Biopreservation Beyond the Biosphere: Exploring the Ethical, Legal & Social Implications of Suspended Animation in Space

Roel Feys[1], *Korkut Uygun*[2], *Irina Filz von Reiterdank*[2], *Susan M. Wolf*[3], *and Rosario Isasi*[1]

1. UNIVERSITY OF MIAMI , MIAMI, FLORIDA, USA. 2. HARVARD UNIVERSITY, BOSTON, MASSACHUSETTS, USA. 3. UNIVERSITY OF MINNESOTA, MINNEAPOLIS, MINNESOTA, USA.

Keywords: Biopreservation, Hibernation, Suspended Animation, Space, Astronaut, Research Ethics, ELSI

Abstract: In the evolving field of advanced biopreservation technologies, the development of suspended animation (SA) is inspired by real-world challenges. In the context of space exploration, SA is seen as a solution to enable humans to undertake missions far beyond low Earth orbit, including routine travel to other planets in our solar system and beyond. While work on the socio-ethical and legal implications (ELSI) of space exploration continues to evolve, NASA has committed to make ethics a priority issue, making this a fruitful field for further examination.

I. Introduction

From the Hibernaculum in *2001: A Space Odyssey* (1968) to the Hypersleep Chamber in *Alien* (1979) and the hibernation pods in *Passengers* (2016), suspended animation (SA) figures prominently in science fiction. These imaginary depictions of SA are inspired by real-world challenges. The distances spacecrafts must travel to reach other planets, let alone other stars, are vast. For example, a one-way journey to Mars, one of Earth's closest neighbors, takes six to nine months using current propulsion technology.[1] En route to other planets in our solar system and to other planetary systems, astronauts will face physical and mental

Roel Feys, Ph.D., *is an ELSI Research Associate at the John P. Hussman Institute for Human Genomics, University of Miami Miller School of Medicine.* **Rosario Isasi, J.D., M.P.H.,** *is Associate Professor of Human Genetics and Adjunct Professor of Law in the Dr. John T. Macdonald Foundation Department of Genetics, the John P. Hussman Institute for Human Genomics, and the Interdisciplinary Stem Cell Institute, University of Miami Miller School of Medicine and School of Law.* **Korkut Uygun, Ph.D.,** *is Associate Professor of Surgery (Bioengineering), Harvard Medical School; Deputy Director of Research, Shriners Hospitals for Children; Director, Cell Resource Core, and Director, Organ Reengineering Lab, Center for Engineering in Medicine & Surgery, Massachusetts General Hospital; and Director of Research, NSF Engineering Research Center for Advanced Technologies for Preservation of Biological Systems (ATP-Bio).* **Irina Filz von Reiterdank, M.D.,** *is a Research Fellow at Harvard Medical School and Massachusetts General Hospital.* **Susan M. Wolf, J.D.,** *is Regents Professor; McKnight Presidential Professor of Law, Medicine & Public Policy; Faegre Drinker Professor of Law; Professor of Medicine, University of Minnesota; and Lead, Ethics & Public Policy component, NSF Engineering Research Center for Advanced Technologies for Preservation of Biological Systems (ATP-Bio).*

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics. DOI: 10.1017/jme.2024.148

health challenges due to the inhospitable environment of outer space and the living conditions aboard their craft, challenges that will be exacerbated on missions lasting months or even years.

Cognizant of these obstacles, scientists have contemplated the possibility of SA since the start of the Space Age. In 1954, Hubertus Strughold — a Nazi physician who migrated to the United States as part of Operation Paperclip — first introduced the concept of cold hibernation to space medicine.[2] As early as 1958, Wernher von Braun, a vocal supporter of Mars exploration, suggested hibernation could help to solve the physiological and psychological problems astronauts would experience during a voyage to Mars.[3] More recently, NASA has funded studies on the architecture of a "torpor-inducing Mars transfer habitat"[4] and the hibernation of Arctic ground squirrels.[5]

On Earth, biopreservation technology is sought as a solution to extend the storage times of organs for transplantation and to stabilize patients in critical condition after a mass casualty incident.[6] While SA of whole human bodies belongs to the realm of science fiction for the time being, biopreservation research is advancing rapidly. The hope is that SA technology will someday enable humans to undertake missions far beyond low Earth orbit (LEO), so-called "exploration missions,"[7] including routine travel between Earth and other astronomical bodies such as Mars.

SA, hibernation, and biopreservation are terms that, while related, each denote distinct concepts within the field of biological preservation. SA refers to the deliberate slowing or halting of life processes by external means without causing death, allowing for later reanimation. This term is often used in medical or futuristic contexts where metabolic activities are drastically reduced, including in methods such as vitrification. Hibernation, in turn, describes a naturally occurring state of reduced metabolic activity in animals, facilitating survival during periods of scarce resources or extreme environmental conditions. Biopreservation encompasses the extension of viability and integrity of biological tissues, including cells, organs, and entire organisms, through processes like cryopreservation. Although SA and hibernation share conceptual similarities in reducing metabolic functions to preserve life, they are not synonymous due to their differing origins — artificial induction versus natural occurrence. To ensure clarity, our discussion will employ the term "suspended animation" (SA) for the preservation of whole organisms, including human beings, and the term "biopreservation" for the preservation of isolated tissues, cells, and organs.

In this article, we discuss the ethical, legal, and social implications (ELSI) of SA applied to astronauts, proposing an ELSI framework. We use the example of astronaut SA to elucidate several key ELSI issues posed by crewed space exploration. We begin by discussing the rationale for astronaut SA, providing an overview of the health challenges of space travel and the expected benefits of SA for astronauts. We then look at the current state of SA research and make recommendations for a framework to identify, analyze, and mitigate ELSI and governance issues in the development of biotechnologies for space travel. We limit our analysis to issues that emerge from the use of SA by professional astronauts in preparation for and during early exploration missions. Hence, our analysis excludes potential ELSI issues that could arise earlier in the development of the technology (e.g., in animal testing[8] and earthbound research on non-astronauts) or in terrestrial applications. Our rationale for doing so is twofold: First, ELSI issues arising early in the development of SA are covered by current research on advanced biotechnologies and existing regulations on animal and human subjects research. Second, SA is a nascent technology that will take decades to develop. The technical and ethical challenges along the translational pathway are formidable and uncertain, but focusing on the transition from Earth to space allows for a preliminary conceptual analysis of the ELSI issues. Moreover, our proposed ELSI framework is largely focused on the US context, while the recommendations could be extrapolated to the international context.

In this article, we discuss the ethical, legal, and social implications (ELSI) of SA applied to astronauts, proposing an ELSI framework. We use the example of astronaut SA to elucidate several key ELSI issues posed by crewed space exploration.

Given our focused scope, we center on the technology to be used by professional astronauts, thus pur-

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

posely excluding issues specific to "spaceflight participants" or space tourists on commercial missions.[9] Moreover, the development and use of SA will most plausibly be carried out under the auspices of a government space agency (e.g., National Aeronautics and Space Administration (NASA), China National Space Administration (CNSA), or Roscosmos State Corporation for Space Activities (Roscosmos)). We thus frame our arguments in the context of NASA-led efforts. We hypothesize about missions that will take place in a distant future. In the decades to come, we can anticipate that public-private partnerships may become more complex and private actors — in the United States or abroad — may ultimately take the lead in space exploration. Technological breakthroughs in the context of an accelerating international and multi-actor space race will inevitably pose complex ELSI issues, testing the adequacy of current ethical and governance frameworks. For instance, competing interests between public and private actors could intensify. The issues we identify and the recommendations we propose will serve as a useful starting point for discussion.

II. Scientific Rationale: *Why* Develop Suspended Animation Technology for Astronauts?

Homo sapiens is a species not designed for space flight. Modern humans — and their ancestors — evolved under the boundary conditions present on Earth, including standard gravity (1 *g*) and the planet's geomagnetic field.[10] As a result, humans face a host of physiological and psychological challenges when traveling to outer space. NASA uses the acronym "RIDGE" to summarize the health challenges posed by the conditions of space: Radiation, Isolation and confinement, Distance from Earth, Gravity fields, and hostile/closed Environments.[11] The distance and duration of exploration missions not only compound these issues, but are the primary reason for the development of SA, as it will take months, years, or even decades for astronauts to reach their destinations. SA has the potential to mitigate RIDGE issues.

Exposure to space radiation is one of the most hazardous aspects of both short- and long-term human space travel.[12] Prolonged exposure to space radiation can result in damage to several physiological systems, leading to an increased risk of cancer, cardiovascular issues,[13] and neurological disorders.[14] When it comes to the short-term impact of space radiation, researchers are particularly concerned about the risks posed by major solar or galactic cosmic ray events, which can lead to radiation sickness and even death. Lower doses of radiation still pose risks, as even mild symptoms can impact astronauts' ability to perform their tasks.[15] Shielding can protect against the harmful effects of space radiation but leads to other design challenges when it comes to so-called "upmass" limitations.[16] SA has the potential to markedly slow down or even halt astronaut cell division and metabolism, thereby averting damage done by radiation, which mostly occurs in dividing cells. However, repair mechanisms will also be slowed down and, therefore, damage upon reawakening may not be reduced.[17] Still, SA techniques using liquids or ice formation could provide physical protection barriers against space radiation.

The gravity fields to which astronauts' bodies are subjected vary, for example on a mission to Mars: weightlessness during the journey, Martian gravity (1/3 *g*) at the destination, considerable gravitational force equivalents (*g* forces) during launch and reentry, and Earth's gravity upon return.[18] Weightlessness, also called microgravity, causes a number of physiological changes.[19] The spaceflight environment causes musculoskeletal issues such as bone density loss, muscle loss, and joint damage.[20] The brain is also affected in its ability to process balance and movement.[21] When astronauts move from one gravity field to another, they face new health challenges, some minor (e.g., spatial orientation, orthostatic hypotension) and others serious (e.g., bone fractures, cardiovascular disease).[22] A combination of a specialized diet, exercise, and certain medications can mitigate some of the adverse effects.[23] SA has the potential further to reduce the negative impact of gravity fields as it reduces metabolism and the pathological mechanisms described.

Isolation and confinement, distance from Earth, and closed environments pose interrelated health challenges. Astronauts' immune systems are adversely impacted by the lack of a circadian rhythm and inadequate nutrition, while pathogens behave differently under spaceflight conditions, increasing the risk of illness.[24] Astronauts' mental well-being can suffer from isolation and the constant noise produced by the systems running aboard spacecraft, as the vacuum of space traps sound inside the vessel. SA has the potential to induce a "sleeping" state where astronauts would not require nutrition or be disturbed by their environment.

Some of the adverse effects of spending extended periods in LEO are longer term (e.g., attenuated cognitive function, alteration in certain genes' expression levels),[25] but most disappear once astronauts return to Earth. However, exploration missions pose challenges beyond those encountered during even the longest stays aboard Mir (437 days) and the International Space Station (ISS) (371 days),[26] stations circling the

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

planet in LEO and enjoying the protection of Earth's magnetosphere. SA may be able to attenuate some of the adverse effects.

The impact of the space environment and existing countermeasures on astronauts in LEO are well documented, even if the biological mechanisms are not always fully understood, but the same is not true for travel beyond the Van Allen belts, which protect Earth against high-energy radiation from the sun and galactic cosmic rays. The first mission beyond the Van Allen belts was Apollo 8 in 1968 and the most recent crewed mission beyond LEO was Apollo 17 — over fifty years ago (1972).[27] While current knowledge of space travel could be extrapolated to prolonged missions to the Moon and beyond, there is almost no data "on the risk owing to radiation exposure associated with exploration missions beyond the protection afforded by Earth's magnetic field, including the differences between a 1-year spaceflight in LEO and a 3-year Mars mission."[28] Crewed deep-space missions — during which astronauts will spend months, years, or even decades beyond LEO – will involve "known unknowns" as well as "unknown unknowns." The former are known risks of unknown extent (e.g., biological response to extreme temperature changes under conditions of deep space) and the latter are unforeseeable risks.[29] These unknowns must be addressed in program and policy decisions. SA can provide a solution to some of these risks, but the technology itself will be a source of unknowns.

III. The State of the Science and Path Forward

Since the use of SA in space travel lies in the distant future, how each step of the translational pathway will unfold is uncertain. Examining analogous medical conditions on Earth can provide insights into and solutions to challenges encountered in space. For example, osteoporosis bears similarities to space-related bone loss, muscle atrophy is seen after immobilization due to fractures or surgery, and organ preservation is critical in transplant surgery. Considering familiar health conditions and their treatment can elucidate promising approaches in space. These insights pave the way for implementing and refining biopreservation strategies that are critical for space travel.

In transplant surgery in particular, a range of biopreservation strategies that make use of cold temperatures are currently being developed for whole organs, often inspired by nature.[30] Using an ice-free, supercooled state, extended preservation of animal and human organs has been achieved, increasing organ preservation times from hours to days.[31] Drawing inspiration from the wood frog (*Rana sylvatica*), controlled ice-formation of small animal livers has enabled successful partial freezing up to five days.[32] Building on these successes, partial freezing is currently being translated to porcine and human livers, pushing the boundaries as far as ten days, more than 20-fold the current preservation time.[33] The longest organ preservation presently reported is the months-long storage of rat kidneys, which were then successfully transplanted.[34] The organs were stored for 100 days using vitrification, a technique in which freezing occurs so rapidly that instead of ice crystals, a glass-like state is achieved, enabling the potential for years-long preservation.

While the described cooling techniques focus on separate organs, steps have been made to translate the technology to Vascularized Composite Allografts (VCAs), grafts that are composed of multiple tissue types. Researchers have demonstrated success in storing animal models up to two days, instead of six hours using traditional cold storage.[35] Translation to such composite organs is the first step to whole body SA, as it combines knowledge of preserving diverse individual tissues. The work of researchers like Kenneth Storey and colleagues has been pivotal in illustrating how certain organisms naturally enter states of suspended animation or hibernation under extreme conditions. These studies provide valuable lessons on metabolic downregulation and stress tolerance, which are crucial for developing effective whole-body preservation strategies.[36] Understanding these natural mechanisms offers a roadmap for mimicking such states in humans, particularly in the context of protective strategies against extreme environments encountered in space travel. An exciting development in this direction, researchers recently achieved success in a large animal model, where whole-body Extracorporeal Membrane Oxygenation (ECMO) — not dissimilar to the more well-known heart-lung machine — was used one hour after cardiac arrest to resuscitate the organs and demonstrated cellular recovery by decreasing cell death and revealing molecular and cellular repair processes.[37] This is a promising step showing that application of techniques used in individual organs (e.g., machine perfusion) and techniques developed for different purposes (e.g., ECMO for ICU patients) can lead to breakthroughs in other fields as well (e.g., whole-body preservation).

From a scientific perspective, advances in the field of biopreservation can provide a foundation for the SA of astronauts, but will require adaptation to the unique challenges posed by the space environment. Expanding upon seminal findings in organ preser-

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

vation research, the next phases in the translational trajectory of SA for extraterrestrial applications could focus on the extraterrestrial viability of preserved organs. For instance, a liver subjected to partial freezing could be conveyed to a space environment for subsequent reanimation and functional analysis.[38] Another approach could be to preserve animal organs during a space mission and transplant them upon return to Earth, for in vivo functional assessment and direct comparison to time-matched organs preserved on Earth. To observe long-term function and survival of whole-body SA, small and, subsequently, large animal models could be used. Human investigations on whole-body SA could initially encompass the use of decedent models, in particular, donors after brain death (DBD), extrapolating from normothermic regional perfusion (NRP) methodologies.[39] This phase would aim to elucidate integrated organ system preservation dynamics. Even if the above steps were to be taken and successes were achieved, the technological and ethical hurdles to overcome to make SA of astronauts a reality would be immense. Protecting the brain in the context of whole-body SA emerges as a major challenge. The task of preserving neural tissue integrity and functionality over extended durations presents formidable scientific obstacles, stemming from the intricate nature of neural networks and the fundamental importance of the brain in maintaining consciousness and identity. However, with limited work having been done in this field, the scientific and ethical complexities are outside the scope of this article.

Strategies to overcome these hurdles may not be dissimilar to those shown in science fiction. Intravenous infusions would likely be necessary for controlling body temperature, as well as timely administration of medications to prevent adverse effects such as bone, muscle, and cartilage loss. That medication could be administered either preventatively prior to the cooling phase, throughout preservation, or as part of the reanimation phase. Reanimation will likely be much slower than depicted in science fiction and may resemble care in an ICU, in which astronauts recover from muscle atrophy, ischemia-reperfusion, and chilling injury over the course of days, weeks, or even months. Next, psychological reorientation as well as physical rehabilitation and adjustment to the “awake” state would follow. Preservation will have to be stable and reliable, not sensitive to environmental factors such as vibrations and *g* forces. Necessary equipment will need to be small and light enough to fit aboard a spacecraft. Furthermore, astronauts will have to be able to initiate and end biopreservation themselves or through automated systems which do not require medical personnel. Additionally, these SA techniques will need to work in a microgravity environment.

IV. Space ELSI Research: No Giant Leap … Yet

ELSI research is still young; it became an independent field of study in the context of the Human Genome Project in the early 1990s. Nevertheless, NASA has considered the ethical, legal, and social implications of its activities since the agency’s inception in 1958.[40] For example, NASA is a signatory to the Common Rule, requiring NASA to have an Institutional Review Board (IRB) to oversee human subjects research.[41] To ensure experiments on international missions (e.g., aboard the ISS) are conducted in a safe and ethical manner, NASA has been cooperating with its partner agencies in the Human Research Multilateral Review Board (HRMRB) for decades.[42] The agency’s ongoing interest in ethical, legal, and social issues is also reflected in its policies and commissioned reports, some of which are highlighted below. However, NASA has expressed relatively little interest in ELSI research applied to emerging technologies pertaining to astronauts, at least publicly.

Existing ethical, legal, and social research on space travel can roughly be divided into three categories: current NASA policies, reports commissioned by NASA, and more visionary research on the future of humanity as a spacefaring species. In addition, there is a small body of literature that more explicitly addresses specific issues in space exploration from an ELSI perspective, including papers by Sara Langston on commercial human spaceflight and some of Konrad Szocik’s work on human genetic enhancement for space travel.[43] While the existing literature does not explicitly address ELSI related to SA, that literature provides the background for our discussion of astronaut SA.

Many NASA policies and documents touch on ethical, legal, and social considerations, albeit often implicitly and not through an explicit ELSI lens. Examples are the most recent iterations of NASA’s *Protection of Human Research Subjects* documentation (2022), *NASA Space Flight Human-System Standard: Volume 1: Crew Health* (2022), and *NASA’s Moon to Mars Strategy and Objectives Development* (2023).[44] They range from directly addressing ethical concerns surrounding human subjects research conducted by NASA to listing objectives to guide the development of the technology needed to return to the Moon and travel to Mars (e.g., “return crews safely to Earth while mitigating adverse impacts to crew health”).[45] NASA

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

has considered the ethical and social implications of the Apollo program and, more recently, looked at the agency's historical impact on society (2007).[46]

Since the 1970s, NASA has tasked the National Academies of Science, Engineering, and Medicine (NASEM) to produce reports to assess and make recommendations on certain of its activities, including ethical considerations related to crewed space flight. Two consensus study reports by the Institute of Medicine (the predecessor to the National Academy of Medicine) are of particular interest, *Safe Passage: Astronaut Care for Exploration Missions* (2001) and *Health Standards for Long Duration and Exploration Spaceflight: Ethics Principles, Responsibilities, and Decision Framework* (2014).[47] The analysis and recommendations of the latter serve as an inspiration for our own arguments. However, that report focused on the development of health standards as specified in *NASA Space Flight Human-System Standard* (Volumes 1 and 2).[48] Moreover, while many of the report's conclusions are relevant to SA, *Health Standards* is a decade old and does not explicitly consider the use of new biotechnologies.

In April 2023, the agency convened a workshop on Artemis and ethics. The workshop considered the ELSI of NASA's efforts to return to the Moon and to travel to Mars, resulting in the report *Artemis, Ethics, and Society: Synthesis from a Workshop* (2023). Unfortunately, the report is of limited use to our current discussion, as it focuses heavily on the return to the Moon and does not consider the ELSI issues raised by the emerging science and technologies that will be required for exploration missions, such as SA. Nonetheless, several of the report's general recommendations are relevant, including the need for NASA to reflect on core values to shape newly engineered systems. In particular, *Artemis* addresses common ethical principles, such as sustainability, benefit sharing, and equity in access. Importantly, the report calls for addressing cultural sensitivities, such as issues that will arise from payloads carrying human remains to the Moon, as the Moon is considered sacred by some communities.[49]

A third body of literature examines the future of humanity as a spacefaring species, reflecting on the inevitability of humanity's colonization of space considering existential threats on Earth, and the resulting need for humans to evolve to cope with their new space environment. The argument, discussed in most detail by Szocik, is that humans will have to be genetically engineered in order to adapt to the harsh conditions of outer space, and that these modifications would constitute preventive therapy rather than enhancement.[50] While the time horizon for these developments is distant, Szocik and others cited above raise questions that are relevant to the development of an ELSI framework for SA and other biotechnologies that may be needed for space exploration, for example, concerning the uniqueness of the bioethics of space exploration and the justification for the use of biomedical technologies to protect against the space environment.

V. The ELSI of Astronaut Suspended Animation in Space

The development of SA for use during exploration missions raises ELSI issues relating to the distinction between research and practice, particularly when it comes to the role astronauts play in developing biotechnologies for deep-space missions. Key concerns are informed decision-making, risk-benefit tradeoffs, and astronaut privacy. Moreover, the ELSI issues surrounding astronaut SA point to substantial governance issues related to research on human beings in the context of space exploration, specifically cutting-edge biotechnological research.

A. Space Exploration: Research, Practice, and Experiment

The distinction between research, practice, and experiment is most famously and succinctly discussed in *The Belmont Report* (1979), which summarizes ethical principles and guidelines for human subjects research.[51] It is worth noting that the report's authors preferred the term "innovation" over "experiment," because of the negative historical connotations of the latter. Innovations refer to untested procedures that depart significantly from standard or accepted practices. However, we choose to use the term "experiment," because it captures the unique and complex scenario of first use of new technologies in aerospace (e.g., experimental aircraft), which might not be subject to a formal research protocol nor established standard practice in the industry. The authors of *The Belmont Report* pointed out the difficulties of distinguishing between the categories of research, practice, and experiment. As we will see, this distinction is even harder to conceptualize and navigate in the context of space travel. Unsurprisingly, issues surrounding research, practice, and experiment are discussed throughout the space exploration literature, with *Safe Passage* and *Health Standards* being prominent examples.[52] However, these issues are not systematically elucidated in terms of the three categories and the corresponding ethical and regulatory frameworks. Addressing the distinctions is important in the analysis of space innovation and research. Despite develop-

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665.

ments in research ethics since *The Belmont Report*, and criticisms of the report,[53] we believe a "back-to-basics approach" is useful to facilitate discussions of SA-related ELSI issues in the context of crewed space exploration.

The Belmont Report defines research as the systematic testing of hypotheses with the goal of developing generalizable knowledge, while (clinical) practice refers to health interventions with the aim of restoring or enhancing an individual's well-being with a "reasonable expectation of success."[54] Astronauts engage in both research, as participants or human subjects in research protocols, and practice, as recipients of established interventions to maintain their well-being. For example, astronaut participation in a protocol to test a hypothesis for clinical care on Earth is research, but astronaut use of accepted pharmacological countermeasures to mitigate the adverse health effects of the space environment is practice.[55] Many activities, however, do not fit the research-versus-practice binary mold and may be both. To illustrate, the routine collection of astronaut health data can be used to monitor an individual astronaut's health and, if necessary, to intervene in their care. However, the same data can also be used to generate knowledge to better monitor, diagnose, and treat astronauts on future missions. The third category, experimentation, is relevant as well. In the process of developing and first using technologies, certain astronaut activities are experimental, meaning the astronaut uses new and (partially) untested technologies in a manner that departs from standard practice, whether on Earth or during spaceflight. As *The Belmont Report* states, "The fact that a procedure is 'experimental,' in the sense of new, untested or different, does not automatically place it in the category of research."[56]

The question is how the development and use of SA — and other new biotechnologies — relate to the categories of research, practice, or experiment. The answer depends on where along the translational pathway the technology is and whether it is being researched, used, or tested. In general, the early development of SA should be research, while the routine use of the technology on journeys to Mars and beyond will eventually be considered practice. Meanwhile, early uses of the technology will plausibly be experimental, given that SA may have gone through a research phase but still not be accepted for routine use, especially for prolonged travel beyond LEO. As we have seen, however, determining where exactly the boundaries between research, practice, and experiment lie is difficult. Indeed, it is possible to move back and forth along the translational pathway. For example, while the first version of SA may be entering routine use, scientists may be researching an upgraded version of the technology.

Given the tension between research, practice, and experiment in the development and use of advanced biotechnologies for spaceflight, central questions should be: Which safeguards should be applied, specifically if using SA for space exploration? Are such measures adequate? Do such protections also consider the collective or societal implications? And how will they impact benefit sharing and stewardship of resources?

Difficulty distinguishing research, practice, and experimentation pervades the space literature. For instance, the authors of *Health Standards* base their discussion of ethics principles for health standards for space travel on the ethics of research involving human participants on Earth, drawing parallels between human subjects research and the 'practice' of human spaceflight (e.g., in considering risk-benefit, informed consent).[57] Along the same lines, Ashle Page argues that principles used for biomedical research on Earth should be applied to human space exploration (i.e., autonomy, justice, beneficence, and nonmaleficence).[58]

The reflex to extend Earth research ethics to space practice is understandable. Not only does the approach err on the side of granting astronauts more protections, but research ethics offers a familiar toolbox for space ethics. However, it is important to highlight the differences between research ethics and space practice, which in many instances more closely resembles the third category of experiment.

Space ELSI research needs to further elucidate the three domains, but also map the relationships between them in the context of space exploration. While theoretically separating the spheres is important to identify and mitigate conceptual issues that arise in each

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

sphere, it is equally important to remember that these distinctions are inevitably going to be somewhat problematic when applied to space travel. As we have seen, there are good reasons to apply research ethics to space, but this approach risks insufficiently addressing the unique features of space exploration, leaving the ELSI of space practice undertheorized.

Given the tension between research, practice, and experiment in the development and use of advanced biotechnologies for spaceflight, central questions should be: Which safeguards should be applied, specifically if using SA for space exploration? Are such measures adequate? Do such protections also consider the collective or societal implications? And how will they impact benefit sharing and stewardship of resources? Which governance mechanisms should be established? As stated above, the main concerns should be whether astronauts are afforded appropriate health and ethical safeguards, as well as whether there are robust governance mechanisms to monitor such protections and consider the ELSI of the activities.

B. Astronauts: Research Participants, Professionals, and Testers

The difficulty of distinguishing between research, practice, and experiment is mirrored in the potential triple role of the astronaut as research participant, professional, and/or tester. In the context of the development and first use of new biotechnologies for space exploration, one of the key challenges is to pinpoint the role of the astronaut, as astronauts can seemingly fulfill any of these three roles at any time. However, astronauts' rights, responsibilities, and protections — whether ethical or legal — plausibly differ depending on their role. While the triple role of the astronaut is often acknowledged in the literature, or at work in the background, the distinction is rarely analyzed.

As research participants, American astronauts are protected under the Common Rule (45 C.F.R. part 46 Subpart A), for example, when they are participating in an approved research protocol aimed at generating new knowledge on board the International Space Station (ISS).[59] The Common Rule provides a robust set of protections for research subjects. These protections plausibly extend to astronauts participating in research of advanced biotechnologies, like SA. However, the extension of the Common Rule beyond research protocols is problematic. Consider, for example, early use of SA during an exploration mission but after the initial research — a set of circumstances that resembles Chuck Yeager breaking the sound barrier or Alan Shepard journeying into space for the first time. Yeager and Shepard were test pilots (even if the latter was called an astronaut once he joined Project Mercury) and their role may best fit in the category of experimentation. Similarly, the first astronauts to use SA during an exploration mission might be considered testers rather than research participants, or maybe they will be both at the same time. Astronauts will be using a still novel technology (untested under the conditions of prolonged use in deep space) to reach their destination, but telemetric data collection to create generalizable knowledge will also take place. Of course, astronauts are also professionals who go through rigorous training to develop a highly specialized skill set to perform a very specific role, that is, to crew a spacecraft. Only when exploration missions using SA become routine, will astronauts exclusively be professionals making use of an established technology to do their job, as exotic as both job and technology may seem today — at least, until a next major technological breakthrough in space exploration pushes them in the role of research participant and/or tester, again triggering questions about appropriate ethical safeguards and governance.

How should we determine which role the astronaut is playing at a given time — participant (research), professional (practice), and/or tester (experiment)? In space, there may be a unique overlap and interplay among these categories. Szocik calls the space environment a "new moral ecology."[60] While existing moral principles and rules still apply, they are used in a new and dangerous environment, requiring flexibility in their application to a point that may conflict with moral intuitions and habits on Earth. Similarly, Paul Wolpe argues that space bioethics is akin to practicing ethics in other extreme environments, such as Antarctica or extreme-altitude mountaineering.[61] For new space technologies, such as SA, drawing clear lines between research, practice, and experiment can be difficult.

So what rights, responsibilities, and protections should astronauts enjoy in their roles as research participants, testers, and professionals? *Safe Passage* argues for an occupational health model, thinking of astronauts primarily as employees rather than research participants and granting them fewer protections, while *Health Standards* (2014) uses research ethics as the model to develop astronaut health standards. While providing astronauts with more rather than fewer protections has much to commend it, the health research model does not neatly translate to the role of the astronaut as tester and professional. Even if we grant that astronauts on space missions should be covered by protections similar to those enjoyed by research participants in biomedical research per-

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

formed on Earth due to the similarities between these activities, the protections might differ to accommodate the realities of space travel. For example, are astronauts as government employees able to provide voluntary and informed consent? Are potential conflict of interest issues (employer-employee-research participant) properly addressed? Is there an appropriate balance of benefits and risks? What would withdrawal of consent look like? An astronaut who chooses to withdraw from a SA study on Earth in preparation for an exploration mission should be able to do so, but an astronaut who does not want to hibernate while their craft is en route to Proxima Centauri may not enjoy the same protection, but instead may have the responsibility to enter a state of SA to ensure mission success and crew safety.

The ethical questions surrounding the role of the astronaut have corollaries in the legal questions, "Who is an astronaut?" and "What is their status according to space law?" The legal literature, which tries to define who is an astronaut based on international space treaties and national space law, does not adequately address the issue of astronauts as research subjects.[62] Instead, legal scholarship focuses on the role of the astronaut as "personnel" aboard a spacecraft, thus emphasizing their role as professionals or employees, which in turn has implications for astronauts' rights, responsibilities, and protections.[63] The discrepancy between the ethics and legal literature shows a need for more work to bridge ethical issues and regulatory concerns, including by considering international treaties, national legal frameworks, or institutional policy.

The role of the astronaut needs to be further explored and defined, both ethically and legally, to determine astronauts' rights, responsibilities, and protections. It is clear the astronaut's role is dynamic and complex, requiring a model that moves beyond the dichotomy between research and occupational health, while at the same time drawing on both models. Astronauts should be key stakeholders in this process of defining their role and in the development of crewed space strategy, addressing the ethical issues surrounding exploration missions.[64] Governance mechanisms will be needed to ensure that astronauts' interests are safeguarded and to foster accountability and trustworthiness.

C. Risks and Benefits: Beyond Acronyms

The use of SA, whether during its development process or on a mission, requires that NASA and the space community determine that the technology's risks and benefits are acceptable. The challenge is how to adequately assess the risks and benefits, given that both will be difficult to establish.

Risk assessment is central to the conception, development, and execution of NASA programs.[65] But how do NASA and the space community assess risks? In the literature, the acronyms ALARA and ASARP, which stand for "as low as reasonably achievable" and "as safe as reasonably practicable" respectively, are regularly cited as illustrative of risk assessment at NASA.[66] Both approaches involve a tradeoff between the safety performance of a technology and other variables, including the additional cost of an incremental improvement in safety (e.g., money, upmass) and "other societal and socioeconomic considerations."[67] However, these acronyms are often limited to use in a particular context (e.g., radiation exposure), at least historically. More importantly, by themselves these concepts are inadequate as a comprehensive approach to risk assessment. NASA's Risk Management program does provide a more systematic approach to governing agency-wide risk with the aim of reaching "an optimal balance between minimizing the potential for loss while maximizing the potential for gain (opportunity)," including in NASA's *Risk Management Handbook* (2011).[68] While a detailed discussion of NASA's approach to risk management is beyond the scope of this paper, the question is to what extent it is suited to assess and mitigate the risks involved in the development and use of SA or other advanced biotechnologies for space exploration that further complicate risk management. While NASA and the space community have experience with risk assessment and mitigation, disruptive biotechnologies add a new level of uncertainty and potential for harm, especially in the early stages of their development and use. Examples of these risks are practical challenges such as the stability of thermal states in space environments as well as medical challenges such as the long-term effects of biopreservation during space travel. They also raise questions about appropriate governance and oversight to iteratively assess evolving risk-benefit thresholds.

Assessing the potential benefits of SA is equally difficult, both when it comes to the technology itself and the broader justification for exploration missions. As we have seen, the major benefit of SA is that astronauts would be able to "sleep" en route to their destination, which could have psychosocial health benefits and confer protection against the space environment (e.g., radiation exposure), while at the same time solving certain technical issues (e.g., resource use, upmass). At this time, however, it is uncertain to what extent these theoretical benefits can be realized in practice. When it comes to some benefits, like protection

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

against the harsh conditions of deep space, researchers may only be able to fully assess the benefit during a mission, or even after the crew returns to Earth. This leads to a broader question about the value of crewed exploration missions given the risk and uncertainty involved. Why should we send astronauts to Mars and beyond? As former NASA Administrator Daniel Goldin often said, NASA is good at addressing *how* to proceed with space exploration, but does a poor job explaining *why*.[69] There are many potential justifications, from the expansion of scientific knowledge, to the exploitation of space resources, and the mitigation of existential risk.[70] Moreover, some of the technologies that are developed to explore space may have useful — or even lifesaving — applications on Earth, for example, the potential use of SA in emergency medicine. The question of the societal value of crewed deep-space travel becomes even more pressing in light of alternative exploration and exploitation strategies, such as uncrewed probes or AI-powered robots; these alternatives also factor into the risk-benefit tradeoffs surrounding exploration missions.

NASA and the space community have a long history of weighing risks and benefits, which includes reflecting on the risk-benefit tradeoffs surrounding exploration missions. Thus far, however, the agency has insufficiently considered the role that new biotechnologies will play in the exploration of deep space. These technologies will radically alter the assessment of the adequacy of consent and of the balance between risks and benefits, calling again for robust governance. As new biotechnologies move along their translational pathways, NASA and the space community should iteratively assess their risks and benefits relying on the input of the astronaut corps and the broader scientific community, including ELSI researchers. Langston, for instance, takes a first look at such an approach discussing risk governance in the context of commercial human spaceflight.[71] Moreover, NASA and its partners should engage in a broader societal debate about the value of crewed exploration missions, as this is a key factor in weighing risks and benefits individually and collectively.

D. Astronauts' Informed Decision-Making

The difficulties surrounding risk-benefit assessment feed into the issue of informed decision-making, which arises in the context of astronauts participating in SA research as well as crewing a mission that makes use of this technology. The issue of informed consent raises ethical concerns, centered around the principle of autonomy, as well as legal concerns, such as employment-related contractual issues of waiving liability.

Informed decision-making could be problematic when it comes to both astronaut participation in SA research and the use of the technology during a mission (i.e., practice). The issues are similar in both contexts, which goes back to the difficulty of distinguishing between research and practice. The broader question is how to model and implement informed decision-making in space science and exploration. As we have seen, the *Safe Passage* report presents this as a choice between the research and occupational health models, favoring the latter and suggesting the Common Rule needs to be reinterpreted when it comes to research with astronauts.[72] The translational pathway of SA points towards a more dynamic approach to astronaut-informed decision-making, where the consent process is more stringent early on, identical to or closely resembling consent in a research setting, perhaps becomes less demanding when the technology is used later on a space mission (experiment), and then still less so when SA is routinely used (practice). What this less-demanding consent when it comes to the use of new biotechnologies for space travel would look like exactly needs to be specified further.

Astronaut consent is problematic for at least three reasons: (1) As we have seen, the risk-benefit tradeoffs of using SA are poorly understood, to some extent inevitably so (for example, in first use of the technology on a crewed mission beyond LEO), making it difficult for astronauts to make informed decisions. Disclosing benefits and risks is essential for an adequate informed consent process. Szocik goes so far as to argue that informed consent can be ignored or is simply impossible to implement in the context of deep-space exploration.[73] Gibson stresses the importance of consent, but notes that consent can be overridden in certain circumstances (e.g., mandatory anthrax vaccination for military personnel), which may be extrapolated to space travel.[74] (2) The voluntariness of consent is a major concern, due to astronauts' fear of being removed from a (future) mission and their desire to "boldly go where no man has gone before," even if that requires them to make use of a novel technology in an extremely hostile environment. (3) Consent can presumably not be withdrawn. Astronauts will spend long periods in SA, whether to test the technology or en route to their destination, and during that time they cannot rescind their consent. A robust and prospective informed consent process will be needed to address this issue.

Of course, much will depend on the specifics of SA. For example, some animals are able to wake themselves from a state of torpor if necessary. When it comes to space travel, one might argue that astronauts already

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

find themselves in a situation where "their consent becomes binding and irrevocable at the moment the mission launches."[75] However, it is important to conceptually separate assent to mission participation from consent to SA, even if in practice the former appears to imply the latter. For example, an astronaut who enters SA en route to their destination may not want to do so on the way back, a refusal that would have serious practical implications (e.g., resource usage, control over craft) to the point that it raises the question of whether that astronaut can be forced to enter SA. This again requires assessing the triple role of the astronaut as participant (research), professional (practice), and tester (experiment), highlighting the importance of voluntary and informed decision-making.

The issue of informed decision-making also raises legal concerns about the possibility of contractually waiving liability. For example, does the doctrine of *volenti non fit injuria* apply? In lay language, can astronauts who knowingly and voluntarily risk danger bring a claim for any resulting injury? And can informed consent include all the necessary information to decide on a waiver of legally protected interests like life and health?[76] While these questions apply to all crewed spaceflight, they become more pressing in the context of exploration missions in general and the use of SA in particular.

E. No Privacy in Space?

The routine collection of astronauts' health data raises well-known privacy concerns. Space crews are small. To illustrate, for a mission to Mars a crew size of six or eight is considered ideal to accomplish mission objectives and to safely return to Earth.[77] However, small crew sizes make it easy to re-identify individual astronauts based on the data, even if efforts are made to protect confidentiality via de-identification approaches. The issue of privacy already arises in spaceflight (e.g., data collection on ISS), but will plausibly become more pressing with the introduction of SA, as use of the technology will imply the constant collection and communication of vast amounts of health data. The data that is collected by SA technology may also be qualitatively different from the data that is currently collected. For example, hibernation pods may be able to detect the early onset of serious health conditions (e.g., cancer) or even have access to astronauts' mental states (e.g., memories) through a brain-computer interface. Moreover, when in SA astronauts will find themselves in a particularly vulnerable position, without control over the collection process and their health data for prolonged periods of time, thus making their initial voluntary and informed consent imperative.

While privacy issues also arise in the context of defined research protocols, we focus on the routine collection of data by SA technology, given that the boundary between research and practice is blurry in space. When it comes to current data collection practices during spaceflight, opinions differ as to how to approach privacy concerns. The *Safe Passage* report identifies privacy as a key concern and discusses the issue at length. According to the report, astronauts have a strong incentive to keep their medical information private, as they do not want to be disqualified from participation in future missions, an issue we return to shortly. The culture of the astronaut corps, valuing stoicism and a can-do attitude, further reinforces the underreporting of health data. Rather than limiting the disclosure of health data to the flight surgeon, who is the astronaut's personal doctor in preparation for and during a mission, the report points towards exceptions to doctor-patient confidentiality in instances where a clinician's duties extend to an organization (e.g., the military) or the public (e.g., the requirement to report infectious diseases), while not specifically addressing ensuing conflict of interest issues.

In the case of space exploration, the routine collection of astronaut data has the potential to improve the health and safety of current as well as future space travelers. The authors of the *Safe Passage* report rely on Earth-based analogues for balancing confidentiality and public health (e.g., employees at the first nuclear power plant) to argue for an occupational health model for the governance of astronaut health data, including the routine collection of a variety of health data.[78] Walter M. Robinson, who served as a committee member for *Safe Passage*, echoes the report's conclusions, arguing that individual astronauts should cede some privacy in order to promote health and safety for the astronaut corps.[79] Wolpe, at the time NASA's Chief of Bioethics, nuances the privacy issues as presented by the Institute of Medicine and Robinson, noting that the incidence of astronauts refusing to report health data is quite low. While some sorts of data should indeed be collected within an occupational health model, he points to the problematic distinction between research and practice in space science to caution against applying the occupational health model across the board. The development and use of invasive or hazardous technologies require additional protections, including when it comes to data gathering, suggesting a health research model.[80]

At least initially, SA would be an invasive and hazardous technology, suggesting a health research approach to data collection and governance. However,

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

the technology would also allow for the routine collection of massive amounts of health data, some unrelated or unimportant to the further development of SA, reminiscent of an occupational health model. In other words, the introduction of SA would heighten the tension between the two models. From the astronauts' perspective, SA will cause them to lose control over much of their health data, which may lead astronauts to resist the technology, because they fear not being selected for future missions based on the collected data. To navigate the complex relationship between the occupational and research models, and to assuage astronaut concerns, NASA and the space community will have to rethink their approach to data collection and privacy protections.

F. Justice: Fair Crew Selection and Beyond

The Artemis homepage prominently states the program aims "to land the first woman and first person of color on the Moon," showing that diversity, equity, and inclusion (DEI) will be key considerations for NASA and the space community in making crew selection decisions for exploration missions.[81] This is not mere lip service to a DEI agenda. Research has shown that increased diversity among Earth-bound space mission teams can reduce risk, a result that plausibly translates to crews traveling into space.[82] Concerns surrounding fair crew selection feed into other justice concerns, as a career as an astronaut opens doors in science, industry, and policy. SA has the potential both to alleviate and to aggravate issues of justice.

Humans respond differently to the conditions of space travel in LEO, and this heterogenous response will likely be more pronounced during exploration missions. *Health Standards* discusses the possibility of excluding women from early exploration missions because they experience more adverse effects from exposure to the space environment (e.g., muscle loss, bone density loss). Others have suggested selecting space crews for exploration missions on the basis of genomic risk factors (e.g., radiation exposure) or from peoples who live in low-oxygen, high-radiation environments (e.g., the Himalayas).[83] While these proposals challenge our sense of justice, it is important to keep in mind that the loss or temporary disability of even a single crewmember can endanger mission success or threaten the safety of the entire crew. To minimize risk, NASA already uses a rigorous selection process for astronauts, excluding some from the opportunity to travel into space.[84]

SA has the potential to level the playing field for participation in exploration missions, provided that the technology can indeed protect astronauts against the space environment.[85] En route to their destination, astronauts will spend significant amounts of time in hibernation, which could limit the detrimental effects of exposure to the conditions of space, even if they will be awake — and be exposed — upon arrival. Of course, much as humans respond differently to space travel, they may show a heterogeneous response to SA, reinforcing existing inequities or creating new ones. While much will depend on the specifics of the technology, justice in general and equitable crew selection in particular can be considerations in the development of SA. For example, if there are two competing technologies, where one elicits a more heterogeneous response than the other, then equity could be a reason to invest in the latter. SA's potential to ensure equitable access to space could be an important motivation to develop the technology.

G. Broader Governance Challenges

The adoption of SA has implications beyond the astronauts who will test and first use the technology, as others will be impacted by the use and development of the technology, including astronauts' families, future astronauts, and NASA as the responsible institution. Much like the first landing on the Moon, initial exploration missions will engage the American public — and the global population — in concern over astronaut health and safety. For example, the serious injury or death of biopreserved astronauts could lead to a loss of trust in NASA, the space community, and the government.[86]

Health Standards points out that governance challenges are aggravated by the fact that NASA's structure has the potential to give rise to "significant conflicts of interest."[87] For example, the *National Aeronautics and Space Act* (1958) tasks NASA with the expansion of human knowledge of space (§102(c)(1)) as well as the improvement of space vehicle safety (§102(c)(2)).[88] With regards to SA, NASA is obligated both to engage in deep-space exploration, which may require the use of advanced biotechnologies, and to mitigate health and safety risks.[89] Additional conflicts may arise among the increasingly complex and heterogeneous network of stakeholders in the space community, for example, between NASA and its international partners, private subcontractors, and public-private partnering projects.

While our discussion is US centric, it is important to briefly address the international dimension. A challenge for governing space exploration is that much national and international space legislation stems from the Cold War era and is poorly equipped to deal with recent developments,[90] including the use of

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

advanced biotechnologies and the increased heterogeneity of the actors participating in space exploration. The *National Aeronautics and Space Act* has seen only minor amendments since it was signed by President Dwight Eisenhower. The five United Nations treaties on outer space were developed and adopted in the context of the Space Race. To give an example, the treaties were written at a time when space exploration was the exclusive domain of nation states. According to Art. VI of the *Outer Space Treaty* (1967), states "bear international responsibility for national activities in outer space, even if those activities are carried out by non-governmental entities.[91] Moreover, the article specifies, "The activities of non-governmental entities in outer space [...] shall require authorization and continuing supervision by the appropriate State Party to the Treaty."[92] However, this article may make governments hesitant to adopt novel technologies, in turn impeding their development by private industry. To plug the gaps in space governance at the international level, the American Institute of Aeronautics and Astronautics has suggested the need for a "World Space Conference" to bridge the programmatic and political levels of space governance, a sort of United Nations for spacy policy.[93] Astronauts, and other stakeholders, should play a key role in such a governing body.[94] The question is, however, how useful such a metalevel governance approach is when it comes to regulating new technologies, especially given the increased heterogeneity of actors and jurisdictions involved in space exploration, some of whom may adhere to different priorities and social values. The challenge is to institute policies that are general and flexible enough to account for different technological developments without being so general that they become meaningless.[95] While space exploration has become a global enterprise, and some degree of international harmonization is desirable, the development of technology happens more locally (e.g., nation, state, province) and aligns with local interests. Therefore, a combination of adaptable metalevel global governance and local governance frameworks will be more suitable in addressing the complex issues arising in space exploration, including the use of advanced biotechnologies.

Finally, any combination of governance mechanisms must provide protections to adequately safeguard the well-being and the interests of astronauts, regardless of how their roles are conceptualized (as research participants, professionals, and testers). To ensure this is the case, one possibility is the creation of multidisciplinary, independent oversight bodies beyond the traditional ethics review committees that already operate at space agencies (e.g., NASA, ESA). The mandate of such governance bodies might resemble an ethics review committee, but with an expanded role. Beyond ensuring traditional human research participant protections, they should also be entrusted to assess scientific merit and integrity as well as societal value. Of course, many questions must be answered before this tentative proposal can be implemented. For example, what is the precise scope of these independent bodies? How do they relate to traditional ethics review committees? And how do we ensure their independence from other stakeholder interests? The key is the need for ethical reflection beyond traditional ethics review committees, particularly in light of the use of new (bio)technologies in space exploration.

The successful development and uptake of disruptive technologies, such as SA, are contingent on governance and regulatory mechanisms that consider the individual, community, and societal impacts of such technologies. In turn, promoting trustworthiness and actual public trust relies on deliberative engagement of stakeholders, accounting for the historical, sociocultural, and political contexts that might impact their assessments of benefits and risks.

VI. ELSI Recommendations

Astronaut SA is in the early stages of development and there is considerable uncertainty regarding the technology's translational pathway. It is evident, however, that SA and other advanced biotechnologies will require NASA and the space community to consider ELSI issues and the needed governance for crewed spaceflight. Given this context, we make two broad recommendations: (1) investment in ELSI research by NASA and the space community, and (2) the development of governance and regulatory frameworks for the use of advanced biotechnologies by astronauts.

A. Investment in ELSI Research by NASA and the Space Community

As we have seen, there is a need for space ELSI research, which can build on the recent surge of interest in ELSI at NASA in the context of the Artemis program and the space agency's plans to send astronauts to Mars.[96] These complex, long-term endeavors raise a multitude of ELSI questions beyond those related to the development and use of advanced biotechnologies, including the broader ethical, legal, and social ramifications of such missions.

A straightforward first step for NASA is to promote transparency and accountability via meaningful, representative stakeholder engagement. To be more transparent and accountable about both its existing

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

operations and plans for future exploration missions, NASA should actively solicit ELSI researchers — and other stakeholders — to provide feedback on the agency's policies and procedures, together with ensuing impacts. Our suggestion echoes calls for increased transparency in the *Health Standards* and *Artemis* reports.[97] To give an example, NASA's approach to the assessment of risk-benefit tradeoffs surrounding exploration missions could benefit from increased reflection from outside the agency via governance mechanisms and public engagement. Understandably, NASA may be reluctant to be more transparent about its operations, as this will elicit questions of accountability in a context where accidents inevitably happen. However, rather than seeing calls for transparency as a threat, NASA should embrace the opportunity to effect institutional change, becoming a more open and robust institution in the process. In practice, NASA can start by making available to the public information about their ongoing initiatives pertaining to policy and ELSI considerations, and make it easier to navigate the agency's many online resources. NASA could also create an online repository with (new) policies that would benefit from feedback.

Of course, NASA can also more actively engage in ELSI research, which may be advisable considering the agency's ambition to launch crewed exploration missions. The *Artemis* workshop and resulting report fit within such an approach. Workshop participants suggested several options for NASA to address ELSI issues moving forward, including integrating ELSI research into existing policy structures and establishing research capacity at NASA to address ELSI. They suggested drawing lessons for the successful implementation of ELSI research in the Human Genome Program.[98] Moreover, the agency can consider existing ELSI programs, like the European Commission's research programs on responsible innovation.[99] Whatever shape ELSI initiatives at NASA will take, they should include socio-ethical reflection on the development and use of advanced biotechnologies for future exploration missions.

For now, most of the responsibilities, public investment, and risk management for crewed spaceflight rest with NASA. As previously stated, we can envision ELSI issues becoming more diverse and complex in the future due to the increasingly commercial and international nature of space exploration, the growing number of stakeholders, and the expanded accessibility of space science and technology. The identification and governance of ELSI issues within that broader space community poses yet another challenge for the emerging area of space ELSI research. Given the pace of innovation and the lack of established governance systems in many areas of space science and exploration, ELSI frameworks can play a central role in informing stakeholder policies, procedures, and best practices.[100]

B. A Flexible ELSI Framework for the Governance of Advanced Biotechnologies

The development and use of advanced biotechnologies — including SA — for crewed spaceflight is only one area of space exploration that can benefit from an ELSI and governance framework to inform research and practice. The aim is to distill a set of ethical, legal, and social principles and values that can inform the implementation of governance mechanisms, including policy and regulatory frameworks. We define governance here in the traditional sense, as the process by which authority is administered and oversight is exercised through rules (e.g., standards of practice, codes of conduct, legislation, professional guidelines) and the process by which actors (e.g., individuals, institutions, communities) are held accountable. Under this notion, robust governance mechanisms entail administration and supervision at all levels, nationally and internationally.[101] Applied to SA, an ELSI framework can help guide the translational pathway of the technology through a process of iterative reflection. A deliberative, ongoing dialogue between biopreservation scientists, ELSI researchers, and other key stakeholders can direct the development of the technology, by reflecting on the core values (e.g., respect for persons, justice, transparency, accountability) that need to be built into SA. Early choices can shape technologies and institutions, often in ways that cannot easily be changed later. By prospectively reflecting on the ELSI issues raised by SA, we can avoid being locked into a suboptimal technology decades or centuries in the future that disregards important socio-ethical deliberation and the perspectives and values of impacted individuals and communities.

Similarly, mission planners — in dialogue with ELSI researchers — must start thinking about policies for the use of astronaut SA now, relying on the interrelated principles of autonomy (ethical), *volenti non fit injuria* (legal), and broad accessibility, stewardship, and benefit sharing (social). The results of this exercise, which should be iterative, can help inform the development of SA. Over time the ELSI framework will evolve — for example, with increased attention to DEI.

NASA and the space community need not start from scratch to develop such a framework but can draw on current research. First, researchers and poli-

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

cymakers can use existing ELSI initiatives as models, such as ELSI analyses related to human genomics research and the aforementioned European programs on responsible innovation. Second, while *Health Standards*' scope is limited to the development of specifications as described in the *NASA Spaceflight Human System Standards*, the report's overall approach is similar to what we propose, that is, the development of a set of general principles to inform policymaking.[102] Third, Langston has considered the ethical, legal, and policy implications of commercial human spaceflight, taking an approach that resembles those taken in ELSI research. While Langston falls short of developing a full-fledged ELSI framework for commercial space travel, instead relying on a combination of existing frameworks (e.g., *Health Standards*) and principles (e.g., precautionary principle), the richness of her analysis can inspire a more general space ELSI framework.[103] Finally, the research on the future of humanity as a spacefaring species contains important elements that can be used to inform space ELSI.[104] Bridging the gaps between these existing bodies of research will go a long way in providing the basis for a space ELSI framework.

The development and application of an ELSI framework has several advantages: First, the framework should not be construed as a "one-size-fits-all" approach, but should be flexible, allowing the same framework — or parts thereof — to be applied to different ELSI issues related to space exploration and provide the underpinnings for robust governance and regulation. While our focus has been limited to a specific context (i.e., the use of SA by professional, American astronauts), the proposed ELSI framework could be extrapolated to a future scenario where regular citizens (i.e., non-astronauts) will be working and living beyond Earth. Being flexible also means that the framework can evolve over time in response to rapid developments in space science. Moreover, such a flexible framework can potentially be adopted to other contexts, for example to commercial actors within and beyond the United States.

Second, by adopting an ELSI framework, NASA and the space community can govern their activities in a way that does not stifle innovation and fosters public trust. The challenge is not simply to legislate or regulate, reducing ELSI to its more legalistic aspects, but to prospectively explore the field of space ELSI, giving it a chance to mature together with space exploration.[105] In the case of SA, the early state of the technology offers an opportunity to develop an ELSI framework to guide technology development, testing, and application.

Third, and closely related to the previous point, a governance framework can serve as a toolbox for NASA and the space community to address ELSI issues earlier in project lifecycles, making it easier and less costly to identify and mitigate future issues.[106] Of course, doing so can be challenging early in the development of a new technology, given the uncertainty involved. However, this uncertainty shows the importance of mapping out the translational pathway for new space technologies, including SA, allowing a dialogue between the space community and ELSI researchers to steer the technological development process.

VII. Conclusion

SA technologies seek to address real-world challenges. Terrestrial applications of SA could prove beneficial in medicine. In the space context, SA could eventually enable humans to explore the solar system and beyond, allowing for a universe of scientific discoveries. Whole-body SA is still a nascent technology which will not be available for use in space for decades to come. Yet focusing on the potential of SA technology to enable astronaut hibernation is important, as it allows for a prospective conceptual analysis of the socio-ethical, legal, and governance issues. Indeed, progress on the ELSI and governance issues raised by SA will help advance thinking that can be applied to other new biotechnologies in space.

The ELSI of space exploration offers a fruitful field for visionary reflection. The development of SA for use during exploration missions raises important ELSI issues including how to deploy the categories of research, experimentation, and practice. The relationship among these activities will influence astronaut rights, responsibilities, and protections.

Moving forward will require well-developed governance mechanisms to ensure appropriate oversight, accountability, and trustworthiness. Applications of disruptive biotechnologies, such as SA, might radically alter the assessment of the adequacy of a consent process during exploration missions and of the balance between risks and benefits, calling not only for robust governance, but also for iterative and meaningful public engagement. Beyond astronauts' individual considerations, there are wider societal or collective issues that an ELSI approach must consider. They range from justice issues pertaining to equitable crew selection, benefit sharing, colonization, and stewardship of resources, to thoughtful attention to communal socio-cultural views regarding the value and appropriate treatment of astronomical bodies (e.g., the Moon) within and beyond the solar system. Investment in

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

ELSI research by NASA and the space community is essential to attend to these issues.

A solid ELSI framework is essential to moving forward with revolutionary technologies such as SA that will fundamentally change space travel. A successful translational pathway for technologies like SA is predicated on governance and regulatory mechanisms that are responsive to individual, community, and societal impacts. Public trust must be gained and nurtured. This will require transparency and the deliberative engagement of all stakeholders.

Acknowledgments

Preparation of this article was supported by the National Science Foundation (NSF) Engineering Research Center for Advanced Technologies for the Preservation of Biological Systems (ATP-Bio), Award #1941543. Any opinions, findings, and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of NSF.

Disclosures

Korkut Uygun has patent applications relevant to tissue and organ preservation and has a financial interest in and serves on the Scientific Advisory Board for Sylvatica Biotech Inc., a company focused on developing high subzero organ preservation technology. His competing interests are managed by Massachusetts General Hospital and Mass General Brigham in accordance with their conflict-of-interest policies. All other authors have no relevant disclosures. All disclosure forms are on file with the Journal.

References

1. A.G.C. Guerra et al., "Comparison of Four Space Propulsion Methods for Reducing Transfer Times of Crewed Mars Missions," *Journal of the Astronautical Sciences* 69, no. 2 (2022): 284–311.
2. J. Bimm and P. Killian, "The Well-Tempered Astronaut," in S.B. Ziauddin et al., eds., *Nach Feierabend: Der Kalte Krieg* (Zürich: Diaphanes, 2017): 85–107, at 86–100.
3. W. von Braun and C. Ryan, "Can We Get to Mars?" *Collier's Magazine* (New York), April 30, 1954, at 27–28, *available at* <https://www.unz.com/print/Colliers-1954apr30-00022> (last visited September 5, 2024).
4. C. Aditya et al., "On the Precipice of Life: A Contractarian Analysis of Suspended Animation," *Ethics in Biology, Engineering and Medicine: An International Journal* 6, nos. 1–2 (2015): 27–36, at 30–31.
5. S. Mann, *Could NASA's Studies on Hibernating Squirrels Help Astronauts?*, NASA, *available at* <https://www.nasa.gov/centers-and-facilities/armstrong/could-nasas-studies-on-hibernating-squirrels-help-astronauts/> (last visited September 5, 2024).
6. See Aditya et al., *supra* note 4.
7. Institute of Medicine, *Health Standards for Long Duration and Exploration Spaceflight: Ethics Principles, Responsibilities, and Decision Framework* (Washington, DC: National Academies Press, 2014) [hereinafter cited as *Health Standards*].
8. K. Damjanov, "Accounting for Non-Humans in Space Exploration," *Space Policy* 43 (2018): 18–23, doi: https://doi.org/10.1016/j.spacepol.2018.01.001.
9. V. Rahimzadeh et al., "Ethically Cleared to Launch?" *Science* 381, no. 6665 (2023): 1408–1411.
10. D.A. Hart, "*Homo sapiens*—A Species Not Designed for Space Flight: Health Risks in Low Earth Orbit and Beyond, Including Potential Risks When Traveling beyond the Geomagnetic Field of Earth," *Life* 13, no. 3 (2023): 757, doi: https://doi.org/10.3390/life13030757.
11. A. Guzman, *Human Research: Studying Astronaut Physiology*, NASA, *available at* <https://www.nasa.gov/missions/station/human-research-studying-astronaut-physiology/> (last visited September 5, 2023).
12. NASA, *Hazard: Space Radiation*, *available at* <https://www.nasa.gov/hrp/hazard-space-radiation/> (last visited September 5, 2024).
13. C. Krittanawong et al., "Cardiovascular Disease in Space: A Systematic Review," *Progress in Cardiovascular Diseases* 81 (2023): 33–41, doi: https://doi.org/10.1016/j.pcad.2023.07.009.
14. NASA, *Space Radiation Element*, *available at* <https://www.nasa.gov/hrp/radiation/space-radiation-risks/> (last visited September 5, 2024).
15. See *Health Standards*, *supra* note 7.
16. P. Wolpe, *The Unique Challenge of Ethics in Extreme Environments: Bioethics at NASA – and Beyond*, Emory Grand Rounds in Medicine, February 7, 2023, *available at* <https://www.youtube.com/watch?v=u80KTukXne4> (last visited September 5, 2024).
17. T.G. Sazykina and A.I. Kryshev, "Manifestation of Radiation Effects in Cold Environment: Data Review and Modeling," *Radiation and Environmental Biophysics* 50, no.1 (2011): 105–114, doi: https://doi.org/10.1007/s00411-010-0336-7.
18. NASA, *Hazard: Gravity Fields*, *available at* <https://www.nasa.gov/hrp/hazard-gravity-fields/> (last visited September 5, 2023).
19. G.C. Demontis et al., "Human Pathophysiological Adaptations to the Space Environment," *Frontiers in Physiology* 8 (2017): 547, doi: https://doi.org/10.3389/fphys.2017.00547.
20. R. Baran et al., "Microgravity-Related Changes in Bone Density and Treatment Options: A Systematic Review," *International Journal of Molecular Sciences* 23, no. 15 (2022): 8650, doi: https://doi.org/10.3390/ijms23158650; B. Ganse et al., "Joint Cartilage in Long-Duration Spaceflight," *Biomedicines* 10, no. 6 (2022): 1356, doi: https://doi.org/10.3390/biomedicines10061356; I. Takahashi et al., "Disuse Atrophy of Articular Cartilage Induced by Unloading Condition Accelerates Histological Progression of Osteoarthritis in a Post-Traumatic Rat Model," *Cartilage* 13, Suppl. 2 (2021): 1522s–1529s; P.H.U. Lee et al., "Factors Mediating Spaceflight-Induced Skeletal Muscle Atrophy," *American Journal of Physiology-Cell Physiology* 322, no. 3 (2022): C567–C580.
21. G.G. De la Torre, "Cognitive Neuroscience in Space," *Life* 4, no. 3 (2014): 281–294; A. Demertzi et al., "Cortical Reorganization in an Astronaut's Brain after Long-Duration Spaceflight," *Brain Structure and Function* 221, no. 5 (2016): 2873–2876; E. Pechenkova et al., "Alterations of Functional Brain Connectivity After Long-Duration Spaceflight as Revealed by fMRI," *Frontiers in Physiology* 10 (2019): 761, doi: https://doi.org/10.3389/fphys.2019.00761; L.A. Kramer et al., "Intracranial Effects of Microgravity: A Prospective Longitudinal MRI Study," *Radiology* 295, no. 3 (2020): 640–648.
22. See Krittanawong et al., *supra* note 13; NASA, *supra* note 18.
23. S. Colucci et al., "Irisin Prevents Microgravity-Induced Impairment of Osteoblast Differentiation in Vitro during the Space Flight CRS-14 Mission," *FASEB Journal* 34, no. 8 (2020): 10096–10106; M. Rondanelli et al., "Nutrition, Physical Activity, and Dietary Supplementation to Prevent Bone Mineral Density Loss: A Food Pyramid," *Nutrients* 14, no. 1 (2021): 74.
24. A. Marcos et al., "Changes in the Immune System Are Conditioned by Nutrition," *European Journal of Clinical Nutrition* 57, Suppl. (2003): S66–S69; S. Sephton and D. Spiegel, "Circadian Disruption in Cancer: A Neuroendocrine-Immune Pathway from Stress to Disease?" *Brain, Behavior, and Immunity* 17, no. 5 (2003): 321–328.
25. F.E. Garrett-Bakelman et al., "The NASA Twins Study: A Multidimensional Analysis of a Year-Long Human Spaceflight," *Science* 364, no. 6436 (2019): eaau8650.
26. A. Archie, *A NASA Astronaut Is Back on Earth after a Year in Space, the Longest for an American*, NPR, September 28, 2023, *available at* <https://www.npr.org/2023/09/20/1200374445/

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

nasa-frank-rubio-record-yearlong-flight> (last visited September 5, 2024).

27. *What Are the Van Allen Belts and Why Do They Matter?,* NASA, *available at* <https://science.nasa.gov/biological-physical/stories/van-allen-belts/> (last visited September 5, 2024).
28. See Garrett-Bakelman et al., *supra* note 25.
29. See *Health Standards*, *supra* note 7.
30. K.B. Storey and J.M. Storey, "Freeze Tolerance in Animals," *Physiological Reviews*, 68, no. 1 (1988): 27–84; K.B. Storey and J.M. Storey, "Natural Freezing Survival in Animals," *Annual Review of Ecology and Systematics* 27, no. 1 (1996): 365–386.
31. R.J. de Vries et al., "Supercooling Extends Preservation Time of Human Livers," *Nature Biotechnology* 37, no. 10 (2019): 1131–1136; Y. Berkane et al., "Supercooling: A Promising Technique for Prolonged Preservation in Solid Organ Transplantation, and Early Perspectives in Vascularized Composite Allografts. Review," *Frontiers in Transplantation* 2 (2023): 1269706, doi: https://doi.org/10.3389/frtra.2023.1269706.
32. S.N. Tessier et al., "Partial Freezing of Rat Livers Extends Preservation Time by 5-fold," *Nature Communications* 13, no. 1 (2022): 4008, doi: https://doi.org/10.1038/s41467-022-31490-2.
33. O.S. Ozgur et al., "Extended Storage of Swine Livers up to 10 Days using Partial Freezing," poster presented at the Annual Congress of the International Liver Transplant Society, Houston, Texas, May 2, 2024, *available at* <https://ilts2024.abstractserver.com/program/#/details/presentations/595> (last visited September 5, 2024).
34. Z. Han et al., "Vitrification and Nanowarming Enable Long-Term Organ Cryopreservation and Life-Sustaining Kidney Transplantation in a Rat Model," *Nature Communications* 14, no. 1 (2023): 3407, doi: https://doi.org/10.1038/s41467-023-38824-8.
35. See Berkane et al., *supra* note 31.
36. B.E. Luu and K.B. Storey, "Solving Donor Organ Shortage with Insights from Freeze Tolerance in Nature: Activating Endogenous Antioxidant Systems with Non-coding RNA to Precondition Donor Organs," *Bioessays* 40, no. 10 (2018), doi: https://doi.org/10.1002/bies.201800092.
37. D. Andrijevic et al., "Cellular Recovery after Prolonged Warm Ischaemia of the Whole Body," *Nature* 608 (2022): 405-412.
38. F. Melandro et al., "Viability Criteria during Liver Ex-Situ Normothermic and Hypothermic Perfusion," *Medicina* 58, no. 10 (2022): 1434, doi: https://doi.org/10.3390/medicina58101434.
39. R.D. Truog et al., "Normothermic Regional Perfusion – The Next Frontier in Organ Transplants?" *JAMA* 329, no. 24 (2023): 2123–2124, doi: https://doi.org/10.1001/jama.2023.9294. PMID: 37266949.
40. Z. Pirtle et al., *Artemis, Ethics, and Society: Synthesis from a Workshop* (Washington, DC: NASA, 2023) [hereinafter cited as *Artemis*].
41. Office for Human Research Protections (OHRP), *Federal Policy for the Protection of Human Subjects ('Common Rule')*, US Department of Health and Human Services, *available at* <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html> (last visited September 5, 2024).
42. *HRMRB*, NASA, *available at* <https://irb.nasa.gov/HRMRB/> (last visited April 22, 2024).
43. S.M. Langston, "Space Travel: Risk, Ethics, and Governance in Commercial Human Spaceflight," *New Space* 4, no. 2 (2016): 83–97; S.M. Langston, "Reimagining Icarus: Ethics, Law and Policy Considerations for Commercial Human Spaceflight," in T. Russomano and L. Rehnberg, eds., *Into Space – A Journey of How Humans Adapt and Live in Microgravity* (London: IntechOpen, 2018): 1–16 [hereinafter cited as *Reimagining Icarus*]; S.M. Langston, *Commercial Space Travel: Understanding the Legal, Ethical and Medical Implications for Commercial Spaceflight Participants and Crew*, paper presented at and printed in *2017 8th International Conference on Recent Advances in Space Technologies (RAST)*, Istanbul, Turkey, 19–22 June 2017: 489–494; K. Szocik, "Is the Bioethics of Space Missions Different from Bioethics on Earth?" in K. Szocik, *The Bioethics of Space Exploration* (Oxford: Oxford University Press, 2023): 84–103; K. Szocik and M. Braddock, "Bioethical Issues in Human Modification for Protection Against the Effects of Space Radiation," *Space Policy* 62 (2022): 101505, doi: https://doi.org/10.1016/j.spacepol.2022.101505; K. Szocik et al., "Future Space Missions and Human Enhancement: Medical and Ethical Challenges," *Futures* 133 (2021): 102819, doi: https://doi.org/10.1016/j.futures.2021.102819; K. Szocik et al., "Ethical Issues of Human Enhancements for Space Missions to Mars and Beyond," *Futures* 115 (2020): 102489, doi: https://doi.org/10.1016/j.futures.2019.102489.
44. *OCHMO Policy: Research Subject Protection,* NASA, *available at* <https://www.nasa.gov/ochmo/health-operations-and-oversight/ochmo-policy1/> (last visited September 5, 2024); Office of the Chief Health and Medical Officer, *Human Spaceflight and Aviation Standards. NASA Spaceflight Human-System Standard Volume 1 & 2*, NASA, *available at* <https://www.nasa.gov/directorates/esdmd/hhp/human-spaceflight-and-aviation-standards/> (last visited September 5, 2024); *NASA's Moon to Mars Strategy and Objectives* (2023), NASA, *available at* <https://www.nasa.gov/wp-content/uploads/2023/04/m2m_strategy_and_objectives_development.pdf> (last visited September 5, 2024).
45. See *NASA's Moon to Mars Strategy and Objectives Development*, *supra* note 44.
46. See Artemis, *supra* note 40.
47. See *Health Standards*, *supra* note 7; Institute of Medicine, *Safe Passage: Astronaut Care for Exploration Missions* (Washington, DC: National Academies Press, 2001) [hereinafter cited as *Safe Passage*].
48. See *NASA Spaceflight Human-System Standard*, *supra* note 44.
49. See *Artemis*, *supra* note 40.
50. See Szocik, *supra* note 43; K. Szocik, "Biomedical Moral Enhancement for Human Space Missions," *Studia Humana* 8, no. 4 (2019): 1–9; K. Szocik, "Germline Gene Editing and Embryo Selection for Future Long-Term Space Missions," in K. Szocik, *The Bioethics of Space Exploration* (Oxford: Oxford University Press, 2023): 49–-69; K. Szocik, "Justification of Human Enhancement versus Rationale for Space Missions" in K. Szocik, *The Bioethics of Space Exploration* (Oxford: Oxford University Press, 2023): 70–83; K. Szocik, "The Ethical Status of Germline Gene Editing in Future Space Missions: The Special Case of Positive Selection on Earth for Future Space Missions," *NanoEthics* 17 (2023): 3, doi: https://doi.org/10.1007/s11569-023-00438-1.
51. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (April 18, 1979), *available at* <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html> (last visited September 5, 2024) [hereinafter cited as *The Belmont Report*].
52. See *Health Standards*, *supra* note 7; *Safe Passage*, *supra* note 47.
53. P. Friesen et al., "Rethinking the Belmont Report?" *American Journal of Bioethics* 17, no. 7 (2017): 15–21, doi: https://doi.org/10.1080/15265161.2017.1329482.
54. See *The Belmont Report*, *supra* note 51.
55. See *Safe Passage*, *supra* note 47.
56. See *The Belmont Report*, *supra* note 51.
57. See *Health Standards*, *supra* note 7.
58. A.M. Page, "Bioethics Beyond the Biosphere: Using Human Subject Medical Research to Chart Out Regulation and Liability for Health Risks in Outer Space," *North Carolina Journal of Law & Technology* 20, no. 5 (2018): 37–73.
59. 45 C.F.R. 46 Subpart A (2018).
60. See Szocik, *Is the Bioethics of Space Missions Different from Bioethics on Earth? supra* note 43.
61. See *Health Standards*, *supra* note 7; See Wolpe, *supra* note 16.

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press on behalf of American Society of Law, Medicine & Ethics.

62. Y. Baturin, "The Astronaut's Legal Status," *Advanced Space Law* 5 (2020): 4–13; D. Beamer-Downie, "Considering the Unthinkable — A Review and Discussion of Current International Law and Suggestions Regarding How We Deal with a Catastrophic Incident in Space," *Acta Astronautica* 92, no. 2 (2013): 255–262; B. Cheng, "Definitional Issues in Space Law: 'Space Objects', 'Astronauts', and Related Expressions," in B. Cheng, *Studies in International Space Law* (Oxford: Oxford University Press, 1997): 492–509.
63. S. Sreejith, "The Fallen Envoy: The Rise and Fall of Astronaut in International Space Law," *Space Policy* 47 (2019): 130–139.
64. L.M. Covert, "Multinational and Ethical Issues in Manned-Space Strategy," *Space Policy* 18 (2002): 151–156; J. Zaikowski, "Careers in Bioethics: Interview with Dr. Paul Wolpe," *Voices in Bioethics* 4 (2018), *available at* <https://journals.library.columbia.edu/index.php/bioethics/article/view/6017>.
65. See *Health Standards*, *supra* note 7.
66. See *id.*; Zaikowksi, *supra* note 64.
67. *ALARA*, US Nuclear Regulatory Commission (USNCR), *available at* <https://www. nrc.gov/reading-rm/basic-ref/glossary/alara.html> (last visited September 5, 2023).
68. NASA, *NASA Risk Management Handbook* (Washington, DC: NASA, 2011).
69. L. Billings, "To the Moon, Mars, and Beyond: Culture, Law, and Ethics in Space-Faring Societies," *Bulletin of Science, Technology & Society* 26, no. 5 (2006): 430–437.
70. See Szocik, *Justification of Human Enhancement versus Rationale for Space Missions*, *supra* note 50; M.N. Mautner, "Life- Centered Ethics, and the Human Future in Space," *Bioethics* 23, no. 8 (2009): 433–440.
71. See Langston, *Space Travel: Risk, Ethics, and Governance in Commercial Human Spaceflight*, *supra* note 43.
72. See *Safe Passage*, *supra* note 47.
73. See Szocik, *Is the Bioethics of Space Missions Different from Bioethics on Earth? supra* note 43.
74. T.M. Gibson, "The Bioethics of Enhancing Human Performance for Spaceflight," *Journal of Medical Ethics* 32, no. 3 (2006): 129–132.
75. See *Health Standards*, *supra* note 7.
76. S. Hobe and R. Popova, "Legal Aspects of Human Orbital and Suborbital Spaceflight: Some Legal, Medical and Ethical Considerations," *REACH – Reviews in Human Space Exploration* 7–8 (2017): 1–5.
77. J. Stuster et al., *Human Exploration of Mars: Preliminary Crew Tasks* (Houston, TX: NASA, 2018).
78. See *Safe Passage*, *supra* note 47.
79. W.M. Robinson, "Ethics for Astronauts," *Medical Ethics* 11, no. 3 (2004): 1–2.
80. P. Wolpe and W.M. Robinson, "Dialogue: Bioethics in Space," *Lahey Clinic Medical Ethics Journal* 12, no. 1 (2005): 10–11.
81. NASA, *Artemis*, *available at* <https://www.nasa.gov/specials/artemis/> (last visited September 5, 2024).
82. K.E. Mandt, "Increasing Diversity on Spacecraft Mission Teams Reduces Risk," *Science* 382, no. 6675 (2023): eadk7373.
83. See Hart, *supra* note 10; M.R. Edwards, "Space Ectogenesis: Securing Survival of Humans and Earth Life with Minimal Risks–Reply to Szocik," *International Journal of Astrobiology* 20, no. 4 (2021): 323–-326.
84. E. Pavez Loriè et al., "The Future of Personalized Medicine in Space: From Observations to Countermeasures. Review," *Frontiers in Bioengineering and Biotechnology* 9 (2021): 739747, doi: https://doi.org/10.3389/fbioe.2021.739747.
85. NASA Office of the Inspector General, *NASA's Efforts to Increase Diversity in Its Workforce* (Washington, DC: NASA, 2023).
86. See *Health Standards*, *supra* note 7.
87. See *id.*
88. Public Law 85-568 (1958).
89. See *Health Standards*, *supra* note 7.
90. M.K. Latimer, "Lost in Space: An Exploration of the Current Gaps in Space Law," *Seattle Journal of Technology, Environmental & Innovation Law* 11, no. 2 (2021): 322–349.
91. Treaty on Principles Governing the Activities of States in the Exploration and Use of Outer Space, including the Moon and Other Celestial Bodies, adopted December 19, 1966, opened for signature January 27, 1967, entered into force October 10, 1967; 18 UST 2410; 610 UNTS 205 [hereinafter cited as Outer Space Treaty], *available at* <https://www.unoosa.org/oosa/en/ourwork/spacelaw/treaties/outerspacetreaty.html> (last visited September 5, 2024).
92. See *id.*
93. See Billings, *supra* note 69.
94. See Covert, *supra* note 64.
95. M.J. Sundahl et al., "Returning to the Moon: Legal Challenges as Humanity Begins to Settle the Solar System – Full Transcript," *Global Business Law Review* 9, no. 1 (2021): 1–117.
96. See *Artemis*, *supra* note 40.
97. See *Health Standards*, *supra* note 7; *Artemis*, *supra* note 40.
98. D.D. Dolan et al., "Three Decades of Ethical, Legal, and Social Implications Research: Looking Back to Chart a Path Forward," *Cell Genomics* 2, no. 7 (2022): 100150, doi: https://doi.org/10.1016/j.xgen.2022.100150.
99. See *Artemis*, *supra* note 40.
100. See Langston, *Reimagining Icarus*, *supra* note 43.
101. National Academies of Sciences, Engineering, and Medicine, *Human Genome Editing: Science, Ethics, and Governance* (Washington, DC: The National Academies Press, 2017), doi: https://doi.org/10.17226/24623.
102. See *Health Standards*, *supra* note 7.
103. See Langston, *supra* note 43 (all references in n. 43).
104. See Szocik, *supra* note 50 (all references in n. 50).
105. J. Arnould, "The Emergence of the Ethics of Space: The Case of the French Space Agency," *Futures* 37, nos. 2–3 (2005): 245–254.
106. See *Artemis*, *supra* note 40.

The Journal of Law, Medicine & Ethics, 52 (2024): 648-665. © The Author(s), 2024. Published by Cambridge University Press
on behalf of American Society of Law, Medicine & Ethics.