Hogan Lovells

Beyond Earth's Gravity

Navigating Legal Hurdles in Space-Based Drug Research and Development

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Foreword: Innovations in Space

Innovative technologies are reshaping every industry, presenting new business cases and changing our daily lives. These technologies are hyper-connecting the world and offering new ways to interact. Particularly in the Space and Satellite arena, technology is ever-evolving, expanding, and combining in ways never before contemplated.

At the same time, these innovations bring many legal, regulatory, and contractual challenges and considerations that need to be kept in mind to support the successful launch of a new business. Along with new business models (some fully or partially still on the drawing board), often come new hurdles, paradigms, and new approaches to partnering and capital raising.

This is the latest in our series of "Innovations in Space," which is the result of a collaboration between our Space and Satellite and Life Sciences and Health Care groups. It explores the growing opportunities of pharmaceutical and biotech companies that engage in space-based drug research and development activities, and the myriad of legal issues raised by this important area.

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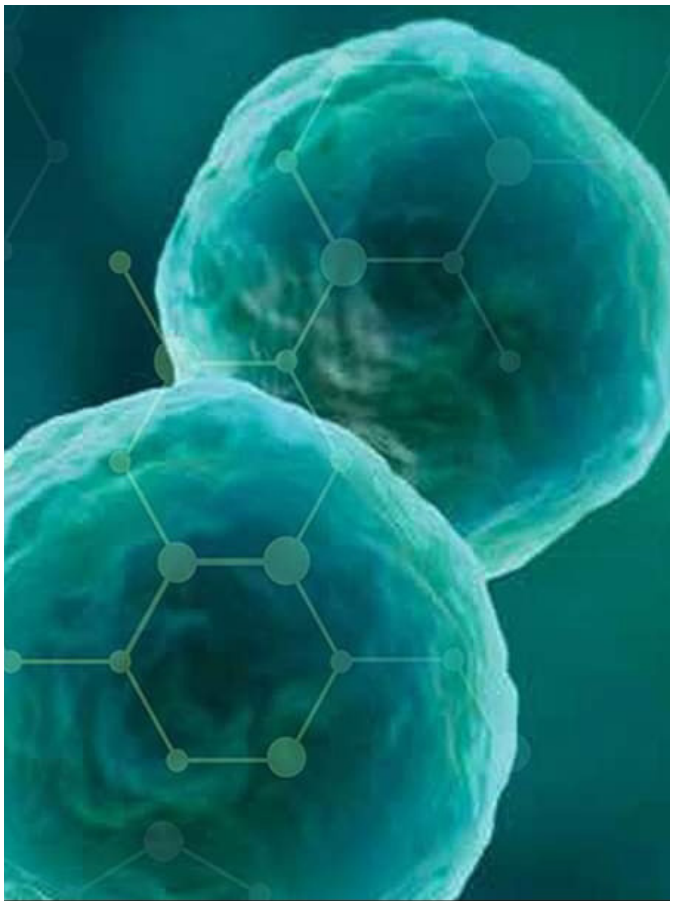
Overview

When it comes to space exploration, we often think of historical milestones like the launch of Sputnik, Yuri Gagarin's journey, and Neil Armstrong's iconic moon landing. However, space exploration has evolved far beyond satellite deployment, space travel, and trips to the moon. It now envisions a future where Mars exploration, commercial spaceflights, movie filming, space mining, and even drug research and development in privately-held commercial space stations are practically within reach.

The history of drug development and research in space can be traced back 50 years when scientists first became concerned about the adverse effects that the conditions of space had on astronauts. As a result, they began exploring ways to counter, prevent, or mitigate these effects. Only recently have researchers aboard the International Space Station ("**ISS**") shifted their focus towards the potential positive effects of space conditions.

In the last 15-20 years, research conducted aboard the ISS has unveiled the profound and positive impact of microgravity on cellular behavior, tissue engineering, gene expression, organism growth patterns, and regenerative medicine. These groundbreaking discoveries have attracted the interest and attention of governments and the private sector. Companies working to develop low-cost access to space (dubbed "**NewSpace**" companies), Fortune 500 pharmaceutical companies, startups, and companies facilitating research activities in low-Earth orbit ("**LEO**"), among other private entities, have recognized the immense opportunities that space-based drug research and development offer.

All these events, coupled with the upcoming decommissioning of the ISS around 2031, have led to a significant increase in the private sector's presence in space. This increased presence is slowly but surely shattering the myth that space is solely the domain of governments, making "access" to space more reachable and affordable. However, with this increased private sector involvement and opportunities, new legal challenges arise that require careful consideration. In this article, we will explore some of these legal challenges and provide a few best-practice tips for companies engaged or intending to engage in these exciting ventures in order to address such challenges.



Why Space?

Opportunities for Pharmaceutical and Biotech Companies in Space

Before exploring the legal challenges associated with conducting drug research and development in LEO, let's first examine the advantages it offers from both a scientific and a business perspective:

Scientific Considerations

Experiments conducted on the ISS National Lab and on Earth have provided valuable knowledge about cellular behavior and interactions, tissue development and regeneration, and aggregate interactions in the context of a whole organism. Additionally, bioengineering experiments on the ISS National Lab in conjunction with ground-based studies have shown that microgravity enables the study of novel features that are not possible under normal gravity conditions. Here are some captivating examples:

a) **3D Cell Cultures.** Cell cultures are important for studying cellular behavior, interactions, and functions. In space, cells grow in three-dimensional structures, which is different from the flatter, two-dimensional structures observed on Earth. The reduced gravity in space allows for more uniform cell growth and enhanced cell-cell interactions, which can lead to better cell differentiation and the formation of more functional tissues. Unlike on Earth, where support structures are needed, cells in microgravity can self-assemble and form structures without external "scaffolds," resembling their behavior within a living organism.

Photo supplied by NASA.

b) **Protein Crystal Growth.** Proteins are vital for human health. Understanding the structure of proteins is crucial for studying how they function and for developing new treatments for diseases. Protein crystallization is a technique used in medicine to determine the 3D structure of proteins. By studying the crystal structure, scientists can see how the protein interacts with other molecules, like drugs or enzymes. This information helps in designing drugs that target specific proteins involved in diseases. Protein crystallization in a microgravity environment is advantageous because it allows the protein molecules to form crystals more slowly and neatly. This leads to higher-quality crystals that can be analyzed on Earth for further research and drug development.

c) **Biofabrication.** Biofabrication is an innovative approach to regenerative medicine that utilizes 3D printing to create biomaterials, cells, tissues, and organs. It involves building 3D tissue structures layer by layer using living cells, resulting in models that closely resemble our own tissues and organs. This method has significant applications in tissue engineering and artificial organ development, potentially addressing the shortage of donor organs and reducing the risk of rejection by using a patient's own cells. In drug development, biofabrication has the potential to make the process more ethical, quicker, and more cost-effective by using bioprinted tissue models to reduce the need to rely on animal or human testing – and perhaps one day to replace such testing altogether. Biofabrication also has shown great promise in accelerating the wound healing process in various tissues through bioprinting.

In addition to microgravity, there are other conditions in space that are also yielding valuable insights. For instance, the **extreme conditions in space** have provided researchers with valuable information on how organisms adapt, which can potentially lead to the development of innovative therapies and technologies for medical applications. Additionally, the study of **high radiation levels in space** may contribute to the advancement of radioprotective measures and therapies, particularly in critical areas such as cancer treatments. Moreover, the **ultra-vacuum conditions in space,** devoid of atmospheric pressure and gases, offer a unique opportunity to study biological samples in their purest form. This vacuum environment allows researchers to delve into the fundamental properties and behavior of biomolecules like proteins and enzymes. By examining these molecules in their native state, scientists can gain crucial insights into their structure, function, and interactions, ultimately aiding in the development of novel drugs, therapies, and diagnostic tools.

Business Considerations

The prospect of utilizing microgravity conditions in space to revolutionize medicine has captured the interest of major pharmaceutical companies such as Merck, AstraZeneca, Eli Lilly, and Sanofi, as well as numerous other companies already conducting experiments aboard the ISS. Additionally, the NewSpace movement has played a pivotal role in democratizing access to space, making it increasingly feasible for smaller biotech companies and startups to enter this exciting market.

However, for these companies, the accessibility of LEO raises important questions. While they may have already surpassed the proof of concept stage and are eager to further develop their assets, the financial hurdle of engaging in space ventures can be daunting. When contemplating the decision to send experiments to LEO, it is crucial for companies to consider several key factors. By carefully weighing these considerations, pharmaceutical and biotech companies can determine whether sponsoring drug research and development in space is indeed the right path for their scientific endeavors. To assist in this evaluation, here are some compelling business advantages to consider when determining whether or not to send experiments to LEO:

- **Increasing Interest.** Significant findings over the last 15-20 years have shed light on the impact of microgravity on drug research and development, sparking scientists' vision of how much can be done and learned in this field. For example, more recently, it has been discovered that these unique conditions can also support biomanufacturing in ways that are not possible on Earth, which could take medicine to a whole new level. This recent discovery has sparked interest in the pharmaceutical and biotech sector, leading innovators to pursue new ways to study drugs and other medical treatments. As more advancements are made, this interest will continue to grow, enhancing all the other business-related advantages discussed in this section.

- **Accessibility.** The increasing presence of private sector entities in the space industry has opened up new opportunities for pharmaceutical and biotech companies, including startups. As space becomes more competitive and contested, the costs associated with conducting research in space will naturally decrease. Further, rapid advancements are being made in space infrastructure technologies that provide increased frequency and lower costs for accessing space. For example, rocket launches with thousands of pounds of research material and equipment bound for the ISS National Lab are now more affordable, reliable, and frequent. This trend is making it easier for both biotech startups and established companies to engage in drug research and development in space.

- **Funding Opportunities.** There are several funding opportunities available for companies interested in conducting biotech research in space. Both the government and private sectors offer support in this area. NASA and the Center for the Advancement of Science in Space ("**CASIS**") provide programs and funding specifically for research on the ISS National Lab, inviting proposals from companies and

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researchers interested in conducting biotech-related experiments in microgravity. The National Institutes of Health (NIH) and the National Science Foundation (NSF) also collaborate with CASIS to encourage biotech research projects on the ISS National Lab. Private sector foundations like the National Stem Cell Foundation are involved in research aboard the ISS and provide funding opportunities as well. Additionally, the ISS National Lab has an investor network that includes venture capital firms, corporate venture investors, angel investor organizations, accelerators, private equity markets, and financial intermediaries. Further, CASIS actively identifies appropriate funding sources and connects qualified research projects with these investors to further support research projects.

- **Potential to Build a Strong Scientific Foundation at a Faster Pace.** The journey from discovery to market can indeed be lengthy and intricate, particularly in emerging fields like cell and gene therapy. Bringing a drug from the lab to the patient requires substantial investment, and pharmaceutical and biotech companies often face the challenge of an insufficient amount of scientifically sound data, which can hinder the progress of drug candidates beyond the pre-clinical stage. However, conducting drug research and development under microgravity conditions shows promise. It has the potential to establish a strong scientific foundation that was previously missing on Earth, and could serve as a crucial link in the drug development process. Moreover, this innovation has the potential to revolutionize the entire process, making it faster, more cost-effective, and more efficient.
- **Opportunity to Develop Collaborative Partnerships.** Collaborative partnerships in space offer significant benefits for pharmaceutical and biotech companies in the field of biotech research. By collaborating with NASA, CASIS, and other industry leaders, companies gain access to advanced resources and expertise, which can greatly accelerate their research and development efforts. These collaborations can also provide opportunities for companies to collaborate with their peers on a global scale, transcending borders and harnessing a diverse talent pool. Through cost-sharing arrangements, companies can also undertake ambitious projects that may have been otherwise financially unfeasible.

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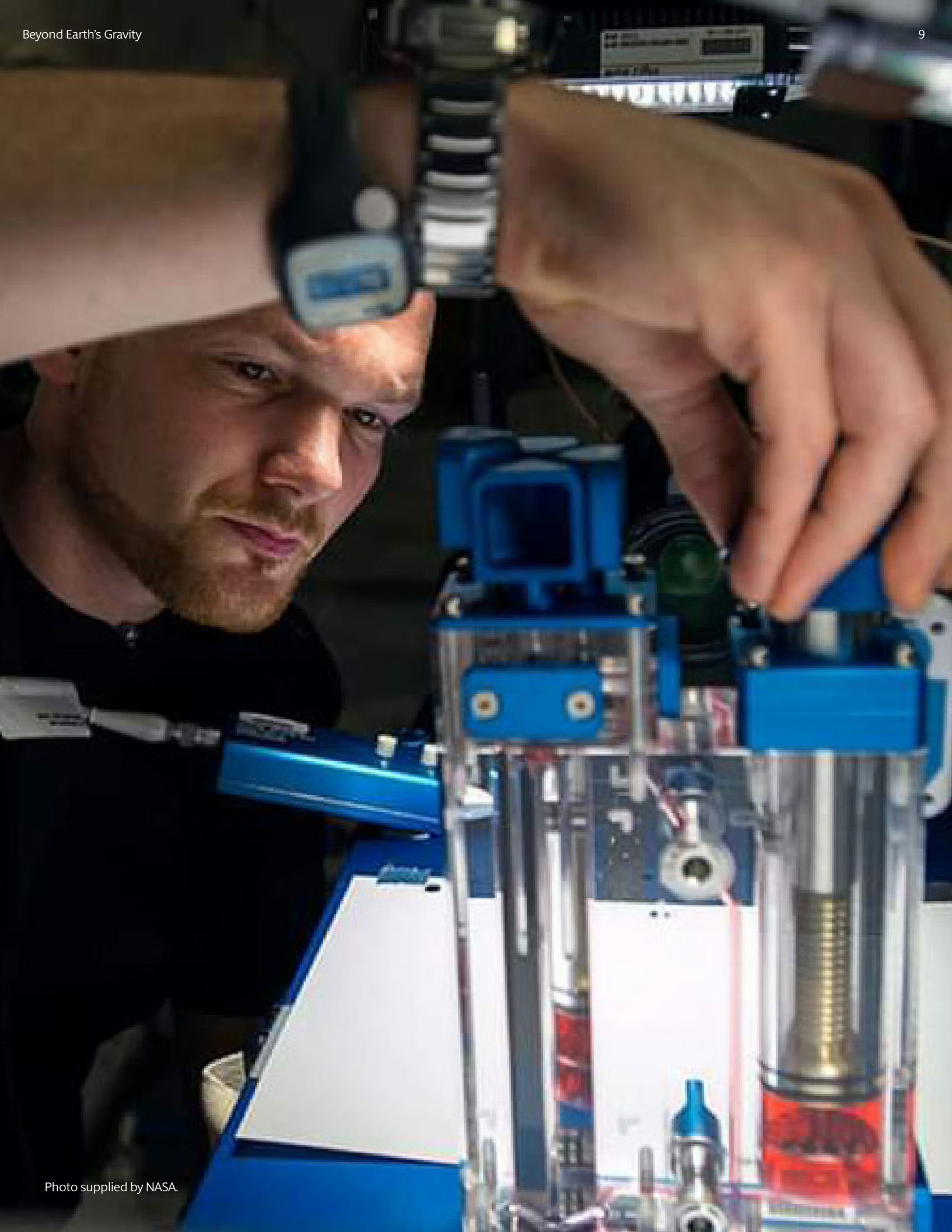

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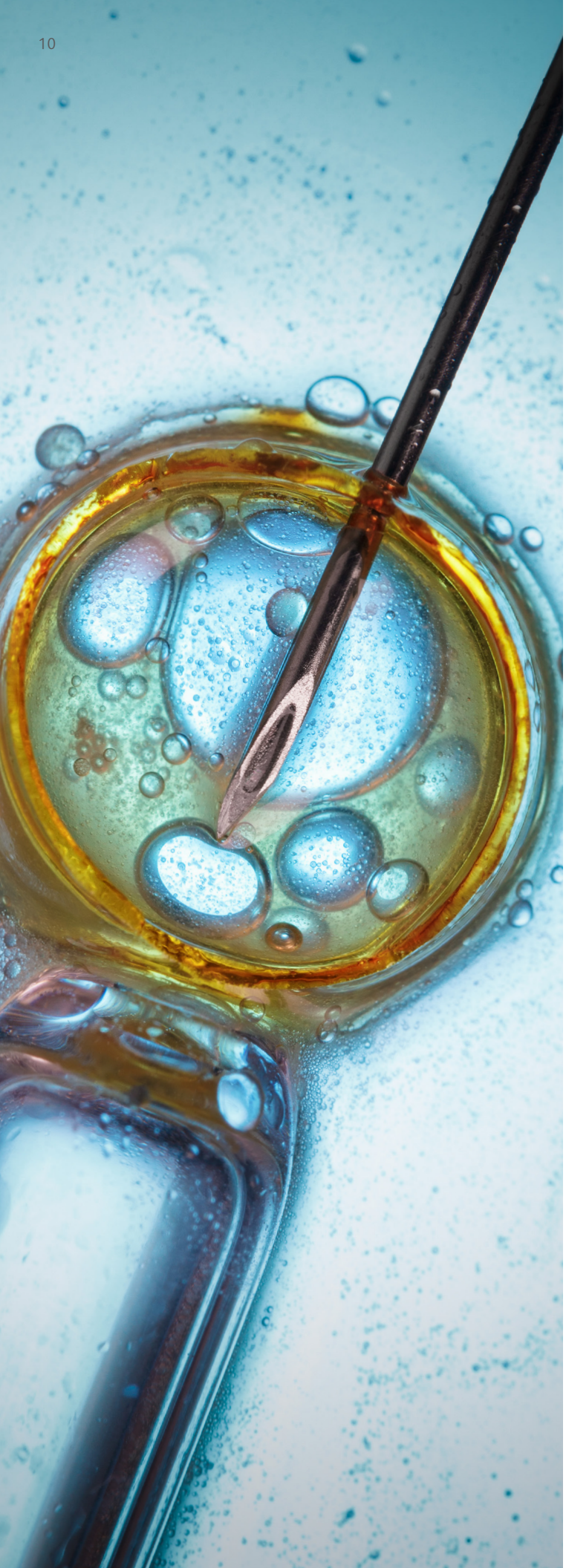


Legal Framework

In order to identify and address the main legal challenges involved in drug research and development in LEO, it is important to understand the sources of law that govern these endeavors. These sources include: (a) international treaties, (b) customary international law, (c) soft law instruments, and (d) US laws that pertain to (i) space-related activities in general, (ii) drug discovery, development, and pre-clinical research in space, and (iii) other relevant laws and regulations such as US export control laws, commercial law, contract law, and intellectual property.

Space Laws and Regulations

US-based pharmaceutical or biotech companies planning to conduct drug research and discovery in LEO, should consider two key layers of space laws: International space laws and US space laws and regulations.

International Space Laws (Treaties)

The Law of Outer Space

While there are soft law instruments that could potentially constitute customary international law in the field of space law and other multilateral treaties, the "Law of Outer Space" consists mainly of five international treaties that form the basis for all space-related activities. These treaties include the Outer Space Treaty, the Rescue Agreement, the Liability Convention, the Registration Convention, and the Moon Treaty. The Outer Space Treaty, also referred to as the "Magna Carta of Space," establishes the core principles of international space law. The main principles, for purposes of this article, include

(1) the exploration and use of outer space is for the benefit and in the interests of all countries and mankind; (2) there shall be freedom of scientific investigation in outer space, and states should facilitate and encourage international cooperation in such investigations; (3) a state party to the Outer Space Treaty should carry out activities in the exploration and use of outer space in accordance with international law; (4) a state party to the Outer Space Treaty on whose registry an object launched in outer space is carried shall retain jurisdiction and control over such object, and over any personnel thereof, while in outer space; and (5) ownership of objects launched into outer space or on celestial bodies is not affected by their presence in outer space or their return to Earth.

The ISS Intergovernmental Agreement

When participating in activities on the ISS, it is crucial to consider the International Space Station Intergovernmental Agreement (commonly referred to as the "**IGA**"). This agreement, signed in 1998 by 15 governments involved in the ISS project (the "**Partner States**"), sets forth a "long-term international cooperative framework . . . on the basis of genuine partnership, for the detailed design, development, operation, and utilization of a permanently inhabited civil international space station for peaceful purposes, in accordance with international law." (Art. 1).

Under the IGA, each Partner State has jurisdiction over the elements it provides on the ISS, treating them as if they were part of their own territory (Art. 5). This means that each Partner State has control and authority over their registered elements and the personnel representing them on the ISS. This extension of national jurisdiction determines which laws apply to activities on a specific Partner State's element of the ISS. It also recognizes the jurisdiction of a Partner State's courts and allows for the enforcement of national laws in areas like criminal matters, liability, and intellectual property rights.

While the United States takes the lead in managing and coordinating the IGA, there are also Memoranda of Understanding ("**MoUs**") between NASA and each cooperating space agency: the European Space Agency (ESA), the Canadian Space Agency (CSA), the Russian Federal Space Agency (Roscosmos), and the Japan Aerospace Exploration Agency (JAXA). These MoUs describe in detail the roles, responsibilities, and management structure necessary for effective utilization of the ISS. In addition to the IGA and MoUs, there are also a few bilateral arrangements between the involved space agencies aimed at both implementing the MoUs and providing specific guidelines for the distribution of roles and responsibilities among the agencies in their respective fields.

Importantly, while the IGA itself is not directly binding on private parties, it does contain certain "flow-down" provisions that mandate the inclusion of these provisions into lower-tier agreements. These provisions include, but are not limited to, the following: (1) the obligation that the ISS shall be utilized in accordance with international law, including the "Law of Outer Space" (Article 2(1)); (2) the retention of jurisdiction and control by each Partner State over the elements it registers in accordance with the Registration Convention and over personnel in or on the ISS who are its nationals (Article 5); (3) the right that each Partner State shall have to access the ISS using its respective government and private sector space transportation systems, provided they are compatible with the ISS (Article 12(1)); and (4) a cross-waiver of liability between Partner States and related entities, such as contractors, subcontractors, users, customers, or entities associated with a Partner State at any tier (Article 16).

US Space Laws and Regulations

The regulations governing the US space industry can be divided into three main sectors; namely: civil, national security, and commercial. The civil sector is managed by agencies like NASA and focuses on non-defense activities such as satellite launching, research, and solar system exploration. The national security sector is overseen by agencies like the United Space Command, the Combined Force Space Component Command, and the United States

Space Force, and is dedicated to defense and intelligence operations. Lastly, the commercial sector involves various federal agencies regulating commercial space activities, such as NASA, the Federal Aviation Administration (the "**FAA**"), the Federal Communications Commission, the National Oceanic and Atmospheric Administration, the Department of State, and the Department of Commerce.

Within the commercial sector, there are four main subcategories: space launch services, commercial communication satellites, remote sensing satellites, and satellite services. Space launch services, which include space flight, cargo transport and space tourism, are mainly governed by the Commercial Space Launch Act of 1984, which also requires a license for launching a vehicle into outer space, operating a launch site, or conducting launch activities. Further, the FAA conducts policy, safety, payload, and environmental reviews as part of this licensing process. Licensees are also required to register all objects placed into space under the Registration Convention.

In addition to the mentioned regulations, there are other US space laws and policies that govern commercial space activities, such as the Communications Act, Inventions in Outer Space, the National Aeronautics and Space Act, the Commercial Space Act, and the US Commercial Space Launch Competitiveness Act. These laws aim to support commercial activities in space, promote scientific advancement, and encourage collaboration between government agencies, private companies, and researchers.

Pharmaceutical and Biotech Laws and Regulations

The old proverb "what goes up must come down" not only reflects a basic law of terrestrial physics, but also holds true in the context of commercial activities in space, particularly in space-based drug research and development in which clinical research ultimately needs to continue or be completed on Earth, at least at present. Even though scientific research aboard the ISS has flourished in the past decade, so far that research is still at a very early stage of pharmaceutical and biotech development, and remains only a precursor to years of subsequent drug and medical treatment development work that must be carried out on Earth.

Currently, pharmaceutical and biotech companies primarily use their space-based research and development activities to gather additional insights to enhance the subsequent stages of their drug and therapy discovery process. Therefore, this section will focus on the laws and regulations that apply to these early-stage activities in space.

International Pharmaceutical Laws and Regulations

Even though the United States is not a party to many international agreements related to biotechnology, the international pharmaceutical and biotech community follows a number of influential soft law instruments. These instruments include, but are not limited to, the OECD Principles of Good Laboratory Practice ("**GLP**") and GLP Compliance Monitoring, UNESCO Universal Declaration of Human Genome and Human Rights (1997), International Ethical Guidelines for Biomedical Research involving Human Subjects (2002), UNESCO International Declaration on Human Genetic Data (2003), UNESCO Declaration on Bioethics in Science and Human Rights (2005), WHO Guidelines on the Quality, Safety, and Efficacy of Gene Therapy Products, and ISSCR Guidelines for Stem Cell Research and Clinical Translation. These standards cover various aspects of the drug development process, such as the quality of non-clinical laboratory studies, ethical implications of human genome research, protection of human rights and privacy, guidance for biomedical research involving human subjects, responsible management of genetic data, and standards for stem cell research. These soft law instruments aim to ensure reliable test results, protect the health and rights of individuals, and promote responsible and reliable scientific research.

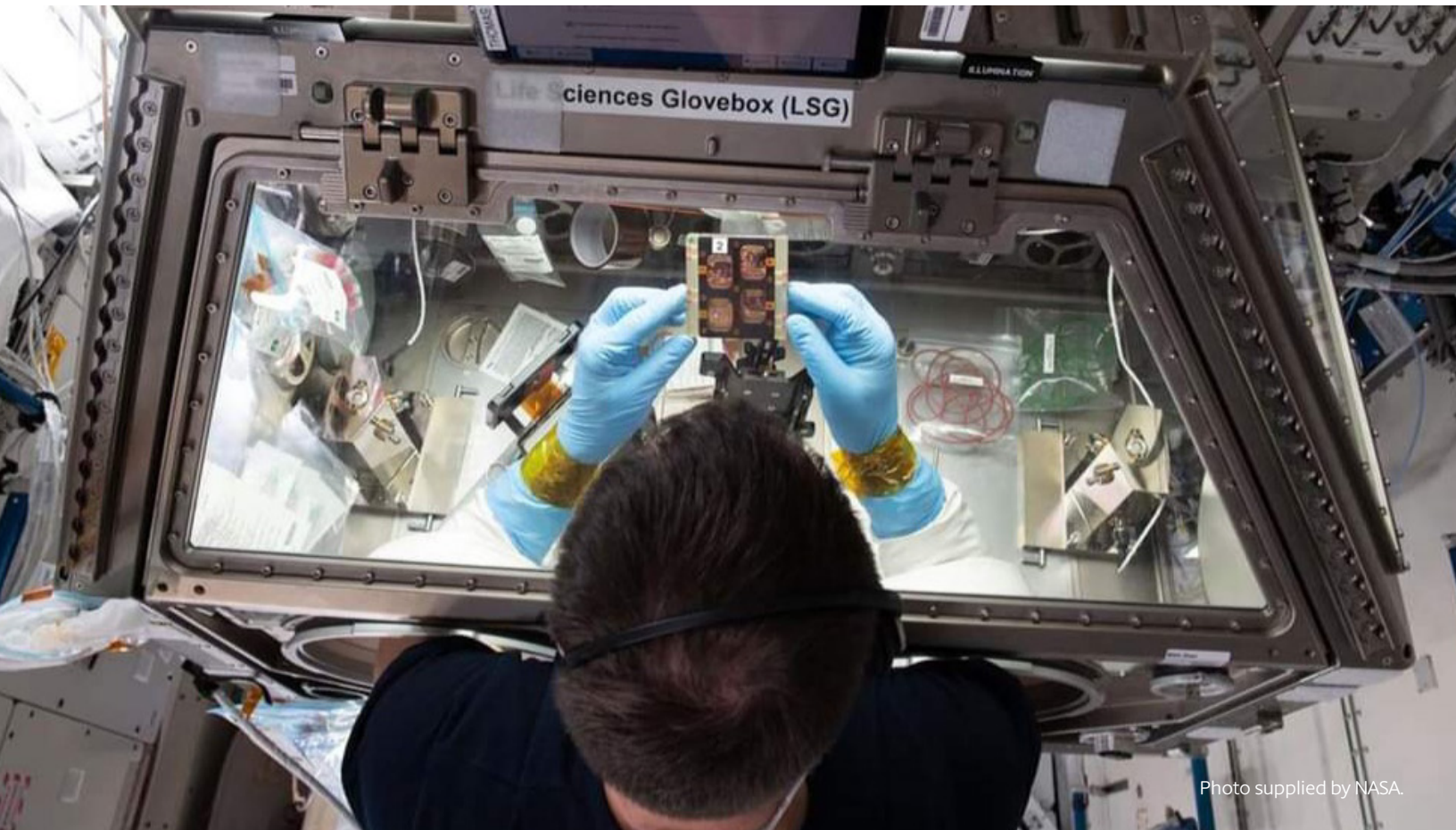
Traditionally, non-clinical research has been used to address basic safety questions through laboratory and animal testing. Sponsors may be able to attain additional valuable nonclinical data from in vitro studies conducted in space that involve human cell lines, stem cells, or tissues, perhaps reducing the amount of animal and human testing that will need to be performed. With this in mind, companies engaged in nonclinical research in space should adhere to the relevant soft law guidelines, principles, and standards, as they have gained consensus among multinational pharmaceutical and biotechnology companies. Those guidelines, principles, and standards could serve as the basis for customary international and space biomedical research law.

US Laws and Regulations

Any non-clinical research activity conducted within an area of the ISS that belongs to the United States and/or subsequently continued on Earth within US territory will be governed by the applicable US laws and regulations, namely The Federal Food, Drug, and Cosmetic Act (FDCA), the Public Health Service Act (PHSA), and the Animal Welfare Act (in cases where animal studies are involved).

Moreover, FDA requires researchers engaged in nonclinical research on which FDA will rely to adhere to GLP, as defined in the medical product development regulations. These regulations establish minimum requirements for study conduct, personnel, facilities, equipment, written protocols, operating procedures, study reports, and a system of quality assurance oversight. These practices help ensure the safety of FDA-regulated products and help determine whether they should be tested in humans.

In the context of biomanufacturing, compliance with current Good Manufacturing Practice (cGMP) regulations is particularly important. These regulations govern the production of drugs and biologics, including therapeutic proteins, antibodies, vaccines, and other innovative products. These regulations cover various aspects of manufacturing, such as facility design, equipment qualification, personnel training, documentation, quality control, and product



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traceability. Additionally, Good Tissue Practice (GTP) regulations may come into play when biomanufacturing involves the use of human cells or tissues. Together, these regulations ensure the safety and quality of human cells and tissues used in applications like regenerative medicine, cell and gene therapies, and tissue engineering. Compliance with cGMP and GTP is crucial to ensure product safety and efficacy by maintaining consistent quality controls and safeguarding the well-being of patients who may receive these products.

Other Laws and Regulations

In the context of drug research and development in space, it is crucial to consider other legal obligations to which a company may be subject. Given the hybrid and multifaceted nature of space law, engaging in these types of activities may also trigger various other laws and regulations at the international and national levels. These additional legal considerations encompass areas such as government contracts, US export control laws and regulations, commercial law, contract law, intellectual property law, insurance, and dispute resolution, among others.

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Legal Considerations

Considering the aforementioned laws and regulations, it becomes apparent that space law and biotech law are intricate and ever-evolving fields. These fields encompass complex subject matters and intersect with other areas of law, giving rise to a wide range of potential legal issues. Since biotech-based activities in LEO are still in their early stages, the legal considerations associated with these activities primarily pertain to pre-clinical research. Within this context, two main focal points where these issues may arise include: (1) research results and intellectual property, and (2) legal and regulatory matters. Keeping this in mind, the main legal issues that may arise can be further categorized into (a) preliminary issues, (b) issues related to drug research and development in LEO, and (c) issues to consider when the research work product returns to Earth.

Preliminary Issues

Before embarking on sponsored-drug research and development in LEO, from a US business perspective, it is important to take into account several legal considerations which include, but are not limited to:

a) **Corporate Formalities.** As most space-related activities are conducted through a juridical person, the most important questions to consider include:

- Is the US entity properly set up?
- What is the entity's corporate purpose?
- Where was the entity incorporated?

- Are there any additional states where registration is necessary for conducting operations?

b) **Ownership or Control of the Asset.** The primary asset of pharmaceutical or biotech companies involved in space activities will most likely be a biological material in the form of a molecular compound, recombinant protein, genetically modified organism, cell line, antibody, or other relevant items. Therefore, the main considerations to keep in mind include:

- Does the company have ownership or control over the asset?
- Have the inventors properly assigned the invention to the company?
- If the company has "control," what are the associated rights and restrictions with respect to the asset?
- Are there any other entities with a title, right, or interest in the asset or its improvements?

c) **Permits or Authorizations.** Before sending biological materials to the ISS (or later to commercial space stations), several essential questions should be considered, including:

- Is an export license or permit required? If so, what are the specific requirements and procedures?
- Are there any licenses that need to be obtained before sending these biological materials to space?
- Are biosafety permits or certifications necessary for handling and transporting the materials?
- Are there any specific biosafety regulations or guidelines to follow?
- If human genome research is involved, what type of approval or consent is required, and what procedures must be implemented to protect human subjects' privacy?
- Are there any specific regulations or guidelines provided by CASIS, NASA, FDA, FAA, or other regulatory bodies?

Drug Research and Development in LEO

When it comes to drug research and development in space, there are several additional factors that need to be considered. One crucial aspect to keep in mind is the future decommissioning of the ISS, which is scheduled to occur around 2031. Following this event, privately-held commercial space stations will step in to fill that void. Therefore, it is essential to address these issues at two distinct points in time: Before the decommissioning of the ISS and after its transition to private commercial space stations.

Before the decommissioning of the ISS, there are several key issues that need to be considered. These include:

- What are the specific objectives of the drug research and development in space?
- Which areas of drug research and discovery should be the focus in the space environment?
- With whom will the company need to contract for purposes of the space-based drug research and development?
- Which companies or entities would be most suitable collaboration partners?
- What logistics need to be coordinated for transporting research payloads to and from space?
- Where will the research take place (i.e., the ISS National Lab or another element within the United States or another country)?
- What are the legal implications and jurisdictional aspects to consider if the research is conducted on a module registered in another country?

- What are the roles and responsibilities of the scientists involved in the research, including considerations of ownership rights if they make inventive contributions?
- What are the terms and conditions for accessing and utilizing facilities, equipment, and resources?
- How will ownership and control of research outcomes (i.e., research results and inventions) be determined?
- Which governing law will apply, and which country will have jurisdiction over any contractual disputes that may arise?

Once the ISS decommissions, the new commercial space stations will likely include portions (**"Modules"**) that will be leased to or owned by governments and/or commercial entities across the world. This will raise a fresh set of issues, in addition to those mentioned earlier, which include the following:

- What will be the rules of law applied to these international endeavors as to pharmaceutical and biotech research and development in space?
- Will government customers of these space stations assert jurisdiction for actions in their Modules (similar to the result of the IGA) or will governments, as well a commercial customers, be subject to a commercial contracting approach as to selecting a choice of laws?
- Or, for all or some of the issues that might arise (such as criminal laws), should and will the law of the country licensing the commercial space station govern?
- And what about the laws of the country licensing the launch vehicles that are returning to earth with the results of these pharmaceutical and biotech materials, as well as the jurisdictions (if different) to which these re-entry vehicles are landing?
- Whose laws and jurisdiction will those products be subject to (which may be in addition to and different from the laws governing the materials on board the space station)?

Work Product Returns to Earth

At this stage, the crucial question to ask is what steps need to be taken from a regulatory perspective to ensure that the data generated in space can be used for further development of the asset on Earth? Additionally, it is important to consider how to perfect any rights and title over the research results and intellectual property generated, developed, and/or arising from the performance of the research in LEO.


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Best-Practice Tips

The following best-practice tips will tackle the primary legal challenges that pharmaceutical or biotech companies might face during drug research and development in space. To ensure clarity, these recommendations will be presented in the same order as the issues previously discussed, which will continue to be focused on safeguarding the predominant factors associated with pre-clinical research, that is: (1) research results and intellectual property, and (2) legal and regulatory matters.

Preliminary Issues

a) **Corporate Formalities.** Ensuring proper incorporation and qualification to conduct transactions in relevant jurisdictions is important for an entity engaging in biotech research in space for several reasons:

- First, proper incorporation with all the relevant corporate documentation in place establishes the entity as a legal and recognized entity. This provides a legal framework for the activities and operations of the entity, including drug research and development in space. It also ensures that the entity has the necessary legal standing to enter into contracts and protect its interests.
- Second, being qualified to conduct transactions in the jurisdiction where pre-space activities are conducted is important for complying with local laws and regulations. Different jurisdictions may have specific requirements for conducting certain activities. By fulfilling these qualifications, the entity can ensure that it is operating within the legal boundaries and is eligible to engage in the desired activities.

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- By properly incorporating and qualifying it to conduct transactions, the entity can also protect its rights to the research results and intellectual property developed or generated in space. This includes contracting with inventors or companies to ensure that the entity has exclusive rights to its discoveries and inventions.

b) Intellectual Property Rights. It is important to ensure that the company has either ownership or control over the asset or biological material (i.e., molecular compound, recombinant proteins, genetically modified organisms, cell lines, antibodies, etc.) (the "**Asset**") that will form the basis of the research in space. To that end, it is crucial that there is a proper assignment of all rights, title, and interest in and to such Asset in favor of the company or that the company is not otherwise restricted in developing this Asset in space.

c) Permits and Authorizations. Before engaging in any space-related activity, an important question that should be addressed is what types of permits or authorizations need to be secured beforehand? The following are some examples of the permits and/or authorizations that should be considered:

i. *US Export Control.* If a pharmaceutical or biotech company is interested in conducting drug discovery, development, and pre-clinical research in space, a question to consider is whether the activity would constitute an "export" and if so, whether prior US government authorization is required to engage in such activity. Contrary to common belief, an "export" not only refers to physically shipping or transmitting items out of the US, but also includes the release of source code or technology/ technical data (e.g., technical drawings, design plans, certain data, or general "know-how") to a foreign person within the United States, including areas of land, sea, or space connected to the United States (known as a "deemed export"). Foreign persons are individuals who are not US citizens, US green card holders, US asylees, or US refugees. In this context, even though the launch or reentry of the space launch vehicle from the United States would not be considered an export under US law (51 USC § 50919(f); 15 CFR § 734.18(a)(1)), any exchange of technology or technical data (which can occur through intangible and electronic transfers, such as conversations, emails, server access, visual inspection, etc.) that takes place on the ISS or within the US (before the initial launch or after the return from the ISS for further evaluation on Earth) may be deemed an "export" if such technology is released to a "foreign person." In such cases, a US company may need to seek and obtain authorization from the US government before exporting certain controlled items, software, technology/ technical data, or defense services.

ii. *Other Permits or Authorizations.* In light of the particular circumstances surrounding the research that will take place in space, any US company intending to engage in these types of activities should determine whether there are additional permits or authorizations that need to be sought and secured prior to engaging in them. These may include (1) biosafety permits or certifications necessary for handling and transporting materials, (2) consents by human subjects if human genome research is involved, and/or (3) other specific permits or approvals required by CASIS, NASA, FDA, or other regulatory bodies.

d) Logistics and Transportation Services. While CASIS collaborates with pharma and biotech companies for logistics and launch services to transport biological materials to the ISS, it is crucial for companies to negotiate appropriate terms and conditions that provide suitable protection. This includes addressing liability, risk of loss of the biological materials, compliance with laws, indemnity, limitation of liability, termination for material breach, insurance, governing law, and dispute resolution.

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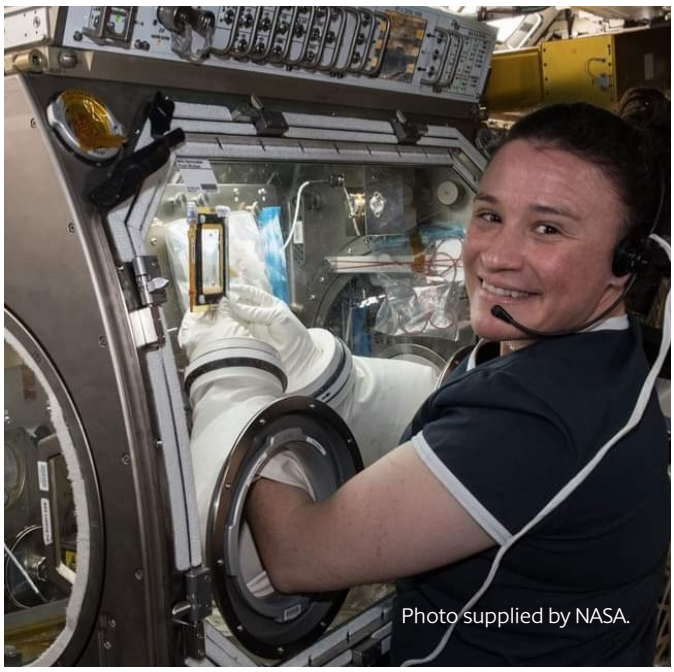
Drug Research and Development in LEO

When considering sponsoring drug research and discovery in space, it is crucial to address the applicable legal and contractual framework that will govern such endeavors. From a legal perspective, this framework includes five international treaties known as the "Law of Outer Space." However, since these treaties were primarily the product of the Cold War and have not been modified since their inception, they do not adequately cover activities related to drug research and development in space, nor for the most part include detailed guidance as to specific required, permitted or prohibited activities. This also applies to any associated soft law instruments and customary international law. Given these limitations, drug research and development activities in space need, for the most part, to be governed by contracts (subject to the standard limitations of freedom of contract, including legal restrictions, public policy, and statutory regulations).

Therefore, it is also necessary to determine the exact structure of the governing contractual framework considering the aforementioned issues, both before and after the decommissioning of the ISS.



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a) **Pre-ISS Decommission.** When considering conducting drug research and development aboard the ISS National Lab, there are important factors to keep in mind:

i. *Research Solicitation Process.* CASIS is responsible for overseeing the ISS National Lab and the research conducted on it. Therefore, all drug research and development projects aboard the ISS National Lab must result from an award granted by CASIS. To that end, CASIS releases research solicitations, either independently or in collaboration with other governmental agencies (i.e., NSF or NIH). These solicitations outline the requirements and criteria for awarding research projects. It is essential for potential applicants to carefully review these requirements and criteria to ensure they are able to comply with them and that they align with their specific asset(s) and needs.

ii. *Considerations for Research Expectations.* Before accepting an award, it is crucial to have clarity on the sponsor's expectations regarding the research. It is important to consider the scope of the research, manner of conducting it, scientists involved, work product and deliverables, ownership and/or right to use research results and intellectual property, jurisdiction, applicable laws, and regulatory compliance.

iii. *Templates and Non-Negotiable Provisions.* CASIS has established templates that serve as a reference for potential ISS National Lab awardees. The templates can be found on the ISS National Lab website: https://www.issnationallab.org/user-agreements/

iv. *Non-Negotiable Provisions.* CASIS emphasizes that certain provisions in the agreements are non-negotiable (some of which are derived from the "flow-down" provisions set forth in the IGA or are obligations related to CASIS-funded research). These provisions, should be identified and assessed to ensure they align with the company's expectations.

v. *Customizing Agreements with CASIS.* Except for non-negotiable provisions, awardees should otherwise ensure that the agreements they enter into with CASIS provide suitable legal, contractual, and regulatory protections based on their specific needs. Key provisions to consider include standards of performance, contractual remedies, confidentiality, intellectual property rights, generation and storage of research results, integrity of data, regulatory compliance, limitation of liability, insurance coverage, indemnification obligations, governing law, and jurisdiction.

vi. *Intellectual Property Rights.* Users who have access to the ISS National Lab will have their rights and obligations determined by the contractual framework they have agreed upon with CASIS. However, it is important to note that according to the IGA, the country of inventorship will be determined by the ownership and registry of the "element" in which the invention took place. This means that if an invention is made on a US element, it will be deemed to have occurred in the US. However, this territorial approach is only used to determine the location and country where the invention took place. In other words, the ownership of the invention and the right to file for a patent in multiple countries are not affected by this determination and inventors may file for a patent in any country of their choosing, as long as they comply with any foreign filing requirements such as foreign filing licenses.

b) **Post-ISS Decommission.** Once the ISS decommissions, it will create exciting opportunities for pharmaceutical and biotech companies interested in sponsoring drug research and development in space. While it is too premature at this point to answer all the questions that were previously posed, these answers will certainly be developing and evolving as privately-owned commercial space stations become closer to reality. What we can anticipate, however, is that as CASIS's involvement decreases or changes, these pharmaceutical and biotech companies will have greater leverage to negotiate agreements that are tailored to their specific interests and needs, without the current limitations. During this phase, it is crucial to ensure that contracts with commercial space stations include standard terms and conditions for projects involving biological materials at a pre-clinical stage. These conditions should cover various aspects such as ownership and use of research results and intellectual property, access and integrity of research data, confidentiality, regulatory compliance, performance standards, remedies and deliverables, liability and indemnification, insurance, modification and termination (including the consequences), and governing law and dispute resolution, among other important provisions.

Work Product Returns to Earth

To ensure that the work product of the research conducted in space can be effectively used on Earth from a legal and regulatory perspective upon its return, we recommend addressing the following key suggestions:

- Ensure that all required permits and documentation have been obtained to comply with applicable laws and regulations regarding the transportation and importation of biological materials. Identify any specific requirements or restrictions that need to be addressed in order to legally bring the research materials back to Earth.
- Implement protocols and systems to securely store and retrieve experimental results while maintaining data integrity. Establish mechanisms to ensure the chain of custody for the biological materials is properly documented, demonstrating their origin, handling, and storage throughout the research process.
- Evaluate whether the research conducted in space followed proper regulations and guidance. Assess whether the protocols and procedures used during the research adhered to the minimum basic requirements for pre-clinical research, both in *vivo* and in *vitro*. Identify any discrepancies or areas that require further evaluation to ensure compliance with applicable regulations.
- Assess whether the experimental design used during the research in space was appropriate. Evaluate the sample preparation methods and data collection techniques to ensure they were sufficient for reliable and accurate results. Address any concerns regarding the quality or validity of the data obtained, and take steps to validate and verify the research findings upon return to Earth.
- Identify whether there are any additional regulatory approvals or assessments required before proceeding with further drug development, including clinical research. Evaluate if the research findings from space raise specific regulatory considerations or need additional safety or efficacy assessments. Address any additional regulatory requirements or considerations that arise upon returning the work product to Earth.

Conclusion

The realm of space exploration has entered a new era, opening up a world of endless possibilities for the future. From satellite deployment and moon landings, we now envision Mars expeditions, commercial spaceflights, cinematic ventures, space mining, and even drug research and development within privately-owned commercial space stations.

One of the most groundbreaking platforms in recent years has been the ISS. Research conducted on the ISS National Lab has revealed the profound impact of microgravity and other space conditions on cellular behavior, tissue engineering, gene expression, and organism growth patterns. This has the potential to revolutionize medicine and take it to new heights.

The advantages of conducting drug research and development in space are enormous, both from a scientific and business perspective. Scientifically, experiments carried out on the ISS National Lab, in conjunction with ground-based studies, have shown that microgravity allows for the exploration of unique features that cannot be achieved under normal gravity conditions. It enables more efficient 3D cell cultures, improved protein crystal growth, and opens up possibilities for 3D printing of biomaterials, cells, tissues, and even organs.

From a business standpoint, pharmaceutical and biotech companies, along with other key players in the industry, have shown increasing interest in the potential of space for drug research and development. The prospects of groundbreaking discoveries, the growing accessibility of space through private sector involvement, funding opportunities from NASA, CASIS, the National Stem Cell Foundation and others, accelerated scientific advancements, and the chance to establish collaborative partnerships with esteemed organizations and industry peers are all driving this interest.

However, it is important to acknowledge the challenges associated with drug research and development in space. A comprehensive understanding of the applicable legal landscape, encompassing international and national space laws, as well as biotech laws and regulations, is crucial. Companies must also be aware of other legal obligations such as government contracts, export control laws, commercial law, contract law, intellectual property protection, insurance, and dispute resolution mechanisms.

Companies intending to engage in drug research and development in space should also be mindful of the issues that may arise at every stage of their efforts. By proactively identifying and addressing these challenges, companies can enhance their prospects of success. Despite the intricacies involved, the immense benefits of conducting research in microgravity conditions and the potential for groundbreaking discoveries make it an exhilarating frontier for the pharmaceutical and biotech industry. The vast possibilities of space beckon, waiting to be explored and harnessed for the advancement of science and humanity.

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