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Short Communication

# Networking for training Level 3/4 biosafety laboratory staff

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ABSTRACT

Worldwide, public health systems are continually challenged by emerging and re-emerging viruses. It is therefore important that high-containment labs coordinate and communicate globally to share their experiences and lessons to improve their capacity to respond to threats. The National Biosafety (Level 4) Laboratory in Wuhan, CAS, which is the first Level 4 biosafety laboratory (BSL-4) in China, has been certified recently and it is expected to play an important role in the prevention and control of highly infectious agents in future. Trained and experienced staff in such organizations is the most important factor contributing to safety and security. Therefore, it is imperative to develop a standard training program. Accordingly, in the present study, we developed an improved training program and assessment system based on policies and practices developed by BSL-3/4s in other countries. It included the following three components: (1) A flexible modularized theoretical training: This training comprised 14 modularized theoretical topics such that staffs with different backgrounds could take this theoretical training with different topic combinations according to their knowledge and skill levels; (2) A standardized practical training assessment: This comprehensive assessment, which could be used with biosafety laboratory staff before, during, and after training, included standard operation procedures to meet the special requirements of trainees with different scores; and (3) An applicable documentation system: A certification system was established to evaluate the ability of all staff working inside or outside the laboratory, implemented by a special committee. This certification was approved and authorized by the director of the laboratory and was classified into three grades with corresponding minimal requirements. Further, the present study examined the importance of and need for networking for training BSL-3/4 staff. The establishment of rigorous standards for training BSL-3/4 staff will instill confidence in the public, policy makers, and security officials. Additionally, the expanded international network of BSL-3/4s will continue to be operated safely and will pose no risk to scientific staff, local communities, surrounding environment, and host nations. The clarification and coordination of training standards will help develop a highly-qualified biocontainment workforce and will result in a series of programs that will enable scientists to develop measures to deal with existing threat agents and new diseases that emerge.



Emerging and re-emerging infections and possible bioterrorism acts will continue to challenge both the medical community and civilian populations worldwide. Such events range from the use of anthrax in terrorist events to real international emergencies such as the severe acute respiratory syndrome (SARS) and 2014–15 Ebola epidemics, and the influenza pandemic that is expected to occur in future. These experiences have taught us a very important lesson; that a national/global health crisis can be effectively countered and brought to an end through a national/international effort involving effective communication and cooperation, as opposed to local initiatives or uncoordinated actions. Networking among Level 3/4 biosafety laboratories (BSL-3/4s) is one of the major approaches to enhancing preparedness for emergencies and tackling potential challenges.

It is fortunate that several international networks such as the World Health Organization's Global Outbreak Alert and Response Network (WHO-GOARN) and the Global Health Security Action Group-Laboratory Network (GHSAG-LN), as well as other networks for "high consequence pathogens" established by the WHO, are in operation. Meanwhile, the European Network for Highly Infectious Disease and European Network of P4 Laboratories are good examples of successful cooperation on the following essential objectives of networking: establishing a coordinated and accessible BSL-4 infrastructure for the surveillance and diagnosis of Risk Group 4

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pathogens; collecting biosafety and training procedures that have been adopted in European P4 laboratories; collecting, sharing, and evaluating diagnostic methods for P4 agents; establishing communication channels for information exchange among national and international health authorities; and standardizing the policies and procedures of biosafety and biosecurity. In the present paper, we would like to highlight the importance of networking for BSL-3/4 staff training.

Good biosafety laboratory practices cannot be developed without a strong safety culture. It is therefore generally agreed that training should be a precondition for starting work in specialized, safety- and security-sensitive BSL-3/4s. A literature review concluded that deviation from general "good microbiological practices" is the most frequent cause of laboratory-acquired infections, and that training for compliance with procedures and regulations seems to be the best method to avoid such infections.[1] As of December 2017, worldwide, at least 54 BSL-4s were in the planning or operational phase[2] and there were many more BSL-3s. The current expansion of BSL-3/4s in more countries has resulted in a demand for experienced workers, which presents a challenge for the establishment of BSL-3/4 training processes. Undoubtedly, qualified personnel are critical for guaranteeing the effectiveness and safety functions of a biosafety laboratory. Given the global demand for BSL-3/4 workers; the increasing national/international collaboration in the areas of high containment laboratory biosafety; and the increase in basic research and its application to the development of diagnostics, therapeutics, and vaccines, there is a clear national and international need for more structured and transparent training processes to establish and verify standards for BSL-3/4 workers. The infrastructure for the National Biosafety (Level 4) Laboratory in Wuhan, CAS, China's first BSL-4 laboratory, was completed in 2015 and it has been certified as meeting the highest biosafety standard by the China National Accreditation Service for Conformity Assessment (CNAS).[3] Recently, research in the Wuhan BSL-4, on Ebola virus, Nipah virus, and Crimean-Congo hemorrhagic fever virus, has been approved by the National Health and Family Planning Commission of China.[4] Therefore, the need for more experienced workers and the development of personnel training would emerge soon in Wuhan BSL-4. National/international cooperation and networking for training will be beneficial, especially because the Wuhan BSL-4 hopes to be a WHO reference laboratory and national research center for highly infectious diseases.

Fortunately, some experienced BSL-4s in the United States and other countries have developed a framework of standards and norms necessary for training scientists and support staff (Fig. 1).[5] Briefly, these standards pertain to the following aspects: 1) formal training should consist of 3 elements, didactic or classroom style theoretical preparation, one-on-one practical training in the facility, and mentored on-the-job training; 2) certification of training; and 3) reevaluation of all persons working in the BSL-4 to ensure that their knowledge and skills remain current. This framework has served as a model for many BSL-3/4s globally[6,7] including the Wuhan BSL-4. Additionally, based on this framework, under the support of National Key Research and Development Program of China, we have developed an improved general training program and assessment system for different staffs of BSL-3/4s in China. This program addresses laboratory management, maintenance, experimental operations, and training biosecurity and other support personnel. It aims to facilitate networking among BSL-3/4s in China and with the global BSL-3/4 community. It focuses mainly on the following aspects:

1. **Flexible modularized theoretical training**. The purpose of the theoretical course is to help the trainees to gain a comprehensive understanding of biosafety and biosecurity principles and regulations, the overview of maximum biocontainment laboratory features, maintenance and management, and the standard operations for working in a BSL-3/4. It comprises lectures and discussions on topics such as biosafety laws and regulations, fundamentals of biosafety, biosecurity, basic knowledge of pathogenic microorganisms, biosafety laboratory management, risk assessment, biological exposures and emergency responses, Biosafety Cabinet (BSC), Personal Protective Equipment (PPE), waste management and decontamination, animal practice in biosafety laboratory, and specialized procedures as well as operations and maintenance in BSL-4s (Table 1). Staffs with different backgrounds could take the theoretical training with different topic combinations according to their level of knowledge and skills. For example, Topic 1–7 and 12–14 are necessary for laboratory managers or biosafety professionals, while researchers or technicians involved in *in vitro* work require Topic 1–4, 6–10, and 12–13. Similarly, Topic 11 would be beneficial for *in vivo* workers. The details of some topics need to be refreshed annually and information on different laws and regulations in different countries or regions should be included for foreign trainees.
2. **Standardized practical training assessment**. The practical training for the specific facility in which the trainee will work usually includes a complete review and documented understanding of all standard operation procedures; overview of all safety procedures, including alarms and emergency operations; an introduction to the care and use of a protective suit or glove box; storage and record keeping of pathogens; clean-up and decontamination following procedures or spillage; solid and liquid waste management; use of autoclaves and other specialized equipment; communication with others inside and outside the facility; and other general procedures. Then the trainee is assigned a dedicated mentor and is introduced to working with live pathogens under his/her close supervision. The final decision of when the trainee will be allowed independent access is subjective and based on an assessment by the mentor and laboratory director. Although it is usually discussed only after the trainee has had extensive experience of working in the facility, and a typical mentor would usually be an experienced indi-

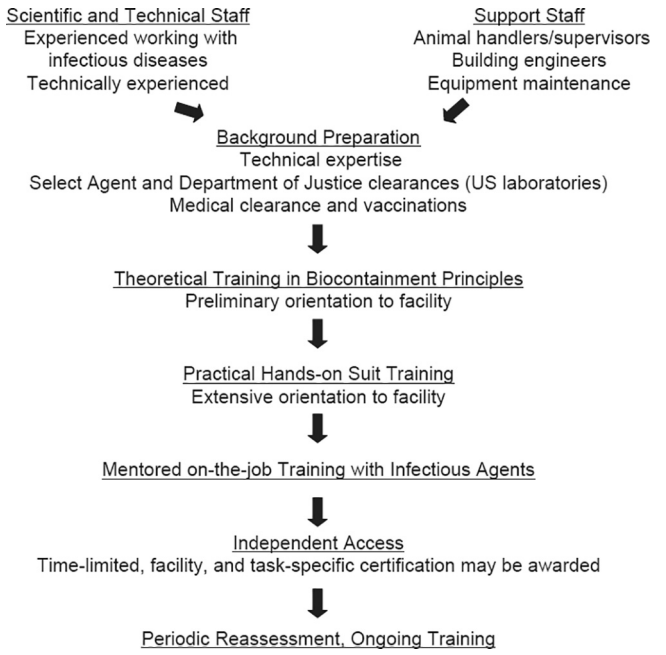


**Fig. 1.** Framework for the high containment laboratory training.[5]

**Table 1**
Contents of the theoretical training.

| Topics | Laboratory users | | | |
|---|---|---|---|---|
| | Management and biosafety officers | Facility and instrument operation | Researcher and technician | |
| | | | *in vitro* | *in vivo* |
| 1. Biosafety laws and regulations | A | A | A | A |
| 2. Fundamentals of biosafety | A | A | A | A |
| 3. Biosecurity | A | A | A | A |
| 4. Basic knowledge of pathogenic microorganisms | A | A | A | A |
| 5. Biosafety laboratory management | A | B | B | B |
| 6. Biosafety risk assessment | A | A | A | A |
| 7. Biological exposures and emergency responses | A | A | A | A |
| 8. Biosafety cabinet (BSC) | B | A | A | A |
| 9. Personal Protective Equipment (PPE) | B | A | A | A |
| 10. Waste management and decontamination | B | A | A | A |
| 11. Animal practice in a biosafety laboratory | B | | | A |
| 12. BSL-4 facility | A | A | A | A |
| 13. Specialized procedures in BSL-4s | A | A | A | A |
| 14. Operations and Maintenance for BSL-4 | B | A | B | B |

A stands for must be completed; B stands for recommended.

vidual with unrestricted access to the laboratory and has the clear confidence of the laboratory director, there is no set time or formal educational requirement to become a mentor. Nevertheless, checklists of specific tasks and skills can be useful to document proficiency during mentored training. We developed such an assessment system. A scored practice standard was suggested like theoretical training, in which we assign different scores according to the completion of an operation and the related risk assessment, with as extensive discussion as possible. More or less key points of standard operation procedures could be listed to meet the special requirements, and the standard would have to be refreshed annually. This assessment system provides a comprehensive assessment of biosafety laboratory staff before, during, and after training. It enables the scientific evaluation of the effectiveness of personnel training and ensures that personnel have continuous technical capabilities. The development of the assessment system helped change and solve the situation in the biosafety laboratory, where often more attention is paid to the training process and the training assessment is neglected. It also provides support for the efficient and stable operation of the high-level biosafety laboratory system.

3. **Applicable documentation system**. It is evident that a tacit internal certification exists and operates formally or informally in all BSL-3/4s. However a more broadly applicable documentation system could provide evidence of consistency in training and demonstrate recognized capabilities with certain tasks, such as those for animal handlers. Therefore, a certification system was established as a part of our program, to evaluate the ability of all staff working inside or outside the laboratory by a special committee composed of biosafety experts, scientists, and laboratory managers. The certification must be approved and authorized by the director of the laboratory in a specific document and can be classified into three grades with the following minimal requirements: Grade Green: Personnel must be under the guidance of internal or external experts/mentors when accessing the BSL-3/4 facility, Grade Orange: personnel have the right to independent access to the BSL-3/4 facility, and Grade Red: Personnel have the right to independent access to the BSL-3/4 facility and are qualified as a mentor/trainer. The minimal requirements for each grade may be a little bit different in every laboratory but they are formally captured and are sufficient to approve a person to work in these specific facilities. The documentation system is intended to be used as a reference for developing an internationally agreed-upon facility-specific, time-limited document to recognize the specific skills and experiences of BSL-3/4 staff.

Every BSL-3/4 is unique, however, every laboratory director should demand that all individuals entering their facility be well prepared and that they have mastered all safety and security procedures required at that facility. Although there is not globally standardized BSL-3/4 training program, our improved training program could facilitate collaboration and personnel exchanges among BSL-3/4s and would help to better certify the national/international workforce.

Furthermore, we suggest that our government should designate specialized and authoritative biosafety training institutions at the national level. It could formulate clarified and standard training content and assessment standards, certify the qualified BSL-3 and BSL-4 workers, and issue a uniform certificate. As such, the qualified BSL-3/4 staff could engage in studies or other works related to highly infectious agents in the same or lower level biosafety laboratories in some jurisdictions or nationwide, and in certain systems. It would be of great benefit to exchange personnel and share samples, technology, information, and lessons learned among BSL-3/4s across the country, and to promote different laboratories do more.

Public health systems and clinical laboratories worldwide are continually challenged by emerging and re-emerging viruses, owing not only to natural outbreaks and potential acts of bioterrorism, but also to importation by returning travelers. To enhance preparedness for emergencies, it is essential that all BSL-3/4s coordinate with each other and share their experiences and lessons learned to improve their capacity of responding to such natural or deliberate threats. Besides expeditious channels of communication for exchanging diagnostic protocols, samples, and regents when feasible, mutual recognition of laboratories and a personnel training network will be essential to secure effective response to highly infectious disease emergencies. Following the implementation of China's "One Belt, One Road" initiative, the risk of exotic pathogens being imported to China has increased dramatically. Wuhan BSL-4 must play a more active role in the prevention and control of highly infectious agents. It is therefore imperative to develop and improve a structured and standard BSL-3/4 training program to ensure that all personnel meet national and international standards for working in maximum-containment labs, and to provide assistance to the countries and regions along the "One Belt, One

Road" route. The establishment of rigorous standards for BSL-3/4 training will instill confidence in the public, policy makers, and security officials, such that the expanded international network of BSL-3/4s will continue to be operated safely and will pose no risk to scientific staff, local communities, the surrounding environment, and host nations. Clarification and coordination of training standards will help develop a highly-qualified biocontainment workforce and will result in a series of programs that will enable scientists to develop measures to deal with existing threat agents and new diseases that emerge.

## Conflict of interest

The authors declare that they have no conflict of interest.

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All authors have read and approved the final version of this manuscript.

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