MOBILE/MODULAR BSL-4 FACILITIES FOR MEETING RESTRICTED EARTH RETURN CONTAINMENT REQUIREMENTS.

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Introduction: NASA robotic sample return missions designated *Category V Restricted Earth Return* by the NASA Planetary Protection Office require sample containment and biohazard testing in a receiving laboratory as directed by NASA Procedural Requirement (NPR) 8020.12D [1] – ensuring the preservation and protection of Earth and the sample. Currently, NPR 8020.12D classifies *Restricted Earth Return* for robotic sample return missions from Mars, Europa, and Enceladus with the caveat that future proposed mission locations could be added or restrictions lifted on a case by case basis as scientific knowledge and understanding of biohazards progresses.

Since the 1960s, sample containment from an unknown extraterrestrial biohazard have been related to the highest containment standards and protocols known to modern science. Today, Biosafety Level (BSL) 4 standards and protocols are used to study the most dangerous high-risk diseases and unknown biological agents on Earth. Over 30 BSL-4 facilities have been constructed worldwide with 12 residing in the United States; of theses, 8 are operational [2, 3]. In the last two decades, these brick and mortar facilities have cost in the hundreds of millions of dollars dependent on the facility requirements and size. Previous mission concept studies for constructing a NASA sample receiving facility with an integrated BSL-4 quarantine and biohazard testing facility have also been estimated in the hundreds of millions of dollars.

As an alternative option, we have recently conducted an initial trade study for constructing a mobile and/or modular sample containment laboratory that would meet all BSL-4 and planetary protection standards and protocols at a faction of the cost. Mobile and modular BSL-2 and 3 facilities have been successfully constructed and deployed world-wide for government testing of pathogens and pharmaceutical production. Our study showed that a modular BSL-4 construction could result in ~ 90% cost reduction when compared to traditional construction methods without compromising the preservation of the sample or Earth.

COSPAR/NASA Facility Requirements: Under the UN Space Treaty of 1967, the Committee on Space Research (COSPAR) maintains a planetary protection policy at the international level for all space faring nations. The policy provides "international standard on procedures to avoid organic-constituent and biological contamination in space exploration" [4]. The policy also promotes the prevention of "adverse changes in the environment of the Earth resulting from the introduction of extraterrestrial matter" as stated in the UN Space Treaty. NASA Policy Directive (NPD) 8020.7G [5] complies with the UN Space Treaty and COSPAR planetary protection policy stating "the Earth must be protected from the potential hazard posed by extraterrestrial matter carried by a spacecraft returning from another planet or other extraterrestrial sources."

NASA NPR 8020.12D [1] outlines requirements for meeting the NPD 8020.7G [5] as well as specifies planning documents and reviews for *Category V Restricted Earth Returns*. However, international space treaties, COSPAR policies, and NASA planetary protection policy directives and requirements do not impose specific construction design requirements on a BSL-4 facility nor biocontainment architecture.

BSL-4 Facility Standards: In the U.S., the *Biosafety in Microbiological and Biomedical Laboratories* [6] publication authored by the U.S. Department of Health and Human Services (HHS): Public Health Service, Centers for Disease Control and Prevention, and the National Institutes of Health houses the primary recommendations, standards, and design requirements for all BSL labs. There are two models for modern BSL-4 laboratories:

- *Cabinet Laboratory*: Manipulation of agents must be performed in a Class III Biosafety Cabinet (BSC); i.e., negative pressure glovebox.
- *Suit Laboratory*: Personnel must wear a positive pressurized protective suit inside a negative pressure laboratory.

Negative pressure gastight BSL-4 BSC III cabinets and suit laboratories have special engineering and design features to prevent microorganisms from being disseminated into the environment. BSL-4 laboratory personnel are highly trained with rigorous procedural handling of extremely hazardous infectious agents, understand the primary and secondary containment functions, and know the design characteristics of containment laboratory equipment. For the design/construction requirements of a mobile/modular BSL-4 containment, we used the established HHS document standards and protocols for a cabinet laboratory that are currently followed in operational BSL-4 facilities in the U.S.

Mobile BSL-4 Containment Facility: A mobile containment facility could secure a sample return capsule (SRC) at the landing site. After biocide decontamination procedures, the facility could be transported anywhere in the world by land, sea, or air. The mobile facility could attach to an existing BSL-4 laboratory that could be used to conduct biohazard analyses on a sample subset while the mobile lab could provide primary clean containment of the science samples awaiting biosafety results. A second usage scenario could attach the lab to a dedicated NASA receiving facility that could conduct the primary containment and biohazard testing. Additionally, a third scenario could have the mobile facility remain at the landing site as primary containment and a small sample is transported to an existing BSL-4 facility for biohazard testing. After completion of biohazard testing, decisions could be made to sterilize the sample or transport all or portions to a permanent quarantine storage facility.

The transportable laboratory preliminary design for these scenarios was sized at 48 ft x 14 ft, 9.5 ft high, met BSL-4 requirements for pressurization, and was designed with appropriate number of containment system redundancies and emergency back-ups. The mobile container could be transportable on a flatbed trailer and fit into a Boeing C-17 Globemaster III or Lockheed C-5 Galaxy for air transport. The facility could be self-contained with the exception of the effluent decontamination system and electrical power supply during transport (dual diesel electrical generators positioned on the trailer).

The facility could contain separate rooms for control/administration, outer change, entry anteroom, shower room, inner change room, mechanical, and main BSL-4 lab. The laboratory would be a negative pressure ISO class 5 cleanroom with ultra-low penetration air (ULPA) and high efficiency gas adsorber (HEGA) filters. The BSL-4 lab would be outfitted with a negative pressure nitrogen enriched Class III BSC glovebox chain. This could include (in-order):

- SRC antechamber/decontamination
- SRC hardware de-integration chamber
- Antechamber/decontamination
- Primary sample quarantine/opening science canister chamber
- Double door autoclave/gas sterilization chamber for retrieval of biohazard testing sub-sample

Material selection for lab finishes and Class III BSC would be based on organic and inorganic compounds of scientific concern. All welded stainless steel HVAC system exhaust and supply housings could include HEPA, ULPA and Teflon (PTFE) filters with automatic scanning for leak integrity and He leak tested. HEGA gas/vapor adsorbers and/or absorbers could be used if chemicals need to be removed. Gas sterilization/decontamination system (*e.g.,* vapor H_2O_2 system) could be plumbed into each room of the facility. The facility would also be manufactured in a dedicated cleanroom to maintain control of the engineering, fabrication, assembly, integration, testing and commissioning before deployment.

Modular BSL-4 Sample Receiving Facility: A modular BSL-4 sample receiving facility could be assembled into any shell building or high bay using the same construction methods as the mobile laboratory. The modular construction could use standard 40 ft containers, assembled together to create a large lab space with BSC III cabinet chains. Testing and certification of the BSL-4 laboratory could be conducted at the manufacturing cleanroom facility and then transported and assembled on-site. Several modular Animal BSL-3 facilities have been successfully constructed world-wide. With added system redundancies, these facilities could be reclassified as BSL-4 laboratories.

Gas-tight Standards: Class III BSC glovebox gas-tight (leak rate) criterion is $< 1\times10^{-5}$ cc/s with 100% He tracer gas under 3 inH_2O pressure in the cabinet. [7] Dependent on mission science requirements, specialized double walled glovebox seals could be required for maintaining nitrogen or other gas environment purity under negative pressure. Non-glove storage isolators can achieve a He leak rate of $< 1\times10^{-7}$ cc/s. However, achieving a better leak rate on gloveboxes may require additional engineering development and challenges.

Summary: Mobile and modular BSL-2 and 3 facilities have been constructed and deployed world-wide with great success. A mobile/modular BSL-4 receiving facility can meet all current standards and protocols, including redundant systems and critical biological containment/pressurization requirements. Manufacturing in a dedicated cleanroom can maintain better control of the engineering, fabrication, assembly, integration, testing and commissioning of a facility. Future studies of sample receiving facilities that require BSL-4 containment may wish to include a comparison review of modern mobile/modular labs as an alternative construction option.

Reference: [1] NASA NPR 8020.12D (2011) *Planetary Protection Provisions for Robotic Extraterrestrial Missions.* [2] Van Meter (2015) *Microbiology for the Healthcare Professional. Elsevier.* [3] Gronvall et al. (2007) *Biosecurity and Bioterrorism*, 5(1):75-85. [4] COSPAR Planetary Protection Policy (2015) *Space Research Today*, 193. [5] NASA NPD 8020.7G (2013) *Biological Contamination Control for Outbound and Inbound Planetary Spacecraft.* [6] HHS (2009) Biosafety in Microbiological and Biomedical Laboratories, 5th ed. HHS(CDC) 21-1112. [7] Stuart, D. et al. (2012) *Applied Biosafety*, 17(3):128-131.

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