascular diseases (e.g., diabetes, Alzheimer's disease, fibromyalgia, Loe Gerhings, muscular dystrophy, Autism, Epilepsy, Parkinson's disease, Huntington's disease, cardiomyopathy, and cancer). A growing body of evidence suggests that aging and age-related diseases are tightly related to an energy supply and demand imbalance, which might be alleviated by a variety of interventions, including physical activity and calorie restriction, as well as naturally occurring molecules targeting conserved longevity pathways [12].

In an excellent review article, Amorim, et al. explain that cellular metabolism interconnects the nine hallmarks of aging, and deregulation of energy metabolism by environmental variations is an essential process leading to mitochondrial dysfunction during aging. A better understanding of mitochondrial dysfunction during aging and age-related metabolic diseases is providing fundamental knowledge to develop therapies to combat late-life morbidities. All these factors are of course accelerated by inflammation caused by the harsh and toxic environments of outer space, as previously described. A growing body of evidence suggests that aging and age-related diseases are tightly related to an energy supply and demand imbalance, which might be alleviated by a variety of interventions, including physical activity and calorie restriction, as well as naturally occurring molecules targeting conserved longevity pathways [12].

Mitochondrial dysfunction and inflammation can be slowed and reversed by nutritional supplementation utilizing glutathione, *N*-acetyl cysteine, riboceine, NRM, NMN, quercetin, astaxanthin, B vitamins, magnesium, carnosine, alpha lipoic acid, CoQ10, and other micro- and macronutrients along with exercise and mindfulness practices (e.g., yoga, and cognitive behavioral therapy [CBT]). All these nutritional, exercise, and mindfulness techniques should be utilized by our astronauts.

20.3.1.2 Endothelial glycocalyx

One of the most important and largest organ systems of the human body is the vascular or blood flow system made up of arteries, veins, and capillaries. The importance of the endothelial glycocalyx (EGX—the lining of all our blood vessels) for human health needs to be emphasized again. A deteriorated EGX can be healed, improved, and maintained with individualized diet, exercise, and toxic substance avoidance. Therefore a reversal of vascular disease, which is one of the most important contributors to aging, should be the cornerstone of any antiaging protocol (see Figs. 20.8 and 20.9).

The EGX is an area of exploding research because it is the microthin, dynamic, permeability regulator that is essential to systemic health. A healthy EGX supports all systems in the body by transporting nutrients to our organs and waste/toxins from our organ systems. Fundamental to a healthy EGX is the use of sulfated polysaccharides in the diet (e.g., green cruciferous vegetables such as broccoli) and supplementation. It is the integrity of the EGX that allows LDL cholesterol to migrate behind the endothelial single-cell wall and form an atherosclerotic plaque as illustrated in

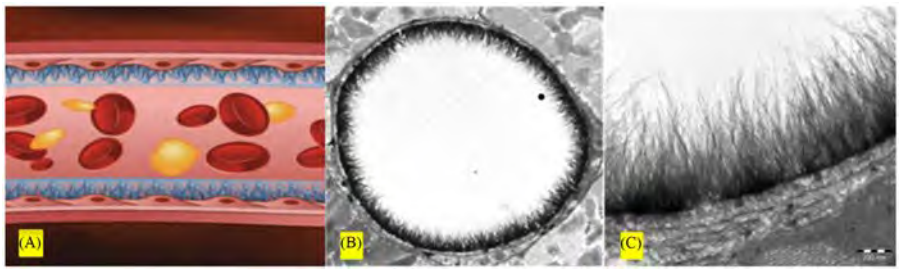

FIGURE 20.8 Healthy blood vessel [8]. (A) Diagram of a healthy blood vessel; (B, C) normal EGX function with no atheromatous plaque (EGX—endothelial glycocalyx).

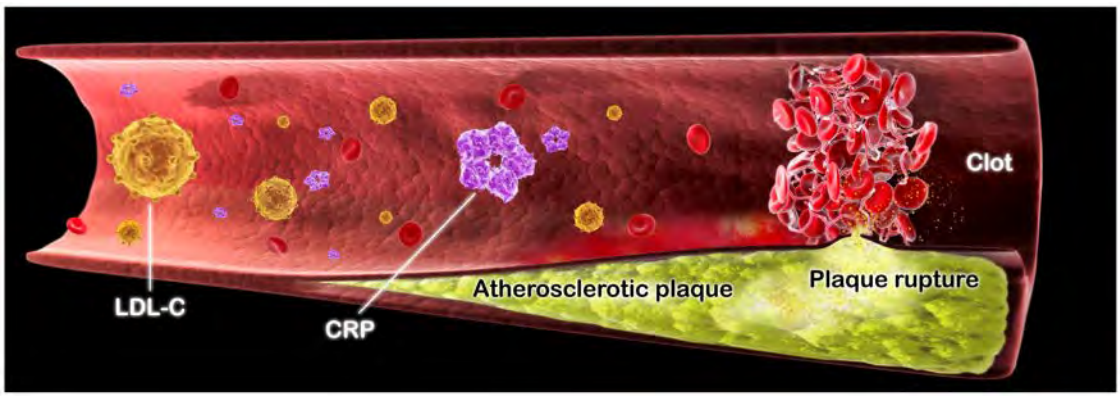

FIGURE 20.9 **Unhealthy blood vessel** [8]. Abnormal disease progression in the human artery.

the above figure. Immunologically unstable plaques can then rupture through the endothelial lining of the EGX and cause arterial clots with blockage and cause myocardial infarction or a stroke with cardiac and brain tissue loss.

Some of the interventions mentioned earlier will be discussed in more detail below, and a detailed presentation on all these factors can be reviewed online (particularly the presentation by Dr. Helen Meisier, MD, PhD) from the Baker Institute at Rice University International Space Medicine Summit—Astronaut Longevity [8].

20.3.2 Individualized DNA profiles for all space travelers

Paramount to understanding a space travelers optimal health will be by obtaining an individual's bioanalysis and informed monitoring of a crewmember's genetics, epigenetics, proteomics and metabolic parameters.

Whole body genomic sequencing should be performed on all exploration-class astronauts to analyze individual genetic strengths and weaknesses, such as clotting factors, atherosclerosis or organ system body blood flow markers (e.g., cholesterol, lipo-(a), APOE4, food immune sensitivities, cancer risks) (e.g., melanoma, breast, and colon, and others) with periodic targeted liquid biopsies, along with periodic epigenetic testing and biologic marker analyses of organ and cellular function maintenance such as individual vitamin, mineral, hormone and immunologic levels (e.g., Vit D, and B-12, magnesium, testosterone, estradiol, Thyroid, CA-127, PSA, CRP-HS, and many others) during selection, pre-, in-, and postflight analyses along with an individual's aging DNA biomarkers (e.g., DNA methylation, telomere length and telomerase activity, senescent cell analysis, and others). All these parameters would help to individualize the astronauts' countermeasures, whether it be with nutritional supplementations and/or pharmaceutical interventions, along with individualized exercise and sleep programs, and countermeasures against toxic environmental exposures to in-flight contaminants (CO_2, VOCs, and microplastics) and external radiation exposures.

Also, understanding how genes repair themselves in LEO is essential to understanding how to mitigate going beyond LEO, where the radiation damage is at a minimum, tenfold that of terrestrial radiation exposure depending on the amount of time and distance from our Sun. The first CRISPR experiment to take place in space showed that DNA can repair itself in microgravity. As part of the "Genes In Space-6" experiment, astronauts on board the ISS created breaks in the DNA of a common yeast and then analyzed how it repaired itself [13]. During the investigation, the yeast's DNA was cut across both strands to create significant damage. In a recent paper published in the journal PLOS, one of the researchers explained how the DNA was restored to its original order [14,15].

Therefore maintaining and augmenting this kind of laboratory capability presently on the ISS should be prioritized on the Moon and/or the surface of Mars.

20.3.3 Individualized genomic nutritional analysis

Dr. DuPont states that the intestinal microbiome comprises more differentiated cells than the human body and controls our body functions through neural connections, orchestration of the immune system, and production of hormones [16]. A proper individualized diet and avoidance of unnecessary antibiotics are essential for microbiome health. A healthy diet of fiber and resistant starches prebiotics plus greater than 90% microbiota strict anaerobes equals healthy short-chain fatty acid composition within the gut, which has positive effects on immune cells, neurotransmission metabolism, and mood. Therefore a diet high in soluble and insoluble fiber along with key nutrients and avoiding antibiotics, which

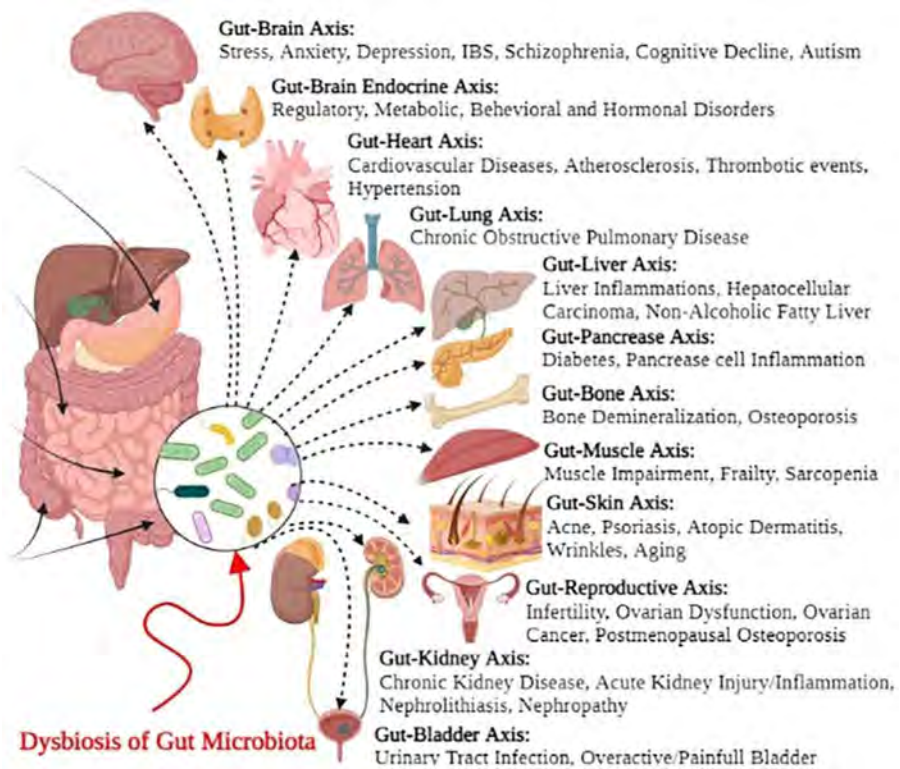

FIGURE 20.10 Dysbiosis of the gut microbiota [8]. This diagram displays the adverse effects that an unhealthy or diseased gut microbiome can have on various organ functions.

are known to damage the microbiome such as Clindamycin, will preserve the microbiome assuring healthy gut flora throughout a mission [16]. This may require periodic assay of the fecal microbiome looking for the proportion of healthy bacteria (e.g., firmicutes/bacteroidetes) versus unhealthy species (e.g., Proteobacteria/Enterobacteriaceae bacteria), which is now possible in orbit with present technologies. Fig. 20.10 illustrates how important the gut biome is in regulating the human biosystems and certain diseases.

NASA Nutritional Sciences Department has been at the forefront of the biome's role in health in space [5,17,18]. The next step is to individualize the nutritional support for our astronauts with genomic testing for food sensitivities (e.g., gluten and lectins), which can cause your immunologic system to burn resources and can lead to a leaky gut syndrome. It is also a comprehensive assessment of an individual's nutritional status for vitamins, minerals, amino acids, energy and fat metabolism, and antioxidant status and immune function (e.g., Micronutrient analysis performed by SpectraCell Laboratories [18]).

20.3.4 Stem cells and cellular senescence

Stem cells play a vital role in tissue repair and regeneration. With age, their numbers and functionality dramatically decrease, leading to compromised tissue maintenance and repair (at the age of 1 we have approximately 100% of our stem cells, by the age of 65 years of age we only have 5%). A stem cell is a single cell that can replica itself and also can differentiate into many other cell types, such as bone, nerves, muscle, and other organ tissue.

The accumulation of senescent cells, which are nondividing and dysfunctional cells, can lead to chronic inflammation and impair tissue function.

An individual's immunologic system and T-cells are constantly working to recognize and rid our body of damaged and or senescent cells and strengthen the body's stem cells for tissue repair and regeneration. With aging, our stem cells dramatically decrease, and our senescent cells increase. Targeting therapies (such as umbilical or placental stem donation and infusion along with an individual's banked stem cells and or cloned NK T-cells are in clinical trials) and may prove to be beneficial for antiaging and a countermeasure against the deleterious effects of radiation and toxic environments of spacecraft and Moon bases.

Animal studies have shown that if you bank (save) stem cells from an early age and then reinfuse those cells in later life you could improve muscle tissue by 40%. Some animal models are living 2−4 times their normal lifespan. Humans

have been banking their cells for use in later years in case they have a genetic predisposition for forming blood cancer and would therefore need a future bone marrow transplant after having their cancerous blood cells wiped out with chemo and radiation treatments. They could replace the bone marrow with their own banked stem cells (verses using donor cells from another person) and replenish their bone marrow to have functioning stem cells that differentiate into pluripotent cells of the body. Human studies are ongoing utilizing banked umbilical or placenta cells and reinfusing those cells with one's own banked older human stem cells. The younger stem cells upregulate the older stem cells, and the older stem cells communicate with the younger cells to help program the younger cells to attack inflammation, repair cellular and tissue damage, and also eliminate senescent cells. Human studies are ongoing and astronauts should be investigated for future stem cell and senescent cell therapies. *See generally, for this section:* International Space Medicine Summit 2023 [8], work by Harari [10], and Giampapa [19,20].

At present what can be stated now by expert opinion is the need to bank all our present active astronauts' stem cells, which could be used later on in case there is a need for a bone marrow transplant for a hematologic malignancy (which has occurred in an astronaut with a successful outcome). Also, if crew members travel outside the protective Van Allen belt (protective magnetic forcefield of the Earth) and are exposed to a solar flare with potentially lethal dosages of radiation, then the crew members could shield their banked stem cells and infuse them therapeutically to counter DNA damage that might result from such catastrophic solar radiation events. Noteworthy is that such potentially lethal solar flares occurred in August 1972 between Apollo missions 16 and 17. Banking of crew members' stem cells with proper ionizing radiation shelters/protections for future therapeutic interventions in space and on return to Earth (RMI studies) is advisable.

20.3.5 Bone density

Fortunately, the nutritional and exercise teams at NASA and the ISS partners have developed countermeasures that are very effective at counteracting bone loss from spaceflight. Individualized nutrition and exercise programs further guided by an individual's genetics could have exponentially significant influences for countermeasures for bone loss and aging in zero gravity and therefore terrestrially.

Another promising new passive countermeasure should be considered for extended periods of time living in microgravity (>30 days, such as the ISS). Specifically, investigating the utility of a passive osteopenia and sarcopenia mitigating garment that uses mild longitudinal as well as circumferential compressions, much like a hospital antideep vein thrombosis garment, and/or one that uses a combination of a circumferential garment plus a near-and-far infrared light therapy modality during sleep or sedentary operations. This may prove to be a promising countermeasure against bone or muscle loss experienced during spaceflight.

The lessons learned from the ISS program concerning accelerated bone loss and aging is that the stronger an astronaut is when he or she goes into Space, and the more they work out in Space, and on return, the stronger they are later in life. Astronauts, even if they have lost significant bone matter and/or muscle upon return to Earth, are still able to regain most, if not all of their bone and muscle loss. This is promising data for antiaging countermeasures [21–26].

20.3.6 Advanced imaging

Advanced imaging technologies are and will continue to revolutionize how medical care evolves for Space- and Earth-based medicine, which includes the following:

- Full-body MRI for skeletal and organ system evaluations with research and development of portable deployable systems
- Utilized functional brain MRI and or PET scan imaging capabilities to follow high-functioning brain physiology and early-to-late-stage neurological progression over the life of the astronaut
- Continued DEXA bone density and body composition measurements (sarcopenia and osteopenia)
- Cardiac/carotid CTA/ultrasound with AI interpretations for evolving cardiovascular plaque detection and repair and stabilization

The Translational Research Institute for Space Research (TRISH) recently sponsored the Brains in Space workshop, which focused on the above cutting-edge technologies for helping maintain brain health during spaceflight. This included brain assessment and stimulation technologies, as well as novel ways to support brain-based health and performance in space; see the example in the following section [27].

20.3.7 Ultrasound, near-and-far infrared, and laser light diagnostic and therapeutic technologies

Onboard diagnostic and therapeutic use of ultrasound (high-frequency focused ultrasound), near-and-far infrared, and laser modalities all have great promise for the hostile environments of space. Space-focused ultrasound utilizes intersecting beams of high-frequency sound concentrated accurately and precisely on tissues deep in the body. Some of the effects include the following:

- Thermal ablation, which is the precise heating and destruction of tissue
- Focal drug delivery, which is the delivery of a very high concentration of drugs precisely where they are needed
- Blood−brain barrier opening, which temporarily gives access of drugs to the brain
- Immunomodulation, which stimulates the immune response allowing the body to fight cancer
- Neuromodulation, which is reversible and either stimulates or inhibits the activity of neural tissue
- Radiation sensitization of tumors to the effects of radiation, which allows the use of lower therapeutic doses
- Stem cell delivery to affected tissues

These therapeutic effects are being studied in over 70 medical conditions worldwide, with 21 conditions approved outside the United States and 5 conditions approved by the US FDA (including uterine fibroids, benign prostatic hypertrophy, essential tremor, bone metastases, and prostate cancer). These technologies show great promise for the future terrestrially, but also for the space environments and should be pursued for the remote and harsh environments of space.

20.3.8 Environmental monitoring

Spacecraft environmental monitoring for CO_2, VOCs, and off-gassing particulates has been routine on the ISS for almost 3 decades. It is proposed that the addition of microplastics such as perfluoroalkyl and polyfluoroalkyl substances (PFAS or PFOS) be included in onboard monitoring in the future. Multiple studies have shown in animals and humans the deleterious effects of these chemicals on health and longevity. A recent article in the NEJM showed increased microplastics in atheromatous plaques of humans with increased instability and rupture contributing to strokes and heart attacks [28].

There is also a recent study on firefighters who all had high levels of PFAS chemicals in their blood (due to their exposure to fire-suppressing foam use) and were treated by simply donating their blood or plasma for 12 weeks for a year with significant reductions in their PFAS levels compared to those firefighters who were told to avoid plastic containers, cutting boards, and microwave use for plastic wrapped foods [29]. Another modality for accelerating this therapeutic approach is the possible use of therapeutic plasma exchange, which has been used all over the world for decades for autoimmune disorders. Astronauts need to have their blood levels measured for PFAS and if such results show elevated levels of PFAS, they should likely undergo either plasma donation or therapeutic plasma exchange (TPE). This type of treatment could be accomplished in LEO and beyond. *See also* [30−32].

20.3.9 Therapeutic plasma exchange

TPE can be thought of as an "oil change for the body." It replaces plasma volume and helps rid the vascular system of toxic substances (e.g., mercury, inflammatory proteins, autoimmune antibodies, and microplastics). It has been utilized in clinical medicine for decades and is now a therapeutic treatment for long-term COVID-19 and autoimmune diseases such as Guillain-Barre. It also has great promise for helping the body clear microplastics and also has antiinflammatory and antiaging properties, which could be of great benefit to our space travelers [33−36].

20.3.10 Circadian rhythm, lighting, and fatigue management

A circadian rhythm, lighting, and fatigue management service provides crew members with a structured implementation plan for fatigue risk management training and personalized guidance on the use of circadian shift schedules, which include advice on light avoidance or exposure, melatonin, caffeine, and other pharmacologic hypnotic and alertness countermeasures to optimize the pre-, in-, and postflight sleep opportunities. It has now been commercialized into a free online app http://www.timeshifter.com for airline travel [37]. A new application will be online in the next few months that can be used for shift workers; this will be an exponential use of established mitigation strategies that NASA has helped fund over the last 4 decades and have been pioneered by the Sleep team at NASA and the Brigham at Harvard School of Medicine (see studies from Lockley [38]). This will be very important for living in the Space environment in LOE with a sunrise and sunset every 45 minutes to living on the planet Mars on a 24.4-hour day [39−43].

20.3.11 Telehealth-communication

NASA JSC and Houston Emergency Medical Services (EMS) has been a pioneer in telemedicine and recently advanced telehealth technologies. On April 10, 1971, the first EMS transmission was sent from an ambulance in Houston, Texas to a hospital and almost 50 years later on October 8, 2021, the first humans were Holoported into Space. NASA Flight Surgeon Dr. Josef Schmid and Alexa Software's Dr. Fernando De La Pena Llaca were scanned live from a Kinect Lidar Camera and were beamed to the International Space Station, joining astronauts in the middle of the US Laboratory module. This live three-dimensional volumetric capture and presentation used 5 MB of bandwidth and an early Microsoft Hololens where the astronaut could place the subjects anywhere in the station to have a real human presence felt on the station. A first in history for extended reality (XR) of humans to Space, this technology demonstration showed not only a new form of Telepresence but a new form of human exploration. The initial use case was the demonstration of a simulated medical examination of cranial nerve function and an orthopedic exam of the knee. Subsequent demonstrations followed including a behavioral health exam and then a two-way holoportation, where the volumetric capture of an astronaut was brought into the mission control center so that a simulated shoulder evaluation could be performed, while the flight surgeons were also captured and beamed to the space station. Future use cases will be bidirectional and augment private family conferences, where the astronaut will be able to join Thanksgiving dinner with their family, tele-mentoring events where the designers of space technology and equipment can be brought to the space station to assist in repairs, crew choice events where VIPs are joined onto the station, and finally the general public who will make their first journey holographically to Space [44,45].

20.3.12 Telehealth-remote treatment, for example, surgery, robotics

Following the COVID-19 pandemic, telemedicine has become normalized and widely used in facilitating virtual doctor–patient visits. However, the origins of telemedicine can be traced back to the space program's necessity to remotely monitor the space crew's health from Earth. This led to the development of various health communication strategies to ensure the health and well-being of astronauts as they manned missions far from home. These innovations have not only improved our space medicine capabilities, but they have also revolutionized terrestrial healthcare by greatly expanding access to medical care across the globe (Fig. 20.11).

In this context, it is useful to consider advanced minimally invasive surgical, dental, and ophthalmologic capabilities, for the present and future. The medical support suite to be utilized on the Mars planetary surface, after systems are tested and proven for lunar colony utilization, will likely include AI-assisted smart analytics, imaging, and several minimally invasive tools to manage everything from a urinary calculus to an inflamed appendix or gall bladder, as prophylactic removal of noncritical organs will not likely be a reasonable approach to risk reduction, since these procedures carry their own risks and potential sequelae (Fig. 20.12).

20.3.13 Hyperbaric oxygen therapy

Advanced hyperbaric oxygen therapy is a therapeutic modality that could be employed on a large space station or a Moon/Mars base. Its immediate need would be for the treatment of decompression sickness due to a loss of pressure during a spacewalk or extravehicular activity (EVA) or in a failed pressurized module.

A series of independent clinical studies have shown that hyperbaric therapies and more specifically the Aviv-hyperbaric clinic protocols can improve the symptoms of a variety of health conditions and ailments, including cognitive decline, long-COVID, poststroke, traumatic brain injury, post-concussion syndrome, Lyme disease, posttraumatic

FIGURE 20.11 Laparoscopic surgery on 0-g aircraft. (A) NASA Flight Surgeon Jeff Jones performs a laparoscopic surgical simulation in the 0-g phase of parabolic flight; (B) laparoscopic surgery in-flight project manager Dr. Azhar Rafiq supervises the results while "weightless."

FIGURE 20.12 Some concepts of advanced medical systems for planetary surface exploration. (A) NASA Flight Surgeon Ricard Scheuring attends an injured lunar surface EVA crewmate while at the Haughton Crater-Mars Project site; (B) notional concept of advanced in-suit EVA biomedical information being relayed via telemetry; (C) notional concept of robotic, or remote teleoperated, evaluation of a crewmember in a planetary surface habitat or large rover medical station.

stress disorder, carbon monoxide poisoning, and fibromyalgia. It has also been shown to increase telomere length and decrease immunosenescent cells (cells that have lost their ability to function in the body) and could therefore have anti-inflammatory and antiaging effects. This should be investigated as a mitigating therapy for the previously mentioned insults from radiation and toxic environments of outer space [46,47].

20.3.14 AI diagnostic programs

AI diagnostic programs are revolutionizing medicine as we know it. The Fountain Life Clinics are leading the charge by training the AI programs to not only diagnose disease from symptoms and abnormal laboratory findings but also from asymptomatic patient presentations of genetic and epigenetic biomarkers utilizing all of the techniques mentioned earlier [48]. AI is likely to play a major role in devising CMO assistance tools for exploration-class spaceflight.

20.4 Conclusion

A medical response program was established to support human space flight for the very first crewed launch and has slowly and progressively evolved along with the mission and vehicle complexities into a robust system of diagnostics, therapeutics, and countermeasures. As the mission duration increased, so did the likelihood of an in-flight medical event, thus the flight surgeons needed to evaluate the risk probability of various medical diagnoses, based on both support of other extreme events, as well as actual human spaceflight, to prepare an appropriate medical support system.

As explained in this chapter, the medical support consists of (1) preflight measures such as selection and retention standards, crew health stabilization, medical flight certification, and preventative regimens; (2) in-flight countermeasures to the effects of microgravity, environmental assessment tools and crew personal protection equipment, and equipment-rich, onboard medical kits for diagnosis and treatment of medical conditions or injuries; and (3) postflight measures including extensive physical, imaging and laboratory evaluation to identify any detrimental effects of spaceflight, prophylactic restrictions on activities, until the crewmember has returned to baseline functioning, and a variable rehabilitation program depending on the duration of the mission.

The number and variety of medical events in professional astronauts mirror those of professional age-matched controls (as compared to the Longitudinal Study of Astronaut Health control population), as might be expected; and a large number of crew members suffer from medical symptoms while they are in flight. Spaceflight continues to be a dangerous profession and entire crews have been lost during either the launch or return phase of flight. The risk of an in-flight medical event is proportional to the duration and complexity of the mission, and significant in-flight events have occurred, including the need to de-orbit the crew members on three occasions in the Russian space program before the ISS era. Fortunately, since the development of the multilateral space medical boards and panels, no crew member's stay on the ISS has been shortened or de-orbited due to medical reasons, which speaks highly for both the preventive measures employed and the ability to diagnose and treat conditions effectively in orbit.

For future space missions, the duration and complexity will again increase dramatically. The need for mission and medical response autonomy will gradually increase as an envisioned lunar surface outpost is established and Mars surface operations are realized. These missions will require the medical support system to further evolve by miniaturization, modernization, and sophistication. We will need to screen for medical risk conditions much more effectively and possess technology that will allow early diagnosis (before even organ system laboratory abnormalities) and intervention before allowing any medical issue to produce a mission impact. This technologically robust program for exploration-class spaceflight will aspire to become like Bones' "Tri-corder," the multifunctional diagnostic and treatment marvel that Dr. McCoy, from Star Trek fame, used to manage all medical conditions that confronted the starship Enterprise crew.

The outcomes of the necessary insights and innovations could greatly improve the viability of future human spaceflights, especially long-duration missions, by helping minimize the inherent medical risk of crew members having a mission-compromising medical incident that is otherwise identifiable and/or preventable and by providing more effective treatment of any medical incidents sustained by crew members during a mission. The ambition is also to develop a roadmap for translation of space medicine findings and countermeasures with the greatest probability for future space applications, into effective future terrestrial applications. One prediction for the future is that some of us could break the barrier of the current 120-year-old age-limited human life span. The race is on for fusion power, the cure for cancer, and the significant slowing of the aging process, with technology that can preserve chromosomal telomeres, for example. Our endeavor is to make the good and best of "science fiction, into science fact." The development of the future spaceflight medical support program will be both a challenge, and an exciting opportunity, for all flight surgeons, biomedical engineers, and space vehicle engineers and designers for many years to come.

Acknowledgment

Aly Alrabaa Officer.

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Overview: Reviews medical screening practices and patterns in in-flight medical events across human spaceflight missions.

Chapter 19

Lessons learned—Part I: Medical screening, standards, and in-flight medical incidents, events, or risks

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19.1 Overview

These two chapters (Chapters 19 and 20) will consider missions being flown during suborbital flight and orbital missions in low Earth orbit (LEO) for astronauts and commercial spaceflight participants ("SFPs," also known as space tourists, noncareer, nongovernmental, or civilian space travelers).Additionally, these chapters will reference exploration class missions beyond the Earth's geomagnetosphere to include destinations such as Lagrange points, near-Earth asteroids, and the Lunar and Martian surface. This assumes nonpolar orbital flight missions between ± 55-degree inclination and exploration class missions that involve both sortie and long stay missions on the lunar surface as stated in the Artemis mission architecture. Mars missions are also addressed, includingboth opposition and conjunction orbital trajectories ,which also include options for short and long term stay. These priorities listed below increase in complexity to execute, as the distance from Earth and duration in space increases (Fig. 19.1).

The priorities emphasized in developing the human spaceflight medical standards and the medical operations program include the following: (1) Risk Mitigation; (2) Safety of Crew and Passengers—Professional Astronaut Standards assume normal physiology in an abnormal environment, while Standards assume abnormal physiology (i.e., comorbidities) in an abnormal environment; (3) Protection of Operations and Equipment—which includes conditions that may: interfere with nominal vehicle operations, result in the need to declare an in-flight emergency, including station evacuation, or compromise the health and safety of the passenger or other aerospace vehicle occupants, and/or the safety of the flight.

Part I (Chapter 19) reviews lessons from medical screening and standards throughout pre-, in-, and postflight phases of a mission, and then examines past and probable spaceflight medical incidents, events, or risks. Part II (Chapter 20) presents lessons learned from in-flight medical equipment and capabilities, in-flight countermeasures, and then examines new medical paradigms particularly promising and useful for future human spaceflight missions. It is important to develop an understanding of the maturation of the medical support program for spaceflight, as the mission profile advanced from crew members staying only a few hours to now many months in space. We describe the current framework for crew medical certification and real-time operational support, along with numerous vehicle and physiological anomalies that have arisen and challenged crew surgeons and biomedical engineers alike. Following this, the discussion will shift to recommendations for new medical diagnostic and therapeutic tools for more complex, longer-duration missions. By examining both past experiences and future innovations, this chapter aims to offer guidance in developing medical protocols and practices for the ever-evolving landscape of space exploration.

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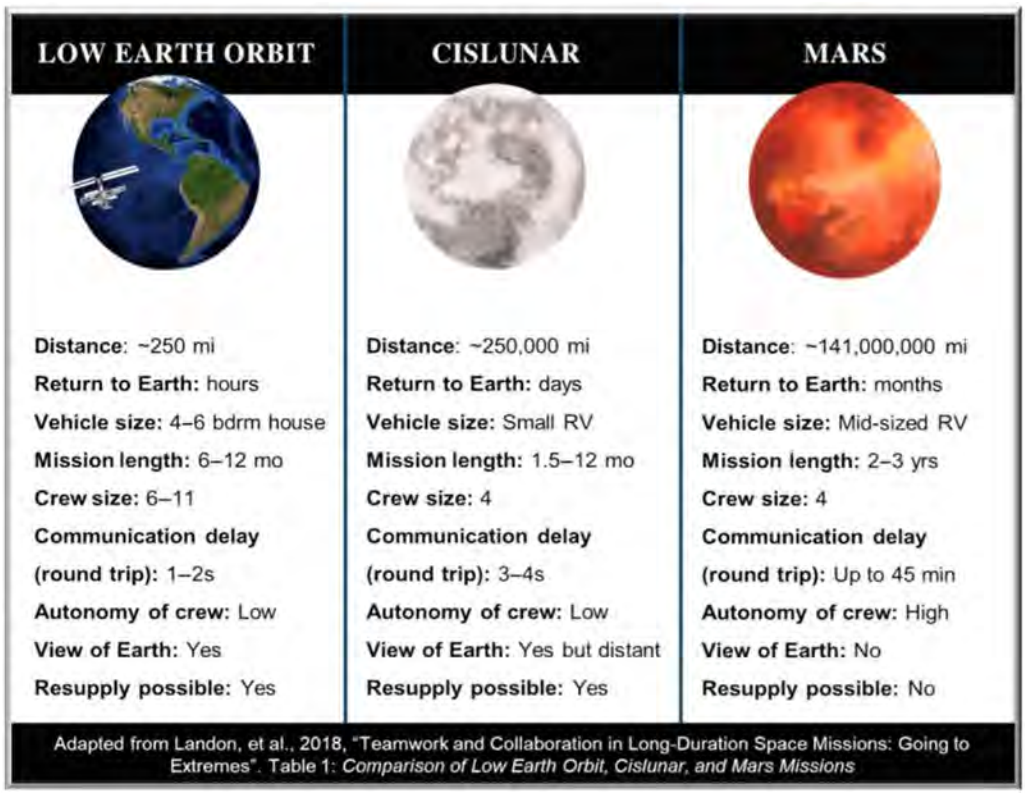

FIGURE 19.1 Comparison of low Earth orbit, cislunar, and Mars missions [5]: The figure highlights key differences and outlines mission parameters based on the ultimate destination goal.

19.2 Introduction

The present state of space medicine for detecting, mitigating, treating, and reversing adverse health conditions is in its infancy. While space medicine depends on both conventional and innovative applications of terrestrial medicine, space medicine itself is significantly advanced compared to many areas of terrestrial medicine as most know it.

A major responsibility of the space medicine community has been, and continues to be, to apply the lessons learned and principles of state-of-the-art medical screening, countermeasures, and interventions to terrestrial medicine. The International Space Station (ISS), for example, has involved unprecedented technological complexity, international cooperation (shown in Fig. 19.2), and coordination. The medical component of the ISS program has evolved into an effective operational system through synergistic input from all partners, including the Canadian Space Agency (CSA), the European Space Agency (ESA), the Federal Space Agency of Russia (FSA), the Japan Aerospace Exploration Agency (JAXA), and the US National Aeronautics and Space Administration (NASA) [1].

Much of the knowledge gained in the practice of space medicine and the development of countermeasures to help astronauts live for short and long durations in the unique habitat of the ISS is applicable to humans on Earth [3]. Living and working in the closed-loop environment of a spacecraft such as the ISS produces an accelerated state of aging. The closed-loop ecosystem of ISS can expose the crew to many unique health challenges, such as approximately 10 times the terrestrial amounts of radiation, significant CO_2/volatile organic compounds (VOC) quantities, bone loss, behavioral health issues, and circadian desynchrony due to sunrise and sunset every 45 minutes. The knowledge and experience gained from living and working in such environments will continue to expand the limits of our medical capabilities. Direct and indirect efforts have been made to translate this gained knowledge and experience to future terrestrial applications. A few examples of evidenced-based countermeasures that have effectively mitigated risk to astronaut health and are ready for translation as solutions to analogous biological health problems on Earth are as follows [3]:

- clinical assessment tools to mitigate coronary artery disease (e.g., AstroCHARM [4])
- exercise prescriptions to mitigate fractures and effects of osteoporosis

FIGURE 19.2 Twentieth Anniversary ISS Logo: This figure indicates the international partners on the logo of the International Space Station. Includes Italy, Germany, France, Denmark, Belgium, Russia, Japan, Canada, the United States, the United Kingdom, Switzerland, Sweden, Spain, Norway, and Netherlands [2].

- use of gradient compression garments (GCGs) to mitigate episodes of orthostatic intolerance
- nutritional guidelines and evidence-based dietary recommendations to maintain fitness and optimal physiology
- renal stone detection through ultrasound
- dynamic lighting systems to mitigate altered sleep patterns and circadian desynchrony
- fatigue risk management
- probabilistic risk assessment within a framework of systems engineering for optimal resource allocation for austere operations

The foreseeable future of space medicine will increasingly be based on emerging new paradigms of medical technology and treatment. By utilizing the latest medical technologies and interventional processes, we will hopefully be able to exponentially improve humanity's terrestrial health, performance, and longevity, as well as the capabilities of conducting human spaceflight missions. Most medical treatments designed for the "average patient" as a one-size-fits-all-approach, may be successful for most, but hazardous for others. Precision medicine, also referred to as personalized, integrated, functional, lifestyle, predictive, and/or biosystems medicine, is the future for tailoring disease prevention, detection, treatment, and reversal. It considers differences in an individual's genetics, environment, and lifestyle. The goal of precision medicine is to target the right treatments to the right patients at the right times.

As missions move into different exploration classifications and extend farther away from Earth,there are three driving concerns: First, medical incidents (including traumatic injuries) are expected to occur with higher incidence with progressively longer missions, and the longer time to definitive care back on Earth may mean that an ill or injured crew member's condition will be more serious if or when evacuation to Earth occurs. Second, future space-vehicle design requirements, such as power, volume, and mass, will be much more significantly constrained, which affects the availability of in-flight medical resources, especially in comparison to what is currently available on the ISS. Third, the development of medical abilities of the crew members themselves, in being able to address medical issues in-flight, will require a high level and fidelity of crew training. Just-in-time and real-time medical assistance and decision support will also be necessary. The crew members will need a suite of low mass, power, and volume diagnostic and therapeutic tools at their disposal; which will allow an autonomous, reflexive, yet holistic response to any medical contingency, even with limited resources.

19.2.1 Lessons learned from medical screening and standards

Like other fields of preventive and occupational medicine, aerospace medicine emphasizes optimizing the workplace performance of essentially healthy individuals. The astronaut population is highly selected, healthy, and receives extensive preventive medical care before launch. Unlike terrestrial medical practice, the potential hazards of the space environment pose unique challenges involving the safety, survival, and successful return to Earth of individual astronauts and even entire crews.

There are numerous environmental sources of crew exposure, either due to the nature of space itself, or the characteristics of the space vehicle. The potential exposures due to being in space include the following:

- barometric pressure changes
- microgravity
- thermal factors—vary from higher to lower extremes depending on solar exposure and distance from the sun
- radiation—three primary sources trapped in geomagnetosphere flux lines around Earth, solar source-wind and solar particle events, and galactic cosmic radiation
- isolation—distance from Earth

Environmental factors associated with the space vehicle and therefore varying in magnitude dependent on the vehicle design and performance characteristics include the following:

- vibration
- acceleration/deceleration (g-loading)
- confined spaces
- perturbed atmospheres
- water source contamination
- combustion events
- noise
- closed life-support system: waste production and management challenges

From exposures to being in space and the environmental factors associated with the space vehicle, there are also several well-known unique physiologic effects of spaceflight. For example, the *effects associated with microgravity* include space adaption syndrome (space motion sickness), fluid shifts, visual acuity changes, neurovestibular effects, Spaceflight Associated Neuro-ocular Syndrome (SANS), deconditioning, cardiovascular effects, muscle atrophy, bone loss, and the development of renal stones. There are also *atmospheric perturbation effects* (hypercapnia, hypoxia, hyperoxia); *radiation-induced effects* (increased markers of oxidative stress, increased chromosomal aberrations as measured on biodosimetry); *immune system effects* (vary from significant hypersensitivity, especially in the form of skin rashes to relative or even complete T-cell anergy to standard antigen exposures); *behavioral and social changes* (psychological/psychiatric changes and impacts measured via several pre/post- or in-flight testing instruments for example, Cognition Test Battery [6] (formerly WinSCAT)); and *cognitive functioning changes* (many crew members have complained of "space brain fog" or "space stupids" due to an increased need for checklists and to write things down, especially items such as steps in a procedure; or via objective measures, e.g., vigilance testing, or reaction time measures).

Long-term spaceflight poses additional inherent risks [7]. For example, spaceflight is associated with significant psychological stressors due to factors such as living in confined spaces, circadian rhythm disruption and fatigue, pressure to perform (work, time), lack of privacy, isolation with lack of real-time communications, decreased social or family support, risk of injury or death, interpersonal relations, and exposure to cultural differences. Underlying behavioral or psychiatric problems can negatively impact a passenger's ability to perform critical functions including nominal and emergency procedures and effective communication [8].

Accordingly, prudence dictates careful deliberation of possible medical events well in advance of their occurrence, including consideration of preflight preparation, in-flight management, return capabilities, potential positive or adverse outcomes, and mission impact. Over several decades, NASA has adopted risk management guidelines aimed at minimizing individual risk while maintaining overall mission effectiveness. While every sort of in-flight medical contingency cannot be predicted, generalized onboard protocols for anticipated medical scenarios can provide a framework for crew and ground personnel decisions [7].

19.2.2 Preflight medical evaluation and selection

Medical selection procedures are designed to identify individuals who are at low risk for a medical event throughout their careers as professional astronauts. Medical testing for space flight is geared to three objectives:

1. detecting individuals with overt disease
2. identifying individuals with asymptomatic disease
3. screening for individuals with increased risk for developing a mission-impact disease process over the course of their careers

This third objective is more controversial since risk factors for developing disease (typically related to biochemical, genetic, or lifestyle factors) are for the most part derived from population studies, from which extrapolation to individual risk is imprecise [9].

Medical screening is carried out against a framework of defined medical standards, developed by the agency or agencies responsible for medical certification. Medical standards should reflect the occupational requirements for the role-specific duties of the crew member. Medical standards for aerospace operations for various organizations can be seen in the table below (Table 19.1).

Three medical evaluation documents (MEDs) have been promulgated for ISS: MED Volume A includes the Medical Standards for ISS Crew members; MED Volume B comprises pre-, in-, and postflight testing requirements for mission-assigned crew members; MED Volume C includes the medical testing and standards for s, which include non-career or nonprofessional astronauts such as tourists or visiting scientists [9]. In addition, various entities have also proposed standards for SFPs:

1. Federal Aviation Administration (FAA) "Guidance for Medical Screening of Commercial Aerospace Passengers"
   - Suborbital and orbital travel
   - Orbital flights of any duration
   - Assumes ≤ 8000 ft barometric pressure and $\leq +4$Gz, -2Gz), ± 4Gx and ± 1Gy; no pressurized or anti-G suits
   - SFPs able to emergency egress (unassisted)
   - List of potentially disqualifying conditions; medical history, exam, and testing guidelines

TABLE 19.1 United States Air Force (USAF).

United States Air Force (USAF)	
Exam Requirements	Air Force Instruction 48−123, Ch 5
Standards	Medical Standards Directory
Waiver Guidance	Aeromedical Waiver Guide
Waiver Authority	Aeromedical Consult Service (USAFSAM)
United States Navy (USN)	
Exam Requirements	Manual of the Medical Department US Navy (MANMED)
Standards	Aeromedical Reference and Waiver Guide
Waiver Guidance	Aeromedical Reference and Waiver Guide
Waiver Authority	Naval Aerospace Medical Institute
United States Army	
Exam Requirements	Army Regulation 40−501, Ch 4
Standards	Army Regulation 40−501, Ch 4
Waiver Guidance	Aeromedical Policy Letters
Waiver Authority	US Army Aeromedical Activity (USAAMA)
NASA	
Exam Requirements	NASA Crewmember Medical Standards—Medical Evaluation Document Vol A (vehicle specific)
Standards	NASA Crewmember Medical Standards (Selection and Periodic Certification)
Waiver Guidance	
Waiver Authority	NASA AeroMedical Board (AMB)
	Appendix F—Space Flight Participants (SFPs)

2. International Academy of Astronautics (IAA) "Medical Safety and Liability Issues for Short-Duration Commercial Orbital Space Flights"
   - Orbital travel
   - Up to 4 weeks of spaceflight
   - Focus on specific hazards for commercial SFPs with only assumption being SFP able to emergency egress (unassisted)
   - Medical history, exam, and testing guidelines
3. FAA/UTMB Health Center of Excellence Commercial Space Transportation "Flight Crew Medical Standards and Spaceflight Participant Medical Acceptance Guidelines for Commercial Space Flight"
   - Suborbital and orbital
   - Time based on SFP mitigation strategy
   - Assumes $\leq$8000 ft barometric pressure and $\leq +6$Gx, $+1$Gy, $+4$Gz (nominal reentry) with up to $+8$Gx (ballistic reentry)
   - SFPs able to emergency egress (unassisted)
   - Medical history, exam, and testing standards; countermeasures based on DRMs

19.2.3 Medical authority groups and standards

Given the complexity of human spaceflight and the number of entities involved, a comprehensive medical operations management structure is required, involving several layers of medical review and oversight for human spaceflight medical support, for ISS crew and visitors. The Multilateral Medical Policy Board (MMPB), Multilateral Medical Operations Panel (MMOP), and the Multilateral Space Medicine Board (MSMB) are the original medical authority groups that play a crucial role in the development, regulation, and implementation of health standards and policies for space participants. These medical organizations, along with many others, collaborate to support human spaceflight to the ISS (Fig. 19.3):

- Multilateral Medical Operations Panel (MMOP): The MMOP comprises one member from each agency. The primary roles of this agency include the coordination of ISS crew medical system support and the development of standards and certification criteria. Provide recommendations to MSMB for approval.
- Multilateral Space Medicine Board (MSMB): The MSMB comprises one member from each agency. The primary roles of this agency include medically certifying ISS crew for spaceflight and qualifying ISS flight surgeons. Presents decisions to MMPB and Multilateral Crew Operations Panel (MCOP).
- Multilateral Medical Policy Board (MMPB): The MMPB serves as the apex of the medical authority. The primary roles of this agency include medical policy formulation and coordination and oversight of crew health issues. Serves as waiver authority and is supported by MSMB and MMOP, which serve as primary working-level groups.
- Multilateral Crew Operations Panel (MCOP): Forum for top-level resolution of ISS crew matters which affect all partners, including RSA (Russian Space Agency), ESA (European Space Agency), CSA, NASDA (Now JAXA—Japanese Aerospace Exploration Agency).

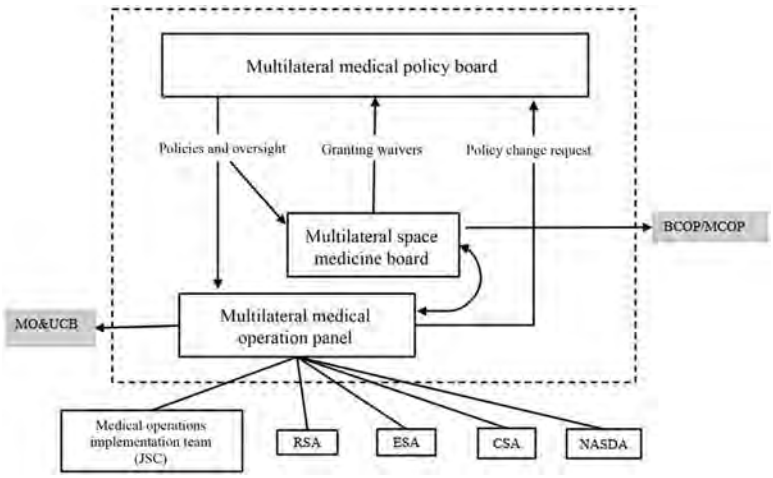

FIGURE 19.3 ISS medical operations management structure [10]: This flow chart represents the coordination of the various medical agencies that play a role in space crew health and safety.

- NASA Aerospace Medicine Board (AMB): Clinical/implementation body for crew medical standards, certification, and waivers.

19.2.4 Premission standards and astronaut selection

For initial selection as professional astronauts, medical standards are generally not waiverable and strictly applied. A noteworthy change to the most recent published NASA standards (OCHMO-STD-100.1A Section 1.2) reads "Any standard invalidated by new medical information may be appended by the AMB with Chief Health and Medical Officer (CHMO) approval" [11,12]. NASA has recently released their latest standards to the public and they can now be accessed online [11,12]. An example of standards in the form of crew health requirements can be shown in the following:

- Premission, in-mission, and postmission crew behavioral health and crew member cognitive state shall be within clinically accepted values as judged by behavioral health evaluation.
- Prelaunch hematological/immunological function shall be within normative ranges established for the healthy general population.
- Premission nutritional status shall be assessed and any deficiencies mitigated before launch.
- Premission muscle strength and function shall be per the values in Table 19.2.
- Crew members' premission bone mineral density (BMD) T-scores for total hip and lumbar spine (L1-L4), as measured by mass dual-energy X-ray absorptiometry (DXA) shall be consistent with age, sex, gender, and ethnic-matched population.
- Premission sensorimotor functioning shall be assessed and be within normal clinical values for age and sex of the astronaut population.

Some standards are considered on a "case-by-case" basis or are designated as requiring special consideration for some findings. However, trained astronauts may develop medical conditions or findings on periodic medical examinations which do not meet the specified standards. Given the extensive and costly process of training astronauts, if a trained astronaut develops a medical condition that does not meet the defined medical standard, a careful risk assessment process is used to assess whether or not they can continue with training and space flight.

Special consideration for waiver of a particular standard requires an evidence-based, risk-based assessment. The risk assessment is based on the probability of an operational-impact medical event occurring as a result of the particular condition and the consequences to the individual should an event occur during space duties [9]. Such a risk assessment involves a detailed, evidence-based review of data derived from the clinical and aeromedical literature, as well as appropriate specialist consultations detailing the potential risks associated with the condition. Based on the review of the literature and specialist opinions, an estimate of the probability of a medical event occurring as a result of the condition is derived. The use of a probabilistic risk assessment (PRA) analysis tool, detailed in Chapter 15 of this book titled "Preparing for the Unpredictable: Facilitating Multi-System Resilience in Human Spaceflight," can further refine the likelihood of an event by providing confidence intervals on the estimated probability. Risk assessment also includes a thorough consideration of the potential consequences of related medical events on crew safety,mission completion, and the potential incremental health risk to the individual due to exposure to the space/weightless environment. This evaluation includes the duration of the mission and the available mission-based medical resources [9].

Medical and psychological screening and preflight preventative strategies ensure the health of the crew member during the preflight, in-flight, and postflight phases of a mission or set of missions. Examples of medical screening conditions can be seen in Table 19.3, Table 19.4, and Table 19.5.

TABLE 19.2 Premission muscle strength requirements.

	Minimum	Microgravity EVAs	Celestial surface EVAs	Unaided egress
Deadlift	1.0 × body weight	1.3 × body weight	1.6 × body weight	1.3 × body weight
Bench press	0.7 × body weight	0.8 × body weight	1.0 × body weight	0.7 × body weight

Note: This table defines muscle strength for two exercises with various degrees of capability required based on the demand of the in-flight scenario.

TABLE 19.3 Medical screening for ISS [9].

Medical Screening for ISS Selection	
Clinical	• Detailed medical questionnaire including past health, detailed family history, occupational, and radiation exposure • Detailed physical examination by an aviation medicine specialist • Specialist consultations including ophthalmologist/optometrist, otolaryngologist, dentist, psychiatrist, gastroenterologist, and gynecologist (for females)
Laboratory	• Hematology—complete blood count, thrombophilia evaluation • Biochemistry—renal, liver function, endocrine/thyroid, cardiovascular risk factors including HS-CRP, PSA (males), HCG (females), iron indices • Infectious disease screen—syphilis; HIV; hepatitis A, B, and C; varicella AB titer; *H. pylori* infection; tuberculosis; methicillin-resistant *S. aureus* (MRSA) infection • Urinalysis—routine and micro. 24-h urine collection for specific gravity, electrolytes (Na, Cl, K), creatinine clearance, calcium, magnesium, oxalate, citrate, uric acid, sulfate, urine volume
Cardiopulmonary	• Resting ECG and maximum effort treadmill exercise stress test • Echocardiography • 24-h ambulatory ECG • Pulmonary function tests • Coronary artery calcium score
Imaging	• MRI of brain, with Mr angiogram • Carotid ultrasound • Thyroid ultrasound • Abdominal ultrasound • Chest X-ray • DEXA bone mineral density • Mammogram or breast MRI • Colonoscopy

Note: This table outlines the clinical, laboratory, cardiopulmonary, and imaging assessments used to determine eligibility for selection to be medically certified to fly to the International Space Station (ISS).

19.2.5 Postselection: periodic assessment and prevention

Periodic medical screening after initial screening and selection has several objectives: first, to ensure that the crew member continues to meet the required medical standards; second, to detect disease processes at an early stage to best ensure a positive health and career outcome; third, to identify and modify unfavorable trends in risk factors; and fourth, to identify unfavorable changes which have occurred as a result of exposure to the spaceflight environment [9]. Examples of medical screening after screening for selection can be seen in Table 19.6. Preflight preventive strategies have also included the following:

- optimization of nutrition,
- vitamin D supplementation,
- triennial imaging of bone mineral density,
- maintenance of optimal aerobic and strength physical fitness,
- maintenance of flexibility, agility, and balance,
- annual physicals,
- preventive dental care,
- vaccinations (influenza, tetanus toxoid, varicella zoster vaccine, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), etc.),
- behavioral health resiliency training,
- total radiation dose control/monitoring,
- premission health-stabilization program (HSP) to reduce the likelihood of contracting an infectious disease before launch, and
- assisted reproductive technology (ART) if desired by the crew member to preserve gametocytes before missions with exposure to radiation.

TABLE 19.4 Space Flight Participants Questionnaire [8].

Otitis, sinusitis, bronchitis, asthma, upper respiratory infections, or other respiratory disorders	Mental disorder, anxiety, or history of hyperventilation
Severe hay fever or allergies	Attempted suicide
Dizziness or vertigo	Use of medications
Significant motion sickness requiring medication	Alcohol or drug dependence or abuse
Fainting spells or any other loss of consciousness	Date of last menstrual period, current pregnancy, recent postpartum (less than 6 weeks), or recent spontaneous or voluntary termination of pregnancy
Seizures, convulsions, epilepsy, stroke, muscular weakness, or paralysis	History of pneumothorax (collapsed lung)
Tuberculosis, hepatitis, AIDS, or other chronic infectious disorders	Kidney stones or blood in the urine
Surgery and/or other hospital admissions	Gallstones or gallbladder disease
Recent significant trauma	Diabetes
History of decompression sickness (DCS)	Cancer
Anemia or other blood disorders	History of radiation treatment or occupational exposure to radiation
Heart or circulatory disorders, including implanted pacemaker or defibrillator	Rejection of life or health insurance
Uncontrolled high or low blood pressure	History of disability requiring accommodation or functional impairment
Visits to a health care provider in the last 3 years	History of previous space flights

Note: This questionnaire is given to nonprofessional personnel who intend to travel to space. It inquires about general health and common morbidities to screen for eligibility for space tourism.

TABLE 19.5 Space flight participant medical testing [8].

Hematology	Chest X-rays (PA and lateral)
Serum chemistry	Visual acuity (corrected)
Urinalysis	Pregnancy
Resting ECG	Audiometric testing

Note: These are the various medical tests conducted on nonprofessional personnel intending to travel to space. (PA is abbreviation for posterior–anterior).

19.3 Lessons learned from in-flight medical incidents, events, or risks

In addition to reviewing medical data from astronauts and cosmonauts in long-duration space flights, epidemiological risk data obtained from ground analog populations provide a source of representative medical events that might occur aboard a space station. Although the astronaut population is highly select, healthy, and receives extensive preventive medical care before launch, ground analogs remain the most appropriate means of supplementing in-flight data to predict background medical events that have never occurred in space flight. Antarctic stations provide useful study

TABLE 19.6 Monitoring requirements after selection [9].

Clinical assessments	• Physical exams, pre-, in-, and postflight • Private medical conferences • ECG • Vision/eye examinations • Hearing assessments • Bone densitometry • Body mass measurements
Laboratory assessments	• Hematology, biochemistry • Screen for infectious disease—TB, *H. pylori*, MRSA, GABHS, stool parasites
Radiation monitoring	• Personal dosimetry • Biodosimetry
Cardiovascular and fitness assessments	• Aerobic functional capacity • Functional fitness assessments
Psychological/psychometric assessments	• Private psychological conferences • Cognitive assessments
Fatigue countermeasures	• Sleep assessments

Note: Following mission selection, space crew members are continually monitored through a series of clinical assessments, laboratory assessments, radiation monitoring, cardiovascular and fitness assessments, psychological/psychometric assessments, and fatigue countermeasures to ensure their ongoing health (ECG is the abbreviation for electrocardiogram).

analogs for space exploration programs. The Antarctic environment is one of the most extreme on Earth, with temperature, humidity, and microclimate providing conditions similar to those on the Martian surface. Much like spaceflight missions, the remoteness of Antarctic stations requires that the isolated facilities have stand-alone medical care capabilities [7].

In consideration of this, it is most appropriate to review past in-flight medical incidents, events, and risks, as well as the in-flight medical equipment, capabilities, and countermeasures available, Additionally, it is essential to consider the medical emergencies that may require evacuation.

19.3.1 In-flight medical incidents, events, or risks: environmental anomalies and events

19.3.1.1 Off-nominal atmospheres

There have been multiple space flight missions where the breathable atmosphere of the vehicle was fouled or perturbed by a variety of causes, especially combustion-related events, including failures of onboard air revitalization equipment or unplanned releases of substances into the atmosphere. While crewmembers enjoy a healthy, breathable atmosphere the vast majority of time in space vehicles, off-nominal air quality has been one of the most numerous recorded spacecraft anomalies that have an impact on crew health, especially during events where combustion fouled the air. See Table 19.7 for a list of example etiologies of off-nominal vehicle atmosphere. Some of the most prominent examples include the crew exposure to ethylene glycol due to a coolant leak on the Mir and the Freon 218 exposure on the ISS. Although events like these are relatively uncommon, we must do our best to ensure that crew members are protected from all potential hazards.

19.3.1.2 Water contamination

The potable water supply has either been noted by crew members or been measured by either onboard or postflight testing, to be off-nominal, even rendered unsafe for consumptiondue to a variety of onboard system failures or via microbial growth. Table 19.8 describes multiple such episodes on several space vehicles. Similar to the air quality exposures, there have been incidents of ethylene glycol coolant leaks in the reclamation system on Mir, which led to contamination of the condensate. Some other prominent incidents include the water provisions being contaminated with cadmium or bacteria on the ISS and Shuttle systems, respectively.

TABLE 19.7 Air Quality upsets during Apollo, Shuttle, Mir, and ISS missions.

Apollo 13	• Critical consumables location • Multiple hardware developers • CO_2 removal
Shuttle	• Teflon sleeve pyrolyzed by electrical short (STS-28) • Wire burned beneath humidifier (STS-6) • LiOH dust escaped from CO_2 removal canisters • Brown dust released from waste management system • Combustion products from electronics pyrolysis in two data display units (STS-35) • Formaldehyde pollution from pyrolysis of motor housing in refrigerator (STS-40) • Undersized capacitor overheated in laptop causing odor (STS-50) • Microbial production of methyl sulfides from liquid waste (STS-55) • Mir airlock adapter coating strongly off-gassed (STS-89)
Mir	• Frequent leaks of ethylene glycol from cooling loops into air • Formaldehyde escaped containment on Mir-18 • Oxygen candle fire produced various thermal degradation products, e.g., benzene (Feb 97) • Overheating BMP beds produced health-threatening levels of CO (Feb 98)
ISS	• Crew sickened in FGB during poor ventilation, probably from rebreathing of exhaled air/CO_2 (Flight 2A.1) • Freon 218 leaks from SM air conditioner (Apr 01 to Mar 02) • Extremely high methanol in a sample of FGB air; exact source never determined (Aug 01) • METOX canister regeneration caused noxious air—many pollutants in air (Feb 02) • Formaldehyde levels periodically exceed long-term limits, especially when debris restricted ventilation • Strong solvent-like odor from Elektron oxygen generator after repair work (Mar 04) • Potential acid preservative aerosol escape from Russian urinal problem (Exp 10/Feb 05) • Electrical odor traced to lamp on Service Module (Exp 10/Mar 05)

Note: A summary of the off-nominal events in the atmospheric composition that have occurred on the Apollo 13, Shuttle, Mir, and the ISS (CO_2, carbon dioxide; CO, carbon monoxide; FGB, Functional Cargo Block of the ISS; METOX refers to metal oxide sorbent for the removal of CO_2 during EVAs).

TABLE 19.8 Water quality incidents on Shuttle, Mir, and ISS.

Shuttle	• High iodine and nickel for multiple flights • Occasional high bacteria
Mir during Shuttle–Mir program	• Ethylene glycol coolant leaks • High levels of chloroform in ground-supplied water • Oxygen candle fire halted condensate reclamation
ISS	• Elevated cadmium from dispenser valve • Incidents of high silver in ground-supplied water • Persistent high bacteria in ground-supplied water • Persistent high turbidity in stored water • Trace lead (Pb) in processed condensate; no breakthrough

Note: A summary listing of the water quality anomalies that have been recorded on Shuttle, NASA-Mir, and ISS missions.

19.3.1.3 Combustion/toxic environmental events

One of the most feared in-flight events is the spontaneous combustion event, commonly known as an onboard fire. In these instances, the crew has both training and equipment not only to protect themselves from the heat and toxic byproducts, but also to extinguish the flames and manage the energy source(s) that may have sparked the event, such as an electrical short circuit. Some examples are outlined in Table 19.9. Notable incidents include the contamination of the atmosphere due to a solid fuel oxygen generator fire on Mir (1997) and a problem with the catalytic oxidizer resulting in the release of carbon monoxide on Mir (1998).

19.3.1.4 Spaceflight radiation exposure

The various space programs have employed a variety of methods to quantify the amount of radiation exposure the vehicle and the crew receive while in space. Missions that stay in LEO typically have lower radiation doses, depending on mission duration, than those that traverse the Earth's geomagnetosphere, through the trapped radiation of the Van Allen's belts, and into interplanetary space where there is no protection from solar wind or solar storm-associated radiation. LEO missions that fly at a lower inclination (nearer to the equator) will have lower exposure than those at higher inclinations, especially near the poles, due to their interaction with the trapped radiation in the auroral horns. Additionally, all flights of sufficient duration, with a procession of the orbits, will encounter the Southern Atlantic Anomaly, a region of concentrated lower-altitude trapped radiation. Several instruments have been developed to detect and measure radiation exposure, including:

- Passive area dosimeters
- Active intravehicular instruments, such as:
  - IVCPDS—Intravehicular Charged Particle Directional Spectrometer
  - TEPC—Tissue Equivalent Proportional Counter
- Active extravehicular instruments, such as:
  - EVCPDS—Extravehicular Charged Particle Directional Spectrometer
- Crew-worn personal dosimeters
- Biodosimetry—WBC assessment of chromosomal aberrations

TABLE 19.9 List of on-orbit events producing combustion or toxic products.

Combustion	• Apollo 1: fire—lethal for three crew • STS-6: arcing in Kapton-PFTE insulation = noticeable odor • STS-28: arcing in Kapton-PFTE insulation = noticeable odor • STS-35: overheating of electronic display unit • STS-40: motor burn (refrigerator/freezer) • Salyut 5: fire, mission abort from headache • (1985): hypothermia during EVA • Mir (1994): wire bundle caught fire • Mir (1997): solid fuel oxygen generator fire—crew on gas masks due to toxic atmosphere • Mir (1998): catalytic oxidizer overheat with carbon monoxide release • Carbon monoxide release (cabin atmosphere measured at 600 ppm, estimated crew; carboxyhemoglobin level of 35 mg/dL)
Other toxic events	• Salyut—CO_2 toxicity (60 ppm) because of CO_2 sensor failure, crew developed severe headaches and fatigue • Apollo Soyuz Test Project—nitrogen tetroxide leaked into capsule on reentry, crew hospitalized postflight for chemical pneumonia • Mir—ethylene glycol leaks, crew developed upper respiratory symptoms (air samples measured 75 ppm) • ISS/STS 96—adhesive off-gassing caused headaches • ISS—Metox off-gassing caused crew headaches • NASA/Mir (1997)—spacecraft depressurization (Progress-Spektr collision)

Note: Brief catalog of the combustion and toxic-release events that have occurred in both Russian and US space missions.

19.3.1.5 Measured bioeffects

The following assays are and have been performed on some professional crew members to measure their exposure to space-related oxidative stress and other health markers: blood and urine measurements of total antioxidant capacity, levels of glutathione, superoxide dismutase, 4-HNE, malondialdehyde, and 8-OH deoxyguanosine.This is of particular concern due to the inherent radiation and microgravity conditions crewmembers experienc during spaceflight.

19.3.2 In-flight medical incidents, events, or risks: trauma and injury

During a spaceflight mission, the crew is exposed to occupational hazards associated with mission training, and living and working in space, including with respect to intravehicular activity and extravehicular activity. This includes the likelihood of sustaining a traumatic injury during such activities. Examples of traumatic injuries occurring during intravehicular activity include:

- Crew members have sustained injuries to muscles and tendons during the execution of countermeasure activities, such as running on the treadmill under load or working against a resistive exercise device.
- Crews have scraped their skin and bruised the peri-orbital region due to collisions with the module structures or payloads during IV locomotion in *g*.
- Debris in the modules, especially shortly after docking of resupply modules, have resulted in corneal abrasion when protective lenses were not worn.

Examples of traumatic injuries occurring during extravehicular activity include the following (Fig. 19.4):

- Shoulder—Injury can be due to the interaction of the shoulder with the hard upper torso of the extravehicular maneuvering unit (EMU) during egress or ingress of the suit, or during repetitive upper extremity actions in the EMU either in training in the Neutral Buoyancy Laboratory (NBL) or in g on orbit.
- Hand/Feet—Fingernails have been damaged due to the forces applied in the 4.3 psi pressurized EMU gloves. Also, the insoles of the feet are often stressed from the pressure of the foot-holds on the robotic arm with the EMU boots.

19.3.3 In-flight medical incidents, events, or risks: behavioral health events

Workload, desynchrony (sleep rest cycle), and off-nominal events are some of the prominent contributing factors for behavioral health issues that have occurred in the US and Russian space missions. The following list outlines a few of the most notable in-flight behavior/psychological stress episodes:

- Acute behavioral change
  - Payload specialist despondent when payload experiment failed, crew concerned about potential for dangerous behavior
- Acute anxiety reaction
- Crew member psychological stress reaction (1988)
- Acute grief reaction
  - Mir: crew member's mother died, withdrew from the crew for 1 week
- Crew−crew interpersonal conflicts
  - Soyuz 21 (1976)
  - Soyuz T14 (1985)
  - Soyuz TM 2 (1987)—Personality incompatibility

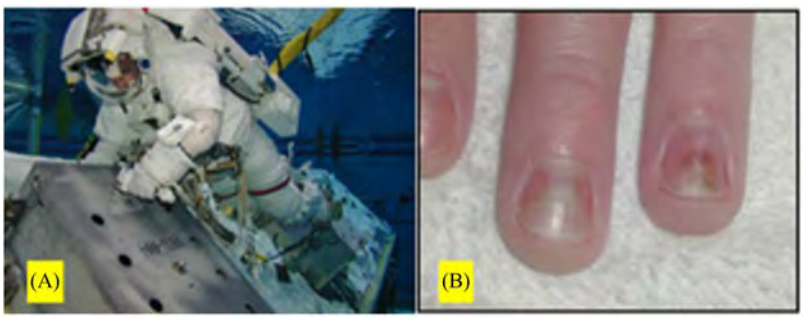

FIGURE 19.4 Traumatic injuries during extravehicular activity: (A) EMU in the Neutral Buoyancy Laboratory (NBL). This is a common source of shoulder injury; (B) Fingernail trauma injury due to forces applied to EMU gloves.

- Crew–ground control team conflicts
  - Sylab 4
  - NASA Mir 4

As the duration of future missions increases and space crews travel farther away from Earth's life-support systems, the likelihood of developing adverse cognitive or behavioral conditions rises due to the extreme, isolated, and confined environments. The extended range and duration of orbital space travel will amplify stressors while simultaneously requiring crew members to maintain mental stability and engage in crew-related duties essential for safety and mission success.

19.3.4 In-flight medical incidents, events, or risks: random medical events

Despite the most meticulously designed and well-executed preventive medical programs in aerospace medicine, random medical conditions can still develop, or crew members may sustain an injury, especially related to mission training activities and the performance of spacewalks (EVA—extravehicular activity). As seen in Table 19.10, most crew members will experience some symptomatology upon arrival into space. Overall, 97% of the crew (588 out of 607) experienced some symptomatology, with 98.1% of men and 94.2% of women affected. Although the majority of cases are readily manageable with onboard capabilities, some may require intervention from ground-based personnel. In such cases, flight surgeons, who conduct regular crew medical conferences, advise crew members or the crew medical officer on effectively managing their onboard symptomatology.

TABLE 19.10 Medical symptoms in US space program.

Symptoms:	97% reported some medical symptom (588 of 607 crew) (98.1% of men and 94.2% of women)
Space motion sickness	79%
Headache	67%
Respiratory complaints	64%
Facial fullness	58%
Space adaptation syndrome	39.6%
Episodic insomnia and fatigue	36%
Gastrointestinal complaints	9%–32%
Musculoskeletal complaints	26%
Injuries and trauma	9%–12%
Genitourinary symptoms	10%
Skin and subcutaneous tissue	8%
Respiratory system	4.5%
Behavioral signs and symptoms	1.8%
Genitourinary system infectious disease	1.5%
Infectious diseases	1.3%
Circulatory system	0.3%
Endocrine, nutritional, and metabolic disorders	0.1%

Note: This summarizes the prevalence of various medical symptoms experienced by crew members in the US space program. These findings highlight the range and frequency of medical symptoms experienced by astronauts during the mission, emphasizing the importance of onboard capabilities and ground-based medical support.

Table 19.11 lists diagnoses that occurred in active astronauts from STS-1 through STS-108, encompassing 106 Shuttle missions conducted between April 1981 and December 2001. These missions, involving 607 crew members, 521 men and 86 women, amounted to approximately 5496 flight days, with 4673 flight days for men and 823 flight days for women. While no medical evacuations have occurred for STS or US crew on Mir/ISS to date, there have been multiple mission-impacting events and 2207 documented medical events,comprised of 1882 events in men and 325 events in women. Notably, 14 astronauts, who were preselected to be nonkidney stone formers, were documented to have experienced kidney stones while serving as active astronauts.

19.3.5 A summary of in-flight medical events in space

Despite numerous advances in space flight, the data presented Table 19.12 emphasizes the inherent risk and the continued challenges of these expeditions. Additional insights are available and presented in Fig. 19.5, which shows in-flight medical events in NASA astronauts during the Space Shuttle Program, from STS-1 through STS-89, April 1981 to January 1998. Various bodily systems are affected during flight, each capable of impacting the mission. In particular, space adaptation syndrome accounts for the majority of the medical events experienced by NASA space crews. Consequently, a flight rule was established prohibiting nonemergency EVAs within the first 48 hours, allowing crew members sufficient time to recover from space motion sickness.

TABLE 19.11 Active diagnoses in US astronauts.

Cervical disk herniation with impingement on spinal cord	Prostate cancer × 5
Kidney stone × 14	Stroke with patent foramen ovale
Clostridium difficile infection	Stroke/TIA from atrial fibrillation
Gastroenteritis/colitis	Bladder outlet obstruction
Inguinal hernia × 4	Ulcerative colitis
Olecranon bursitis r/o septic joint	Flexor digitorum synovitis
Hand bacterial tenosynovitis	Bowel resection
Pneumonia × 2	Fatty liver disease
Corneal ulcer	Bulging disk with radiculopathy × 44 (Cervical 18; Lumbar 26)
Severe epistaxis	Hypercholesterolemia
Right ovarian cyst	Hypertension (essential)
Dysmenorrhea	Atrial fibrillation with ablation × 5
Sudden hearing loss × 2	Brain (pituitary) tumor × 2
Ventricular tachycardia, exercise-induced	Choledocholithiasis × 4
Angina	Pancreatitis × 2
A-fib	Hemorrhagic cyst
Allergic reaction—severe	Lower GI bleeding
Retinal detachment × 2	Duodenal ulcer with upper GI bleeding
Appendicitis × 2	Malignant melanoma
Diverticulitis	Total knee replacement × 2
Asymptomatic coronary artery disease × 18	Shoulder surgical repair × 22

Note: This table documents medical diagnoses observed in active astronauts from April 1981 to December 2001. The data includes 607 crew members (521 men, 86 women).

TABLE 19.12 Spaceflight medically related contingencies, morbidity, and mortality [7].

Date	Mission	Description
03/29/1961	Soyuz ground test	Cosmonaut Bondarenko died on March 23, 1961, in a spacecraft simulator fire with 100% oxygen environment
05/16/1963	Mercury 9	Elevated CO_2 levels and loss of pressure to control system, required manual reentry
03/18–19/1965	Voskhod 2	Manual deorbit service module failed to separate during reentry, landed 1200 miles of target Crew rescued next day
03/16/1966	Gemini 8	Docked vehicles rotated out of control near structural limits. Crew landed early- waited overnight before ocean recovery
06/05/1966	Gemini 9	Astronaut's helmet faceplate continually fogged over during EVA, impairing vision
01/27/1967	Apollo 1	Fire in crew module during ground test, with 100% oxygen environment. Three crew members—Chaffee, Grissom, and White—perished
04/24/1967	Soyuz 1	Parachute system did not deploy after reentry; capsule destroyed on impact, resulting in the death of cosmonaut Komarov
01/18/1969	Soyuz 5	Spacecraft tumbled during entry, landing 2000 km off target, with hard impact. Cosmonaut had minor injuries
04/11–17/1970	Apollo 13	Mission to Moon aborted after oxygen tank ruptured. Crew returned safely. One crew member developed urosepsis
04/23–25/1971	Soyuz 10	Failed docking with Salyut 1. During landing Soyuz air supply became contaminated and cosmonaut lost consciousness
06/29/1971	Soyuz 11	Cabin pressure failure during reentry. Three crew members—Dobrovolsky, Volkov, and Patsayev—perished
12/1972	Apollo 17	Back strain from drilling core sample during walk on lunar surface
04/05/1975	Soyuz-18A	Launch vehicle malfunction, second stage abort subjecting crew to nearly 20 + Gx. Crew landed in Eastern Russia and rescued the next day. Crew member suffered minor internal injuries
07/24/1975	Apollo-Soyuz	Apollo crew members developed airway reactivity/pneumonitis from toxic contaminants during reentry, requiring hospitalization
08/24/1976	Soyuz 21/ Salyut 5	Mission curtailed due to crewmember illness—related to environmental control systems problem
10/16/1976	Soyuz 23	After failure to dock with Salyut 6, capsule landed in blizzard conditions at night into ice-covered Lake Tengiz; rescue team unable to recover capsule until next morning
11/11/1982	Salyut 7	Acute abdominal pain, probably kidney stone, resolved on orbit
09/26/1983	Soyuz T-10A	Launch abort due to pad fire, crew landed safely via capsule escape system
06–09/1985	Soyuz T-13	Hypothermia and CO_2 toxicity during reactivation of Salyut 7
11/21/1985	Salyut 7	Crew member became ill with prostatitis and urosepsis. Return to Earth required 56 days into a 216-day mission
01/28/1986	STS-51L	Solid rocket booster seal failure resulted in Space Shuttle destruction 73 s into flight. Seven crew members perished (Jarvis, McAuliffe, McNair, Onizuka, Resnik, Scobee, Smith)
1987	Mir 2	Crew member developed persistent tachydysrhythmia during EVA, returned early on the next mission opportunity

(*Continued*)

TABLE 19.12 (Continued)

06/1991	STS-40	Freezer motor malfunction causing formaldehyde toxicity and headaches, exacerbated by cabin noise
1995	Mir 18	Crew member experienced episode of asymptomatic, sustained ventricular tachycardia. No mission impact
1995	Mir 18	Traumatic eye injury resolved with onboard treatment
02/23/1997	Mir 23	Fire due to oxygen generator failure; smoke and potentially toxic fumes in station. Mild second-degree burns and reactive airway changes. Onboard treatment given
1997	Mir 23	Three crew members experienced upper airway irritation and dermal reaction following exposure to ethylene glycol
06/25/1997	Mir 23	Progress resupply vehicle collided with Spektr module during manual docking, resulting in station depressurization
08/14/1997	Soyuz TM-25	Soft-landing engine misfire at high altitude; hard landing
02/1998	Mir 24	Three crew members exposed to elevated carbon monoxide levels, with headache symptoms
10/1998	STS-95	Five crew members were exposed to a contaminated water supply leading to ingestions of potentially toxic trialkylamines
02/01/2003	STS-107	Space Shuttle Columbia was destroyed on entry; all crew were lost (Anderson, Brown, Chawla, Clark, Husband, McCool, Ramon)
05/04/2003	Soyuz-TMA-1	Ballistic reentry. Vehicle rolled due to high winds, crew member suffered radial nerve palsy requiring treatment
04/19/2008	Soyuz-TMA-11	Ballistic reentry, nominal landing. Back injury requiring hospitalization
09/16/2011	Soyuz-TMA-21	Kazbek restraint strap failure resulting in knee injury after impacting control panel during nominal landing
03/16/2013	Soyuz-TMA-06M	Seat stroke mechanism, no injuries recorded
07/2013	ISS Expedition 36	During EVA, one crew member experienced water filling the helmet causing difficulty seeing and breathing, requiring early termination of the EVA

Note: This report lists observed morbidity and mortality for various US and Russian missions between 1961 and 2013 (CO_2, carbon dioxide; EVA, extravehicular activity).

19.4 Evacuation and high-risk medical events

Experience with ISS has identified medical events that would require medical evacuation back to Earth if they were to occur in-flight,. Any human spaceflight program is required to assess what kind of in-flight medical events are simply beyond any in-flight capabilities to resolve. For the ISS, a classification system is used for various medical events and the ability of the Health Maintenance System (HMS), a component of the Crew Healthcare System (known as CHeCS), which is currently deployed on ISS, to address them. Table 19.13 describes and provides examples of the classification system of medical events on the ISS.

Retrospective analysis of records from the NASA Johnson Space Center Lifetime Surveillance of Astronaut Health (LSAH) indicates the number of Class III medical events experienced within the astronaut corps by individual astronauts over their lifetime (Table 19.14).

To date, there have been three medical events resulting in crew member de-orbit, all in the Russian space program before ISS: (1) Medical Salyut 5 space station (1976) abandoned 49 days into a 54-day mission for

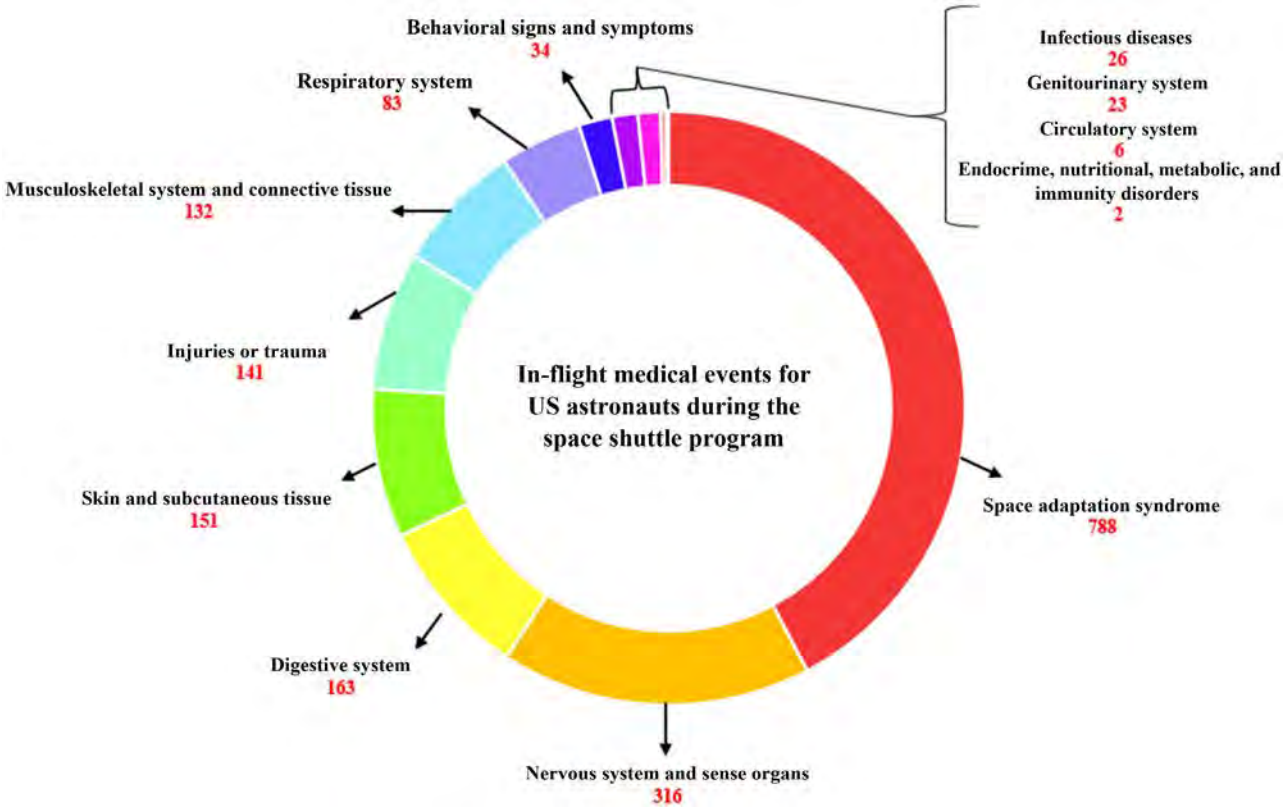

FIGURE 19.5 In-flight medical events in NASA astronauts: This chart illustrates various physiological functions that are affected during flight, each with the potential to impact the mission. Data collected from NASA crew members spans from April 1981 to January 1998.

TABLE 19.13 ISS medical event classification [7].

Class	Description
Class I medical event	No mission impact, e.g., minor muscle strain
Class II medical event	Significant medical events requiring the use of the ISS HMS
Class IIa	Manageable with HMS and not likely to require evacuation or affect mission duration, e.g., prostatitis
Class IIb	Manageable with the HMS but may require the astronaut to return at the next available opportunity for further evaluation and treatment, e.g., breast mass
Class IIc	Manageable with HMS but may necessitate emergent evacuation if the condition does not improve or worsens, e.g., cardiac dysrhythmia
Class IIx	An event unlikely to occur in a microgravity environment or one that would be detected in a premission evaluation, e.g., herniated nucleus pulposus
Class III medical event	An event requiring emergent evacuation from the ISS, e.g., acute appendicitis, cerebral hemorrhage

Note: This table describes the various classes of potential medical events on the International Space Station, the mission impact, and the corresponding outcomes (HMS—Health Management System).

TABLE 19.14 Class III medical events [7].

Class III medical events ($n = 18$)
• 50% total body surface area burn/30% third-degree burn • Diffuse chemical pneumonitis from toxic inhalation of nitrogen tetroxide (three individuals) • Anaphylactoid reaction to intravenous tracer • Acute appendicitis • Ruptured retroperitoneal appendix • Pancreatitis/choledocholithiasis • Pulmonary embolism • Nephrolithiasis • Cholecystitis • Cholelithiasis • Tendon rupture • Retinal detachment • Cervical spinal stenosis with central cord syndrome • Cervical spondylosis with Brown-Sequard syndrome • Metastatic melanoma • Cerebrovascular accident

Note: This table lists the Class III medical events requiring hospitalizations between 1959 and 2018. The data, provided by the Longitudinal Study of Astronaut Health, corresponds to 18 astronauts.

TABLE 19.15 Medical events in-flight with mission impact.

Apollo 8	First American to report space motion sickness
Apollo 9	EVA rescheduled due to SMS/SAS (first timeline change due to medical cause)
Apollo 11	Type 1 DCS in command module pilot
Apollo 13	Urinary tract infection during mission
Apollo 15	Cardiac dysrhythmia (PVC, PAC, bigeminy) during lunar EVA
1975 Apollo Soyuz Test Project	Nitrogen tetroxide chemical pneumonitis on reentry
Salyut 1982	Urinary Stone (near evacuation; passed stone while preparing to evac)
Shuttle	Five cases of urinary retention resulting in bladder catheterization
ISS	Crew member pulled from EVA due to cardiac abnormalities

Note: This table displays medical events that have occurred in-flight in the US program that impacted the mission but did not result in medical evacuation or deorbit.

intractable headaches following probable combustion event; (2) Salyut 7 space station (1985) evacuation 56 days into 216-day mission for urinary tract infection (prostatitis); (3) Mir space station (1987) evacuation 6 months into 11-month mission for heart irregularity during Lower Body Negative Pressure (LBNP) as part of Russian Medical Operations activity called "MO-5". In contrast, the US program has recorded 12 in-flight medical events that impacted missions but did not result in de-orbit. (Table 19.15).

There are also examples of "Medical Close Calls," which required medical staff to determine whether to modify the crew, treat on-site, or evacuate. This includes the following:

- A *preflight* cardiac ischemic event within 3 days of launch (crew changed out)
- Two *in-flight* cardiac ischemic events, followed by myocardial infarction (MI) postflight
  - Case 1: Acute diaphoresis, fatigue and bigeminy on orbit, MI 2 years postflight
  - Case 2: Treated with ASA and beta blocker, MI 6 weeks postflight

Even after a brief examination of specific cases, whether in a terrestrial, aviation, marine, or space environment, it is important to note that the priorities of triage and the principles of medical evacuation remain constant. These are predicated on several factors [7]:

- Severity of the illness or injury
- Environmental conditions at the scene and during medical transport
- Capabilities and proficiency of the first responders
- Available medical equipment and capabilities
- Telecommunications capabilities
- Safety and performance of the transport vehicle
- Flight duration of medical transport vehicle
- Safety of the transport flight profile
- Onboard medical capabilities during transport
- Medical capabilities of the receiving facility

More specifically, the risks associated with spaceflight medical evacuation and transport can be outlined and seen in Table 19.16. Fundamental to spaceflight evacuation is a spacecraft with medical evacuation capability. Minimum environmental control and life-support system requirements for crew return spacecraft can be seen in Table 19.17. Also, noteworthy is that the recovery of a crew in an emergency return is different from the well-choreographed and planned nominal landings. It is not without danger to search and rescue (SAR) forces, in large part due to the many toxic

TABLE 19.16 Risks associated with spaceflight medical evaluation and transport [7].

Timeline event	Risks	Risk mitigation design factors
Decision to transport/ evacuate	– Delayed or premature decision – Incorrect decision (e.g., medical condition likely to worsen with evacuation) – Major mission impact	– Anticipate possible scenarios – Establish standing flight rules to guide decisions – Allow real-time crew decisions independent of ground support if communication fails
Cabin environment	– Space-limited medical access for monitoring, procedures, and resuscitation – Nonsuited configuration is a zero-fault-tolerant cabin environment to entire CRV crew for depressurization or toxic atmosphere event	– Cockpit configuration – Evacuation timeline – Life-support system consumables adequate to the evacuation timeline – Crew time constraint of -3 h from departing station to landing
Medical capabilities of vehicle	Suited configuration limits medical access, especially for airway management and resuscitation	Design allows unsuited transport; seat design allows CMO access to patient
Autonomous Reentry	– Limited landing opportunities – Thermal, noise, and vibration issues – Acceleration profile on reentry—nominal vs. ballistic – Chute deceleration effects	– Large cross-range capability, along with deorbit opportunity every two or three orbits – Low entry G profile – Autonomous, unpowered return – Controlled reentry G limits: 4 + Gx, 1 ± Gy, 0.5 + Gz
Landing	– Limited sight and obstruction avoidance – Land impact vs. water impact – Potential impact injuries	– Maybe autonomous – Inertial navigation system, Global Positioning System guidance – Steerable parafoil to limit landing speeds – Landing site selection and navigational aids – Recumbent crew seating – Landing impact attenuation system

(*Continued*)

TABLE 19.16 (Continued)

Timeline event	Risks	Risk mitigation design factors
Egress and rescue	– Impaired performance in one G due to deconditioning – Unaided egress may not be possible – Land vs. water egress – Remote environment exposure – Risk to search and rescue (SAR) personnel unplanned deployment, toxic propellants, unspent pyrotechnics – SAR/ground force availability and response time	– Prelanding countermeasures: – Fluid loading – Pharmacologic, sympathomimetic agents – Anti-G suits – Crew survival training – SAR readiness and exercises
Evacuation to DMCF	– Additional transport event – Medical facility capabilities at landing site may be diminished	Medical operations contingency support and implementation plan to define requirements for US and international emergency landing sites

Note: This table describes various risks and risk mitigation design factors that are implemented throughout the medical evacuation and transport timeline.

TABLE 19.17 Required parameters for crew return vehicle [7].

Parameter	Range
Total pressure	14.0–14.9 psia
Partial pressure (pp) carbon dioxide	0–0.07 psia
pp oxygen	2.82–3.30 psia
pp nitrogen	$<$11.6 psia
Relative humidity	25%–75%
Atmospheric temperature	18.3–26.7°C
Dew point	4.4–15.6°C
Intramodule circulation	0.051–0.2 m/s
Intermodule ventilation	66 ± 2.4 L/s
Fire suppression oxygen concentration level	10.50%
Particulate concentration (0.5–100 mm diameter)	Average $<$0.05 mg/m^3
Temperature of surfaces	4°C $<$ touch temperature $<$45°C
Atmospheric leakage per module	Max 0.23 kg/day at 14.7 psi

Note: The table outlines the minimum environmental and life-support system design parameters for the crew return vehicle.

substances carried by spacecraft for propulsion and cooling. This is compounded if the vehicle lands in a remote and inaccessible area of the world [7].

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Detsis—Ethics in Space (2022)

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Overview: Discusses ethical foundations and responsibilities shaping future space exploration policies.

Chapter 9
Ethics in Space: The Case for Future Space Exploration

Emmanuel Detsis

Abstract The coming decades will see humans setting foot on the Moon once more and possibly Mars. However, current radiation exposure standards for long duration spaceflight do not allow for such missions. This chapter gives an overview of the discussion in the US and NASA, regarding the way forward and outlines important recommendations that were presented to NASA from the National Academies of Science, Engineering and Medicine in 2021. The ethical issues regarding human spaceflight and radiation exposure are highlighted and examined.

Keywords Ethics of human space flight · Space exploration

9.1 Introduction

The images of the Apollo landing on the Moon are one of the most iconic of the twentieth century. Neil Armstrong's "one small step for man, one giant leap for mankind" inspired millions of people around the world, helped boost the U.S geopolitical image around the globe and was the winning aspect of the US-Soviet "Space Race". Understandably, the Apollo program (11 total missions, 6 Moon landings and 12 astronauts walking on the Moon) was and still is the crowning achievement of human space flight. However, the program ended in 1972, and since then, humans in space have remained very close to Earth indeed. Operating in Low Earth Orbit (LEO), mostly within space stations such as Skylab (US), Mir (Soviet Union and then Russia), the International Space Station (US/Russia/EU/Japan/Canada) and the Tiangong-1, 2 and 3 (China). These stations circle the Earth at orbits between 350 and 450 km.

However, we are entering once again an era of space exploration beyond Earth, with the Moon as a steppingstone and Mars as the ultimate destination. Plans for these kinds of missions have always existed but it seems that the 2020–2030 decade will once again see humans on the Moon, or soon within the decades after. These

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plans for the Moon have gone now beyond the planning phase and are now being "operationalized", with NASA having signed the "Artemis Accords"[1] and other space agencies adapting their own space programs or parts thereof for operations in the lunar vicinity and/or surface, in partnership with NASA or concurrently, as is the Chinese/Russian plan for an International Lunar Research Station on the Moon, as announced at the Global Space Exploration conference on June 16, 2021.

Obviously, there is a plethora of questions to be answered regarding the "how?", encompassing the myriad of technical issues to be solved and worked out in order to make a Moon or Mars landing feasible. There are also several questions regarding "why?", that have to do with the purpose of landing humans on an extra-terrestrial surface, being either scientific or political in nature.

However, this case study will not delve into these aspects, but rather focus on the issue of whether sending humans to another celestial body is an ethical thing to do, and how space agencies currently deal with the ethical issue that the mere presence of humans in space puts them in harm's way.

9.2 Space Exploration and Effects on Humans

"Space is hard" is a common saying amongst people working in the space industry. It signifies the complicated issues surrounding space travel, an issue that is also reflected on the cost of space missions. Space travel beyond LEO is even more so, given the distances involved. Apart from the danger of relying on complicated machinery for transferring the crew to its destination, the space environment itself is extremely harmful to human beings. Many of the problems encountered in human space travel deal with keeping the crew alive. Interplanetary space as well as the lunar and Martian surfaces are extremely hostile environments, including hard vacuum, extreme temperatures, space debris, zero or reduced gravity, as well as harmful radiation. It is this later aspect, the harmful radiation, that this case study will focus on as it constitutes the greatest uncertainty in respect to effects and mitigation. Mitigation efforts regarding vacuum, temperatures and debris are possible, based on proper spaceship and astronaut suit construction as well as effective operational design. The effects of reduced gravity have been extensively studied and countermeasures are in existence (Blaber et al. 2010). These countermeasures cannot eliminate the side effects of long duration space travel but can reduce them to the point that the crew remains operational for the duration of the mission. The issue of harmful radiation is rather more complex. There are currently no effective strategies for complete shielding from space radiation. Any human in space thus will be exposed, with exposure being relative to the duration and type of each mission.

[1] https://www.nasa.gov/specials/artemis-accords/index.html.

9.2.1 Space Radiation Physics

The main sources of radiation in space are galactic cosmic rays (GCRs) and solar particle events (SPEs). GCR are very energetic and thus highly penetrating. They are very difficult to attenuate and essentially cannot be stopped by shielding, since shield mass in space is limited. Spacecrafts cannot carry a heavy amount of shielding material (putting mass in orbit is very expensive), and a "weak" shield might in fact be worse than no shield at all, since a GCR will create a cascade of secondary particles of shield material that will saturate the insides of the spacecraft. It is thus preferable to let GCRs just pass through the human body.

SPEs include particles such as helium ions and other ions. SPEs originate at the Sun. These events occur sporadically with varying frequency. Frequency and intensity of SPEs are unpredictable, although they are related to the Solar 11-year cycle (solar minimum/maximum). Low energy SPE protons cannot penetrate spacecrafts or astronaut suits, but the high energy particles can, and thus contribute to astronaut radiation exposure. However, shielding (especially within a spacecraft) is effective against SPEs. Issues arise with astronauts outside the spacecraft (extravehicular activities) or exposed on the lunar or Martian surface, since when an SPE occurs, astronauts may not have time to seek protective shelter.

GCR flux can be modelled and expected exposure calculated. SPEs can be shielded against based on assumptions about intensity and frequency and planning of activities. Prediction of SPEs is not possible but advanced warning once one has occurred is feasible, albeit with a very small reaction timeframe.

9.2.2 Current Practises

Currently, space agencies have regulations that define radiation exposure standards that astronauts should not exceed. For example, NASA defines space permissible exposure limits (SPELs) for their astronauts which indicate that "astronauts shall not exceed 3% *risk of exposure-induced death* (REID) from cancer". The current NASA standard is adjusted for age and sex, which is not the case for all space agencies. The SPEL indicates an upper 95% confidence limit that the individual will die from cancer associated with the radiation exposure that the individual received while in space. In essence, out of 100 astronauts that have travelled in space, 3 might die from radiation related cancer. This is calculated for each astronaut, based on sex and age.

Radiation exposure dose equivalent unit in dosimetry is measured (in SI units) in sieverts (Sv). For exposure to small doses of ionising radiation, it is easier to use the millisievert (mSv). The current standards of the international space station partners can be seen in Table 9.1.

Table 9.1 Radiation exposure career limits for astronauts. ISS partner agencies. Adopted from NAS (2021)

Space agency	Career dose limit	Sex/age dependency
Canadian Space Agency	1000 mSv	No
European Space Agency	1000 mSv	No
Russian Federal Space Agency	1000 mSv	No
Japanese Aerospace Exploration Agency	3% REID	Yes Lower limit: 500 mSv (female, 27–30 years old) Upper limit:1000 mSv (male, >46 years old)
National Aeronautics and Space Administration	3% REID	Yes Lower limit:180 mSv (female, 30 years old) Upper limit: 700 mSv (male, 60 year old)

Table 9.2 Mission profile and duration with observed radiation dose (averaged). Adapted from NASA's space radiation FAQ[2]

Mission	Radiation dose
Space Shuttle 41-C (8 days, 460 km orbit)	5.59 mSv
Apollo 14 (9 days Lunar mission)	11.4 mSv
Skylab 4 (87 days, 473 km orbit)	178 mSv
ISS Mission (6 months, 353 km orbit)	160 mSv (Solar minimum)–80 mSv (Solar Maximum)
Average human on earth	~2 mSv per year from background radiation (location, lifestyle dependent)
Annual limit for workers dealing with radioactive material	50 mSv
Expected dose for average nuclear facility worker	1 mSv per year (adapted from ncr.gov[3])

To get an indication of how mission profiles affect radiation exposure, Table 9.2 summarises the radiation dose (average) for various mission types. Despite the difference in the type of radiation, 1 mSv of space radiation is roughly equivalent to receiving three chest X-rays.

Radiation doses are cumulative. Thus, under the current standards, a 30-year-old female NASA astronaut might be able to fly once or twice to the ISS before reaching her career limit, whereas a male astronaut can probably fly more times. For Russian, European or Canadian astronauts, longer or more missions can be undertaken. Note

[2] https://srag.jsc.nasa.gov/spaceradiation/faq/faq.cfm.

[3] Occupational Radiation Exposure at Commercial Nuclear Power Reactors and Other Facilities annual reports.

that older astronauts have higher exposure limits, as the overall impact on the rest of their lives is less than the impact on a younger astronaut.

9.2.3 *Effects of Space Radiation on Human Health*

Exposure to large doses of harmful radiation can signify increase risk for the development of cancer and non-cancer anomalies, such as leukaemia, circulatory diseases, vision impairing cataracts, cognitive and memory problems, potential heritable effects and infertility (Cucinotta and Durante 2006; Chylack et al. 2009; NRC 2006). The great degree of uncertainty about whether an astronaut will develop any of these health problems, especially cancer, makes it challenging to communicate these risks to astronauts, the public and policy makers. There are several sources of uncertainty.

As mentioned in the previous section, the average flux of GCR and solar activity can be simulated and modelled. However, SPEs are stochastic events, as there is no way to know exactly when and where an SPE will take place. Thus, it can be treated as a random occurrence, and therefore there is always a risk for a high energy event that exceeds the modelling parameters.

Another source of uncertainty is the actual effects of radiation on the human body. This might be surprising at first, given that radiation sources have been available for decades on Earth. Considering the effects of *long-term* exposure to radiation (rather than acute radiation exposure), however, showcases the difficulty of gathering data over a long period of time (decades) for large groups of exposed humans in order to conduct statistical studies and infer accurate risk rates.

Risk projections for cancer specific illnesses have largely been based on data from the Life Span Study (LSS) of the Japanese atomic bomb survivors. Additional data sources are being made available, such as studies of occupational radiation. Nevertheless, uncertainties remain regarding potential long-term effects (Chylack et al. 2009; NRC 2006).

9.2.4 *Leaving Earth*

The current space radiation exposure standards (see Table 9.1) were developed with short space missions in mind, planning for repeated missions (i.e. multiple stays in the ISS), where it was possible to return to Earth (and have access to health care there) within days. In venturing outside the Earth, to travel to the Moon and Mars, this will no longer be the case. In the case of travel to Mars, the round trip can take more than two years with the projected technology (for 2030+). The mission profile calls for a 6-month cruise, 18 months surface stay (waiting for Mars and Earth to re-align in their orbits and reduce necessary travel time) and 6 months travel back. Thus, once the mission has begun, an astronaut cannot decide that he or she no longer

Table 9.3 Mission profiles for future space exploration scenarios and expected radiation doses. Adopted from (Cucinotta and Durante 2006). Risk calculations can be found therein

Mission type	Effective dose (mSv) from GCR
Lunar Mission (180 Days)	170
Mars Orbit (600 days)	1030
Mars exploration (1000 days)	1070

wants to be part of it. This is quite different from what is typically found in terrestrial occupations that include radiation exposure. Terrestrial workers can choose to leave their job and thus end their exposure. Furthermore, the radiation environment outside Low Earth Orbit changes.

The most important factors that contribute to the heightened risk of radiation exposure for astronauts in Lunar or Mars exploration missions can thus be inferred from the above. Once outside the Earth's protective global magnetic field, which the Moon and Mars do not have (there are localised but not global magnetic fields), the flux of radiation (both GCR and SPEs in origin) increases. Additionally, the response window for energetic SPEs diminishes, as Solar observatories have to observe the event and a signal communicated to the astronauts needs to happen for them to take shelter. The further they are from Earth, the longer it will take for the message to be transmitted to them. In addition, the expected mission durations increase quite substantially, essentially placing future astronauts in a more hostile environment than they operate now, for much longer periods. Contrast Table 9.2 with expected radiation doses for future extra-terrestrial exploration missions (Table 9.3).

9.3 Ethical Space Exploration

The previous section highlights several issues regarding future space exploration destinations.

1. The effects of radiation will probably not have a technological mitigation measure in the envisaged timeframe for these countermeasures to be available. Thus, exposure to harmful radiation is a given for any mission.
2. Uncertainty still remains about the types of adverse effects that astronauts will incur due to long duration spaceflight. This makes it hard to accurately inform the crew on the impact of each mission on the participant's long-term health and quality of life.
3. For missions to Mars, termination of participation might not be an option. If the astronaut so chooses, he cannot just stop participating in the mission. The physical distances and planetary alignment might make it impossible to return to Earth, outside the planned window.
4. Given that exposure is cumulative, Lunar and Mars missions might necessitate inexperienced astronauts as crew (no previous exposure).

5. The current standards for astronaut lifetime radiation exposure do not actually allow participation in missions to Mars, as the nominal mission scenarios would exceed the allowable limits.

The points above ultimately create the situation that a future Mars mission will put the crew in harm's way, regarding career-received radiation, with increased risk of adverse health effects. This section will now describe the official (space agency) response and efforts to deal with this situation.

Spaceflight is an endeavour that brings benefits to many (society, scientists, future astronauts, etc.) but the risks are shared by a few (astronauts and their families), especially health risks. The astronaut corps can be considered an elite group of people, selected from a wide pool of willing candidates. Given the formation and training that the astronaut candidates receive once selected, it is difficult to claim that they are not aware of the risks for space flight and that they are not consenting to them.

The approach of NASA and other space agencies to address Mars as an exploration destination for astronauts is to offer a mission specific waiver for astronauts in such missions. Thus, explicitly informed consent will be needed for each member of a potential crew. As of today, only NASA allows for such a process, although other space agencies seem to agree with this approach.[4] It is highly probable that NASA will lead the way on this issue as the US has more mature plans for future space exploration. Thus, the US response to the problem will most probably define the responses of other agencies.

NASA has asked a committee of experts, brought together by the National Academies of Sciences, Engineering and Medicine (NAS), to review the current process for assessment and management of long-term risk with respect to cancer for crews (NAS 2021). The committee, which was comprised of experts in several related fields, such as radiation dosimetry, clinical oncology, biostatistics, physics, risk communication and management as well as former astronauts, offered recommendations to the agency. The full report also discusses NASA's plan to move to a different exposure limit standard, which will increase allowable career exposure limit that is common for all astronauts (male and female). The standard in question still remains more conservative that other space agencies with a unified approach (600 mSv for all, as opposed to 1000 mSv that is the standard for other agencies, as seen in Table 9.1). However, even with the new proposed standard, Mars missions will still require a waiver, and thus the situation as seen in the previous sections, remains similar.

It is of interest to note some of the recommendations made to NASA by the NAS committee (2021), regarding ethical issues.

Recommendation 2: "*In the near future, NASA should re-examine whether to use risk of exposure-induced death (REID) or other metrics, or a combination of metrics, in setting the dose-based space radiation health standard. NASA should conduct an*

[4] Regarding China, no data on astronaut exposure limits or waiver procedures were readily available so this section might not apply to Chinese practises.

independent analysis of the validity of 3% REID and make explicit the agency's justification for the metrics they choose."

The key element in the above recommendation is the need to make explicit the justification for the metrics to be used, regardless of the standards. This is sage advice and the foundation for creating trust in the standards. The main issue in the case of astronauts is that the current standards differentiate between male and female astronauts, but the proposed future standard is a common standard (based on a 35-year-old female) that, given the physiological differences, will allow more exposure to young, female astronauts but less exposure to older, male astronauts (which they could have been allowed with the older standard). As such, there is a trade-off between equality of opportunity for all versus restrictions imposed on a subgroup. Thus, the need for disclosure on the justification of choice, which will make explicit the argumentation for the change and present the ethical arguments that were evaluated against each other, which will help reassure the subgroup that might feel that their opportunity is being unfairly diminished, and that their position has been considered.

For missions regarding a waiver, it was recommended to follow the previous recommendations of a work on Health standards for spaceflight (IoM 2014), and to "*Adopt an Ethics-Based Decision Framework, NASA should apply the relevant ethics principles and fulfil the concomitant responsibilities through a three-level, ethics-based decision framework that examines (i) decisions about allowing risk to astronaut health and safety in excess of that permitted by health standards, (ii) decisions about undertaking specific missions, and (iii) decisions concerning individual astronaut participation and crew composition*" (IoM 2014, Recommendation 4).

It is understood that current exposure standards cannot apply for future missions to Mars (and some Moon missions). Thus, a waiver is the only way forward. The proposed, ethics-based decision framework, will then be used to decide who can join which mission. The three proposed levels of decision in the framework concern:

(i) the decision that a waiver is indeed ethically acceptable, for which kind of missions and the criteria for the mission objectives and parameters for a waiver to be a possible option. This is necessary to minimise the use of a waiver and avoid a situation where all missions are indeed possible, given that a waiver can be granted.

(ii) The second decision level concerns each individual mission and whether it meets the criteria established in the previous level and thus a waiver is ethically acceptable. Finally,

(iii) the third decision level, which includes the crew composition for the selected mission. The objective here is to acquire *informed consent* and thus, it is necessary to provide as complete information as possible on flight risks, risk management plans and also the state of research knowledge that has informed the risks. The complete framework and decision points can be seen in the IoM report (2014, 145–150).

The way to communicate such risks to astronauts was also a main consideration in the more recent report (NAS 2021). The current paradigm is to use REID (Sect. 9.2.2)

and distribution statistics based on age and gender. As an example (NAS, figure S-2), the risk associated with an effective dose of >600 mSv and thus above the NASA allowable limits, is indicated, highlighted red, as: High Risk—requires Agency Waiver—REID >2.27% mean (0.6, 7.8%) 95% CI for a 35-year-old female.

Even though astronauts are highly trained individuals, with advanced knowledge of risk statistics, it seems that even amongst astronauts the above type of communication is still confusing; effective dose as the main communicating tool would be preferred (NAS 2021, 14). It is interesting to note that it seems (based on discussions between active astronauts and the committee) that communication regarding reproductive health and possible issues from exposure might influence decisions in context for astronauts. The recommendations regarding risk communication to NASA were to:

- Assess and communicate risk at an individual level (rather than generic) for all astronauts
- Follow up the statistical presentation of risks with individualised discussion and answers to possible questions, in order to address questions from individual astronauts.
- Provide access to addition information as needed.
- Develop risk-based communication that is based on what astronauts want, how they process risk information and identify who and what are the most effective sources of information for them.

9.4 Conclusions

Transparency and full informed consent are critical in decision making regarding future exploration missions, even in the context of highly motivated individuals, such as the astronaut corps. It is highly unlikely that there will be no volunteers for a mission to Mars; the opposite is more likely. That, however, does not alleviate the ethical requirement of volunteers to have consented to be placed in such a situation.

There is another concern regarding future space exploration that has to do with the nascent era of commercial space flight. The year 2020 saw the first commercial crewed flight to the ISS, with the Space-X Demo 2 mission.[5] In early 2021, the same spacecraft, Dragon from SpaceX, carried, in addition to the US astronauts, one European and one Japanese astronaut to the ISS.[6] 2021 also saw the first suborbital flights from Virgin Galactic and Blue Origin, which were highly publicised as the respective CEOs were on board. However, both these flights were suborbital, as they did not achieve orbit, but rather flew close to the "edge of space", the Kármán line, an altitude of 100 km that defines the boundary between the beginning of space and Earth's atmosphere (this is an artificial boundary and does differ between nations. Blue Origin's New Shepherd vehicle flew above 100 km and Virgin Galactic's Unity

[5] https://www.nasa.gov/image-feature/demo-2-launching-into-history.

[6] https://www.lefigaro.fr/sciences/thomas-pesquet-a-ete-mis-sur-orbite-par-spacex-20210423.

22 flew below it).[7] Given the brevity of the suborbital flights (4–5 min of microgravity), the issues with exposure discussed in this article do not apply and thus suborbital space tourism is not considered at present.

Commercial spaceflight, and in future commercial space exploration, do need to be considered. There are discussions for commercial crew missions to the Moon and Mars as well, although currently, it is difficult to gauge their preparedness level. SpaceX does indicate future missions on its website to Moon and Mars with their Starship design (see for example: https://www.spacex.com/human-spaceflight/) but as of August 2021, there are not many details about these missions. Nevertheless, one can imagine that given the effects of radiation on the human body and that ill effects can manifest after several years or decades of someone exposed to radiation in space, it might be difficult for commercial companies to offer comprehensive informed consent information to potential astronauts, as they may not have the necessary data. Currently, only the national space agencies can dedicate resources to investigate the uncertainty regarding space radiation effects. Thus, space agency astronaut guidelines, standards and procedures may be adopted by potential commercial endeavours or at least be available as the "industry standard".

The conclusion from this case study is an extrapolation from the very specific group of people that constitute the astronaut corps. If candidates to be the first human to reach Mars or to walk on the Moon once again, still prefer fully informed consent procedures to be put in place, it is therefore evident that such a process should follow any decision regarding any group that is tasked with performing an action that will inherit some sort of risk. Policy makers, as representatives of society in such situations, need to ensure that society demonstrates its appreciation and support to the ones it asks to put themselves in harm's way, by ensuring that they do it knowing the full reasons and consequences of doing so. Thus, public agencies need to be constantly mindful of the ethical implications of their work, incorporate ethical decision making where relevant and ensure a continuous discursive engagement regarding the societal state of what is considered ethical.

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