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Laboratory Biosecurity

Balancing Risks, Threats & Progress



Foreword
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CHAPTER 3

Biosafety Levels

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SAFETY LEVELS

Biosafety Levels (BSL) prescribes procedures and levels of containment for the particular microorganism. The four basic biosafety levels (Figure 3.1), as determined by CDC which describe the microbiological techniques, laboratory practices, safety equipment and laboratory facilities necessary to protect workers and the environment.

Biosafety levels (BSL), agents, factors, and practices are described in the most recent version of the CDC publication Biosafety in Microbiological and Biomedical Laboratories (BMBL), (Table 3.1). The biosafety in microbiological and biomedical laboratories is a guide for the use of hazardous infectious pathogens and toxins in the laboratory, and it should be consulted regarding use of viruses, fungi, bacteria, and tissues that can harbor biological hazard. This section will provide a quick means to compare procedures and requirements for biosafety facilities for conducting work at each biosafety level.

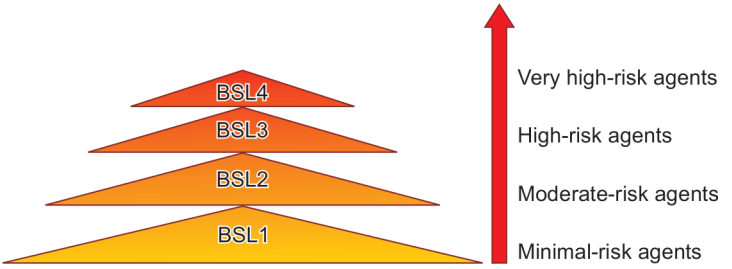

Fig. 3.1: The four basic biosafety levels

Table 3.1 Biosafety levels (BSL), agents, factors, and practices

BSL	*Agents*	*Factors*	*Practices**
1	Agents that are not associated with disease in healthy human adults	None	Standard laboratory and management practices, including appropriate medical surveillance programs
2	Associated with human disease which is rarely serious and for which preventive or therapeutic interventions are often available	Not known to be inhalation transmittable No aerosol production planned	BSL1 practices plus: – Limited access – Biohazard warning signs – Sharps precautions – Biosafety manual Decontamination of all infectious wastes prior to disposal
3*	Associated with human disease; special precautions required for some agents	BSL2 facility with BSL3 controls	BSL2 practices plus: – Controlled access – Decontamination of clothing before laundering – Equipment decontaminated before removed
3	Agents associated with serious or lethal human disease for which preventive or therapeutic interventions may be available (high individual risk but low community risk)	No or limited sharps allowed All work with biological hazard done in biosafety cabinet	BSL2 practices plus: – Controlled access – Decontamination of clothing before laundering – Equipment decontaminated before removed Disinfectant foot bath as needed
4	Indigenous or exotic agents capable of causing severe disease through the inhalation route of exposure, and for which there is no treatment or vaccine (high individual risk and high community risk)	Not allowed at many centers	Not allowed at many centers

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Level 4 Agents

- Crimean-Congo hemorrhagic fever virus
- Ebola virus
- Marburg virus
- Lassa fever virus
- Lujo virus
- Guanarito virus
- Machupo virus
- Juni virus
- Hendra virus
- Nipah Virus
- Smallpox virus
- Foot-and-mouth disease virus (BSL4 veterinarian laboratory only)

	BIOSAFETY LEVEL			
	BSL1	**BSL2**	**BSL3**	**BSL4**
Isolation-"a" of laboratory	No	No	Yes	Yes
Room sealable for decontamination	No	No	Yes	Yes
Ventilation:				
– Inward airflow	No	Desirable	Yes	Yes
– Controlled ventilating system	No	Desirable	Yes	Yes
– HEPA-filtered air exhaust	No	No	Yes/No-"b"	Yes
Double-door entry	No	No	Yes	Yes
Airlock	No	No	Yes/No	Yes
Airlock with shower	No	No	No	Yes
Anteroom	No	No	Yes	-
Anteroom with shower	No	No	Yes/No-"c"	No
Effluent treatment	No	No	Yes/No-"c"	Yes
Autoclave:				
– On site	No	Desirable	Yes	Yes
– In laboratory room	No	No	Desirable	Yes
– Double-ended	No	No	Desirable	Yes

Contd...

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BSCs	No	Desirable	Yes	Yes
Personnel safety monitoring capability-"d"	No	No	Desirable	Yes

"a" Environmental and functional isolation from general traffic

"b" Dependent on location of exhaust

"c" Dependent on agent(s) used in the laboratory

"d" i.e. window, closed-circuit television, two-way communication

Biosafety Level 1 (Risk Group 1—Minimal Risk)

Biosafety level 1 represents a basic level of containment that relies on standard microbiological practices with no special primary or secondary barriers recommended. A sink is required for hand washing. Laboratory signage is not required.

Practices, safety equipment, and facility design and construction are appropriate for undergraduate and secondary educational training and teaching laboratories, and for other laboratories in which work is done with defined and characterized strains of viable microorganisms not known to consistently cause disease in healthy adult humans. *Bacillus subtilis, Nigeria gruberi*, infectious canine hepatitis virus, and exempt organisms.

Biosafety Level 2 (Risk Group 2—Moderate Risk)

Biosafety level 2 represents hazards primarily related to accidental percutaneous, mucous membrane, non-intact skin exposures, or ingestions of infectious materials. Extreme caution with contaminated needles or sharp instruments is emphasized. Even though organisms routinely manipulated at BSL2 are not known to be transmissible by the aerosol route, procedures with aerosol or high splash potential that may increase risk of such exposure are conducted in primary containment equipment, or devices such as a biosafety cabinet or safety centrifuge. Use personal protective equipment as appropriate, including splash shields, face protection, disposable gowns, and gloves. Laboratory signage is required.

Practices, equipment, and facility design and construction are applicable to clinical, diagnostic, teaching, and other laboratories in

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which work is done with the broad spectrum of indigenous moderate-risk agents that are present in the community and associated with human disease of varying severity. With good microbiological techniques, these agents can be used safely in activities conducted on the open bench, provided the potential for producing splashes or aerosols is low. Hepatitis B virus, HIV, Salmonella, and Toxoplasma are representative of microorganisms to this containment level.

BSL2 is appropriate when work is done with any human-derived blood, body fluids, tissues, or primary human cell lines where the presence of a hazardous infectious pathogens and toxins may be unknown.

- Primary hazards to personnel working with these agents relate to accidental percutaneous or mucous membrane exposures, or ingestion of infectious materials. Extreme caution should be taken with contaminated needles or sharp instruments. Even though organisms routinely manipulated at BSL2 are not known to be transmissible by the aerosol route, procedures with aerosol or high splash potential that may increase the risk of such personnel exposure must be conducted in primary containment equipment, or in devices such as a BSC or safety centrifuge cups. Personal protective equipment should be used as appropriate, such as splash shields, face protection, gowns, and gloves
- Secondary barriers, such as hand washing sinks and waste decontamination facilities, must be available to reduce potential environmental contamination.

Biosafety Level 3 (Risk Group 3—High Risk)

Biosafety level 3 represents a level of use at which hazardous infectious pathogens are primarily related to inhalation, and in which the agent in question is known to be or suspected to be spread through inhalation. The biosafety level 3 primarily aims at the protection of the environment to avoid accidental pathogen release. The personal protection of the laboratory worker is in principle similar to BSL-2 level, but is upgraded by additional personal protective equipment according to the risk of the handled pathogen for human health. Work at this level requires that a separate laboratory safety manual be developed by the laboratory

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management, including roles and responsibilities, hazard mitigation and procedures for use and decontamination, emergency response. It is recommended to minimum use of sharps in BSL3 facilities and all procedures with the live agent are to be performed in a type II A/B biosafety cabinet (BSC). Use personal protective equipment as appropriate, including splash shields, face protection, disposable gowns, and gloves. Laboratory signage is required. Entry into and out of a BSL3 facility must be controlled so that only properly trained individuals are allowed unescorted access.

Practices, safety equipment, and facility design and construction are applicable to clinical, diagnostic, teaching, research, or production facilities in which work is done with indigenous or exotic agents with a potential for respiratory transmission, and which may cause serious and potentially lethal infection. *Mycobacterium tuberculosis*, St. Louis encephalitis virus, West Nile virus, Middle East respiratory syndrome (MERS) coronavirus, highly pathogenic influenza viruses and *Coxiella burnetii* are examples of the microorganisms/viruses assigned to this level. Primary hazards to personnel working with these agents relate to autoinoculation, ingestion, and exposure to infectious aerosols. At BSL3, more emphasis is placed on:

- Primary barriers to protect personnel in contiguous areas, the community, and the environment from exposure to potentially infectious aerosols. All laboratory manipulations should be performed in a BSC or other enclosed equipment, such as a gas-tight aerosol generation chamber
- Secondary barriers for this level include controlled access to the laboratory and ventilation requirements that minimize the release of infectious aerosols from the laboratory.

Biosafety Level 4 (Risk Group 4—Very High Risk)

Required for work with dangerous and exotic agents, which pose a high individual risk of life-threatening disease. The facility is either in a separate building or in a controlled area within a building, which is completely isolated from all other areas of the building. Practices, safety equipment, and facility design and construction are applicable for work with dangerous and exotic agents that pose a high individual risk of life-threatening disease, which may be transmitted via the aerosol route and for which there is no available vaccine or

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therapy. Agents with a close or identical antigenic relationship to BSL4 agents also should be handled at this level. When sufficient data are obtained, work with these agents may continue at this level or at a lower level. BSL4 pathogens are exclusively virus. Classified as BSL4 pathogens are: Smallpox virus, Crimean-Congo hemorrhagic fever virus, Ebola virus, Marburg virus, Lassa fever virus, Lujo virus, Guanarito virus, Machupo virus, Junin virus, Hendra virus, Nipha virus. In the veterinary field foot-and-mouth disease virus is classified a BSL4 pathogen.

LABORATORY BIOSECURITY AS A COMPLEMENT TO LABORATORY BIOSAFETY

A good laboratory biosafety practices reinforce and strengthen laboratory biosecurity systems. Since the implementation of specific biosafety activities already covers some biosecurity aspects. Appropriate levels of biosafety may be achieved through carefully designed and implemented work practices, even in modestly-equipped facilities, since **effective biosafety practices are the very foundation of "laboratory biosecurity" activities**. In the absence of careful implementation, various aspects of biosafety may conflict with laboratory biosecurity. For instance, controls that reduce unauthorized access might also obstruct an emergency response by fire or rescue personnel. Mechanisms need to be established that allow entry by emergency responders but ensure uninterrupted and constant laboratory biosecurity, control and accountability. Signage may also represent a potential conflict between biosafety and laboratory biosecurity. In the past, biohazard signs placed on laboratory doors identified the hazardous infectious pathogens and toxins present in the laboratory. However, as a laboratory biosecurity measure to better protection it is recommended that certain information on biohazard signs to the laboratory biosafety level, such as the name and telephone number of the responsible investigator, and emergency contact information should be mentioned.

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Laboratory Biosecurity

Balancing Risks, Threats & Progress

This short but complete book encompasses all aspects related to laboratory biosecurity. It outlines all relevant matter about laboratory setting up of BSL-1 to BSL-4 laboratories. It talks about the manpower and information security of high safety laboratories. Sample transportation and prevention of accidents is amply covered.

All in all, the book presents A to Z of laboratory biosecurity.



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