Significance of High-Containment Biological Laboratories Performing Work During the COVID-19 Pandemic: BSL-3 and -4 Labs

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Abstract

High containment biological laboratories (HCBL) are required for work on Risk Group 3 and 4 agents across the spectrum of basic, applied, and translational research. These laboratories include biosafety level (BSL)-3, BSL-4, animal BSL (ABSL)-3, BSL-3-Ag (agriculture livestock), and ABSL-4 laboratories. While SARS-CoV-2 is classified as a Risk Group 3 biological agent, routine diagnostic can be handled at BSL-2. Scenarios involving virus culture, potential exposure to aerosols, divergent high transmissible variants, and zoonosis from laboratory animals require higher BSL-3 measures. Establishing HCBLs especially those at BSL-4 is costly and needs continual investments of resources and funding to sustain labor, equipment, infrastructure, certifications, and operational needs. There are now over 50 BSL-4 laboratories and numerous BSL-3 laboratories worldwide. Besides technical and funding challenges, there are biosecurity and dual-use risks, and local community issues to contend with in order to sustain operations. Here, we describe case histories for distinct HCBLs: representative national centers for diagnostic and reference, nonprofit organizations. Case histories describe capabilities and assess activities during COVID-19 and include capacities, gaps, successes, and summary of lessons learned for future practice.

Background

This poster highlights our publication and related references (Yeh et al., 2021). Our objective was to reinforce the work among our collaborators at various high containment biological laboratories around the world. Our representative laboratories include three BSL-3 and one BSL-4among three national laboratories and a nonprofit organization. Recognized international norms for enhancing global health security and countering weapons of mass destruction include the Biological Weapons Convention and United Nations Security Council Resolution 1540.

- Additional global frameworks for health preparedness include International Health Regulations 2005 and the Global Health Security Agenda.
- High containment biological laboratories (HCBL) often refer to biosafety level-3 and -4 laboratories designed to contain pathogens and provide safe environment for those performing related work.
- WHO and CDC biosafety guidelines are widely accepted no standard oversight exists (WHO, Meechan and Potts, 2020)..
- WHO and NIH also provide guidance for dual-use research of concern and gain-of-function studies (NAS, 2017).
- Several motivations exist building and commissioning HCBLs. (Hottes et al., 2012)).

This work demonstrates the preparedness for prevent-detect-respond to outbreaks of emerging infectious diseases and importance for creating partnerships before they are needed.

Case Histories

The successes of HCBLs and their trained personnel during the COVID-19 pandemic underscore their critical functions, missions, and preparedness that each were stood up. Several advancements are highlighted here which include research and development, supporting test and evaluation for laboratory diagnostics, vaccine studies, and biosafety and biosecurity expertise.

TABLE 1. Summary of high-containment biological laboratories (HCBL) described in case histories. HCBLs from three continents are listed

	HCBL	Organization Type	Description
BSL-3	Kazakhstan Central Reference Laboratory	National Laboratory	Crucial functions: • Repository for especially dangerous pathogen. • Reference, research, and training center. • Promotes international laboratory practices.
BSL-3	MRIGlobal	Non-profit research	Accreditations and registrations: • CDC registered for Select Agent and Toxins. • CAP, CLIA certified laboratories. • ISO-9001:2015, ISO 17025:2005
BSL-3	Taiwan Centers for Disease Control (CDC)	National Laboratory	Relevant mission: • National reference and research center. • Promotes international laboratory practices.
BSL-4	International Center for Medical Research of Franceville (CIRMF)	National Laboratory	Crucial roles: • National diagnostic center and reference laboratory. • Regional center for diagnosis of pathogens including bacteria (anthrax) and viruses: CCHF, rabies, SARS-CoV-2, Ebola, Marburg, polio • Recognized international center for research.

While our case history laboratories demonstrated laboratory diagnostic capabilities and ability to scale up operations during surge demands, the **Kazakhstan Central Reference Laboratory**, which is one of the newest BSL-3 laboratories, also performed impactful studies to support domestic vaccine development.

MRIGlobal and the **Taiwan CDC** cited BSL enhancements as one way to adapt existing laboratory infrastructure and increase capacity. Experts performed risk-based assessments prior to working in the BSL-2+ laboratories where they implemented modifications as well as additional training on PPE requirements and containment policies. **CIRMF** also had prior experience performing work in BSL-3+ without using their BSL-4 to support COVID-19.

Taiwan CDC example highlights past preparations including avian influenza and MERS-CoV and a strong tiered network of laboratories. The capacity and capabilities within their BSL-3 laboratories provided guidance for laboratory networks at lower containment levels. The initial assessment of pathogens in BSL-3 also enabled the establishment of procedures to handle such pathogens at a lower containment level.

Conclusions

Our case histories of four HCBLs demonstrate their application, intent, design and utility to support laboratory diagnostic and reference activities and respond to surge demands such as COVID-19. Considering high operating costs, the laboratory investments including quality management systems such as ISO:35001 and training whether public or private funded appear justified and there is a track record for sustainable operations. These outputs serve as a model for pandemic response and mitigation.

While these case histories are a small representation of HCBL work, greater efforts are needed that continue to bring awareness and encourage transparency.

- The number of HCBLs continues to increase, that trend will likely continue with COVID-19 worldwide as countries and states will choose to prioritize and build them.
- Since many academic and private laboratories are not under their governmental oversight, it is difficult to obtain accurate counts of HCBLs (4). In our references, we also noted inconsistencies in the HCBLs especially those listed in the BSL-3 category.

While the value of HCBLs is established, the uncertain number of HCBLs also makes it difficult to ascertain capabilities and capacities for future preparedness.

- Some HBCLs especially those at the top-tier of national diagnostic and reference laboratories are connected with infectious disease surveillance programs that become further important as those surveillance programs intersect with tracking and predicting patterns and trends of infectious disease to augment preparedness.
- Regarding new and emerging pathogens, there is a need for higher biological containment for samples obtained from space exploration.

References

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