Guidelines on Biosafety in the Clinical Laboratory

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1. Scope

These Guidelines set out the requirements for the microbiological aspects of safety in laboratories where biological agents are handled. It is primarily intended for laboratories where microbiological work such as diagnosis, research and teaching is undertaken. Biosafety is just one element of laboratory safety which should include other safety aspects like chemical, fire, electrical and radiation safety as well as biosecurity. The Laboratory Director should ensure all workers understand all other safety aspects as well in addition to the requirements as set out in these guidelines.

2. Organization

The laboratory management has the responsibility for the safety of all employees and visitors to the laboratory. The primary responsibility shall rest with the Laboratory Director.

A safety coordinator should be appointed to assist the Laboratory Director in overseeing laboratory safety, giving advice to the management and assisting in the design and maintenance of the safety programme. If warranted, a safety committee with well defined Terms of Reference should be set up.

Individual staff members have the responsibility to follow documented safety procedures to ensure both personal and institutional safety.

3. Biosafety programme

A programme shall be in place, with regular monitoring and review, to ensure a safe work environment and safe work practices in the laboratory, encompassing the following elements:

- Provision of training
- Promotion of appropriate measures
- Implementation of practices in accordance with safety manual
- Management of accidents and incidents
- Management of staff health
- Monitoring of safety systems
- Maintenance of various safety records

3.1 Training

All staff shall be trained to foster correct attitudes and understanding of safe working practices including personal hygiene, appropriate use of personal protective equipment (PPE) with good microbiological techniques, safe use of equipment, recognition of hazards, risks and consequences before commencement of practical laboratory work. Continuing education and training to maintain staff awareness of the safety implication of changing technology and improvements in safety practices should be undertaken and documented. Personal training records shall be kept. For work in BSL-3 or BSL-4 laboratories, more intensive and specialized training should be provided. In addition, staff's experience and competence of working safely shall be formally assessed and documented before commencement of work.

3.2 Biosafety measures

Biosafety measures encompass suitable facility design, availability and appropriate use of PPE and safety equipment and safe work practices. All hazards shall be identified and risk assessment carried out regularly to control the risks.

3.2.1 Facility design

Safety in facility design needs to be taken into account on initial planning and set-up of a laboratory, and ongoing assessments are required to ensure suitability for the work undertaken. Elements which need to be addressed include but are not limited to the followings:

- Location and layout of laboratory
- Air flow and ventilation requirements
- Material of work surfaces, with respect to type of work and disinfection considerations
- Furniture of suitable material and ergonomic design
- Sanitation and handwashing facilities

3.2.2 PPE and safety equipment

PPE and safety equipment provide a barrier to minimize the risk of exposure to aerosols, splashes and accidental inoculation. Such safety equipment selected should be based on the nature of work performed. Examples of PPE include protective clothing, gloves, goggles, etc, and examples of containment equipment include biological safety cabinets and centrifuges with sealed buckets. They shall be used, maintained, disinfected and stored properly. Inventories and maintenance records shall be kept. All PPE should be removed when contaminated or when their use is no longer required, with proper decontamination before re-use or disposal.

3.2.3 Safe work practices

All staff shall adopt safe practices as follows:

- Adopting good microbiological techniques
- Maintaining personal hygiene
- Using appropriate precautions when performing microbiological manipulations, especially when undertaking aerosol generating procedures
- Proper storage of specimens and isolates of microorganisms with corresponding level of access control and maintenance of inventory
- Proper decontamination and disposal as appropriate of infectious materials and wastes

3.3 Safety manual

A biosafety manual shall be developed, adopted and regularly reviewed. The manual shall document the following aspects:

- Organization of safety management
- Safety precautions in microbiological work
- Specific procedures in use of PPE and safety equipment
- Decontamination procedures
- Disposal of laboratory wastes
- Management of accidents and incidents
- Monitoring of staff health including immunization and medical surveillance
- Transport of biological materials

Regular safety audits with reference to the safety manual shall be conducted, with documentation of audit findings and any necessary improvement actions.

3.4 Management of accidents and incidents

Contingency plans and procedures for accidents and incidents, for example, spillage of pathogens, failure of biological safety cabinet and autoclave, shall be in place. Regular drills should be carried out to familiarize staff with the contingency procedures. A reporting mechanism shall be promulgated and made known to all staff such that all accidents and incidents could be promptly reported to the supervisor and safety coordinator and managed accordingly. All accidents and incidents shall be investigated and properly documented. Preventive measures shall be implemented accordingly. A continuous improvement programme shall be in place to review and improve the safety programme. In cases with potential threat to public health, the management shall take appropriate actions and notify the Department of Health without delay.

3.5 Management of staff health

The management shall ensure there is adequate measures to ensure staff health. The staff health programme shall encompass the following:

- Pre-employment check
- Provision of immunization where indicated
- Keeping of baseline sera
- Medical surveillance to monitor staff sickness through reporting and recording of illness and absence
- Provision of medical care as necessary
- Proper record keeping

3.6 Monitoring of safety systems

The overall safety status of the laboratory needs to be reviewed regularly to ensure compliance with safety requirements. Safety inspections and audits shall be conducted regularly to ensure laboratory safety is maintained. Examples of elements to be inspected and audited include: training of personnel, monitoring of equipment and facilities, implementation of safe work practices, maintenance of accident records and surveillance of staff health.

3.7 Maintenance of various safety records

The following records shall be kept, as mentioned in earlier sections:

- Training
- Inventory and maintenance of safety equipment
- Updated inventory of specimens and isolates in storage
- Accidents and incidents
- Staff health including immunization and sickness
- Safety inspection and audit
- Improvement actions

4. Categorization of biological agents

Based on the hazards posed, infective microorganisms are classified according to Risk Groups (RGs) for laboratory work. The following groupings are based on the classification as described in the World Health Organization (WHO) Laboratory Biosafety Manual:

- Risk Group 1 (no or low individual and community risk) – A microorganism that is unlikely to cause human or animal disease.
- Risk Group 2 (moderate individual risk, low community risk) – A pathogen that can cause human or animal disease, but is unlikely to be a serious hazard to laboratory workers, the community, livestock, or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.
- Risk Group 3 (high individual risk, low community risk) – A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.
- Risk Group 4 (high individual and community risk) – A pathogen that usually causes serious human or animal disease and that can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.

When performing work with various infective microorganisms, assessment should be made on the risk of a given procedure or experiment. Human pathogens encountered in a clinical laboratory are mostly RG2 biological agents, such that clinical specimens are handled at least under Biosafety Level 2 (BSL-2) containment. However, higher levels of microbiological practices, containment, and facility design may be required as necessary according to risk assessment, such as in cases when large quantities of cultures are handled.

The following are examples of biological agents recommended to be handled in BSL-3 and 4 laboratories. It must be emphasized that the lists are not exhaustive, and judgement needs to be exercised when determining the level of safety precautions to be adopted, based on known characteristics of the pathogen, and the nature of the procedures to be undertaken.

4.1 Agents recommended to be handled in BSL-3 laboratories

Bacteria
- *Bacillus anthracis*
- *Burkholderia pseudomallei*
- *Brucella* spp. (except *B. ovis*)
- *Clostridium botulinum*
- *Francisella tularensis*
- *Mycobacterium tuberculosis* complex
- *Yersinia pestis*

Viruses
- Dengue virus
- Hantavirus
- Influenza virus type A (subtype H2, H5 and H7)
- Japanese encephalitis virus (pre-exposure vaccination recommended)
- Monkeypox virus
- Rabies or rabies-related virus (pre-exposure vaccination recommended)
- Rift Valley fever virus
- Severe acute respiratory syndrome (SARS)-coronavirus
- West Nile virus
- Yellow fever virus (pre-exposure vaccination recommended)

Fungi
- *Blastomyces dermatitidis*
- *Coccidioides* spp.
- *Histoplasma capsulatum*
- *Paracoccidioides brasiliensis*

4.2 Agents recommended to be handled in BSL-4 laboratories

Viruses

- Crimean-Congo haemorrhagic fever virus
- Ebola virus
- Guanarito virus
- Hendra virus
- Herpes simiae virus (B virus)
- Junin virus
- Kyasanur Forest disease virus
- Lassa virus
- Machupo virus
- Marburg virus
- Nipah virus
- Omsk haemorrhagic fever virus
- Sabia virus
- Tick-borne encephalitis virus
- Variola virus

5. Biosafety requirements

Clinical laboratories need to meet biosafety requirements depending on the pathogens handled. Requirements are classified into:

- Laboratory facilities
- PPE and safety equipment
- Work practices
- Occupational health

5.1 Biosafety level 2 (BSL-2)

5.1.1 Laboratory facilities

a. The ventilation system should preferably have directional airflow from the corridor into the laboratory suite.
b. Work surfaces should be impervious to water and easy to clean and disinfect.
c. The laboratory shall have readily available and preferably foot, elbow or electronically-operated handwashing facilities.
d. Emergency eyewash stations and showers shall be readily available.
e. Autoclave facilities should be available in the same building. If this is not feasible, clinical wastes must be packed and transported in accordance with the code of practice promulgated by the Environmental Protection Department.
f. Biological safety cabinets should be sited away from walking areas and out of cross currents from doors and ventilation systems.

5.1.2 PPE and safety equipment

a. Wear side or back-fastening long-sleeved protective gown.
b. Wear gloves whenever handling human specimens or potentially infectious materials.
c. Wear goggles and face shields for work with potential splashes.
d. Wear closed footwear.
e. Remove all PPE when contaminated or when their use is no longer required, with proper decontamination before re-use or disposal.
f. Use biological safety cabinet (Class I or II) for any laboratory procedures that may give rise to infectious aerosols.
g. Use centrifuge fitted with either sealed rotors or safety cups and open inside a biological safety cabinet.

5.1.3 Work practices

a. Restrict access to laboratory to authorized persons and keep doors closed.
b. No mouth pipetting is allowed.
c. Sharps must handled carefully and disposed of safely.
d. Minimize generation of splashes and aerosols. All aerosol generating procedures involving pathogens shall be performed in a biological safety cabinet.
e. Potentially infectious materials must be stored in a secure location and locked with access only by designated staff.
f. Decontaminate all potentially contaminated areas and materials using appropriate methods/disinfectants before disposal or processing for re-use.
g. All potentially infectious wastes must be rendered non-infectious before disposal. Alternatively, the packaging must be such that it will not pose an infectious hazard to any subsequent handlers before disposal.

5.1.4 Occupational health

a. Baseline serum samples are advised to be kept for all staff for future reference.
b. All staff are advised to receive hepatitis B vaccination if found to be susceptible by serology tests. Other vaccinations should be considered according to the potential for exposure.
c. A system should be in place to detect unusual occurrence of illness among staff.

5.2 Biosafety level 3 (BSL-3)

The requirements below are in addition to those for BSL-2.

5.2.1 Laboratory facilities

a. The laboratory must be separated from other areas and not accessible by the general public.
b. The laboratory is sealable to permit fumigation.
c. Entry into the laboratory is through ante-room with interlocking double-door system.
d. The ventilation system shall maintain directional airflow from entrance into laboratory suite with proper monitoring at all times, and with no recirculation of air to other areas within the building.
e. An autoclave shall be available within the laboratory suite for sterilization of potentially infectious materials and wastes.

5.2.2 PPE and safety equipment

a. Use biological safety cabinet (Class I or II) for all manipulations of potentially infectious materials.

5.2.3 Work practices

a. All manipulations of potentially infectious materials must be performed in a biological safety cabinet.
b. A complete and current inventory of potentially infectious materials of RG3 or above shall be maintained.

5.2.4 Occupational health

a. Medical surveillance should be enhanced. Procedures should be in place for surveillance, early identification and management of illness among staff working with potentially infectious material.

5.3 Biosafety level 4 (BSL-4)

There are currently no BSL-4 laboratories in Hong Kong. RG4 organisms shall not be manipulated. Any material suspected to contain RG4 agents requiring laboratory testing shall be packaged according to corresponding United Nations (UN) recommendations and International Air Transport Association (IATA) guidelines, and sent to overseas laboratories with adequate safety facilities.

6. Specimen packaging, labeling and transport

a. The following triple packaging system shall be used for local surface transport:
   - The primary receptacle containing the specimen must be watertight, leakproof, and the contents appropriately labeled. Specimens should be kept upright to minimize spillage.
   - A second watertight, leakproof packaging encloses and protects the primary receptacle(s). Laboratory request forms must be placed outside the secondary packaging.
   - The third layer of outer packaging protects the secondary packaging from physical damage while in transit and should have adequate strength for its capacity, mass and intended use.

b. For cultures of microorganisms and diagnostic specimens likely to contain organisms above RG2, more stringent packaging in addition to those mentioned above is required. These include wrapping of individual primary receptacles with absorbent material capable of absorbing their entire contents, and use of watertight and robust solid containers as secondary packaging.

c. The specimen package shall be labeled with information that describes its content and identifies the originating and recipient institution and personnel.

d. Corresponding UN recommendations and IATA guidelines should be referred to for international transport.

7. References

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