Principles of Good Laboratory Practice (GLP)

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3.1 What You Will Learn in This Chapter

- The importance of understanding necessary information about good laboratory practice (GLP) as well as implementing relevant standard methods
- The importance of maintaining biosafety in the laboratory and applying correct assessment of the potential risks in laboratory
- The necessity of providing safety of individuals, environment, and chemicals in nonclinical laboratories
- The necessity of conducting GLP guidelines under carefully controlled situations and also traceable, reproducible, and reliable data set
- The importance of implementing standardized and validated procedures to support human clinical trials
- The necessity of setting GLP guidelines by different regulatory agencies to consider organizational structure, documentation (record keeping), quality assurance, personnel training practices, responsibilities, good microbiological techniques (GMT), safety equipment, standard operating procedures (SOPs), records, and sample retention

3.2 Rationale and Importance

In 1972, there were some cases of poor laboratory practice in the United States. Therefore, the FDA decided to do some in-depth researches of 40 toxicology laboratories and increase the number of laws for chemical and pharmaceutical products [1]. They discovered a lot of fraudulent activities and poor laboratory practices such as uncalibrated equipment, wrong measurements, inaccurate data, and inadequate test systems. Accordingly, by setting GLP guidelines, final data can demonstrate a true reflection of results gained during the study [2]. One of the important goals of GLP is promoting safety, quality, consistency, and reliability of products, data, and services in the process of laboratory testing, to improve human health and environmental risk management. Moreover, it is important to know how scientists use quality setting to improve biological products and data. Finally, research authorities should prove that there are no changes in the quality of data [1, 3].

3.3 Good Laboratory Practice (GLP)

3.3.1 An Overview of General Rules

GLP is a set of techniques that provide safety of personnel, laboratory, and environment and also pave the way for better laboratory practices by eliminating poor practices. Safety assessment based on GLP guidelines is a key step before starting clinical trials [4]. Therefore, GLP guidelines have conducted to guarantee biosafety in laboratories [5, 6]. Accordingly, this chapter will describe biosafety aspects of GLP focusing on risk management approaches that should consider risk groups [7]. In accordance with risk groups, each country should design a national classification of microorganisms based on their possibility of increasing harm in humans, animals, and environments according to the following issues [6]:

- Pathogenicity of the microorganism
- Transmission modes and host range of the organism
- Access to effective prevention plans which usually include prophylaxis by immunization, antisera administration, and sanitary measures
- Access to effective treatment measures including antimicrobials, antivirals, and chemotherapeutic agents, passive immunization, and post-exposure vaccination [6, 8]

There are four risk groups based on the classification of World Health Organization (WHO). Infectious microorganisms are categorized in risk groups based on their relative risks. Risk group 1 includes organisms which do not cause disease in humans or animals, risk group 2 pathogens cause diseases such as infections in humans or animals, risk group 3 agents cause serious diseases, and finally risk group 4 organisms cause lethal diseases in humans [9]. The classification of risk groups is used for laboratory work only. In contrast to risk groups, biosafety levels prescribe practices, facility requirements, engineering controls, and personal protective equipment (PPE) for working with infectious microorganisms. Similar to risk groups, there are four biosafety levels which are level 1, 2, 3, and 4 (Table 3.1) [4, 6].

Table 3.1 The association between biosafety levels, laboratory types, arrangements, and equipment [4, 6, 7]

Risk groups	Biosafety level	Laboratory type	Classification of infectious microorganisms	Training requirements and equipment	Treatment procedures
1	Biosafety level 1	Basic laboratory 1	Microorganisms do not cause disease in humans or animals	Pass health test steps, GMT*	–
2	Biosafety level 2	Basic laboratory 2	Microorganisms cause disease such as infections in humans or animals	GMT, protective clothing, biohazard sign	Disease is preventable
3	Biosafety level 3	Containment laboratory	High concentration of group 2 microorganisms and cause serious diseases	As level 2 plus special clothing, controlled access, directional airflow	Treatments and vaccines
4	Biosafety level 4	Maximum containment laboratory	Microorganisms cause deadly disease in humans, and they can transfer from one person to another	As level 3 plus airlock entry, shower exit, special waste disposal	No treatments or vaccines

*GMT** good microbiological techniques

3.3.2 Good Laboratory Practice Training

Trained and well-organized personnel play a key role in the successful performance of procedures in a laboratory. On the other hand, it is necessary to have systems that assess persistent competency and trained personnel to convince suitable responsibility and communication during study conduct. Therefore, all personnel should receive direct and accurate training information to complete and perform their tasks [10]. After initial staff training, qualification assessments should be performed and recorded for all components of the training and practical responsibilities. As a result, the clinical education program should meet all the personnel needs and be documented and available to all laboratory staff [10, 11].

3.4 Biosafety Concepts in the Laboratory

Laboratory biosafety refers to protective measures, containment principles, and relevant technologies to prevent accidental exposure to pathogens and toxins. The association between four biosafety levels and infectious microorganisms based on their potential risks are demonstrated in Fig. 3.1. Effective implementation of biosafety in a laboratory is the base of laboratory biosecurity [7]. Accordingly, laboratory biosecurity refers to personal and organizational security measures that prevent misuse, loss, diversion, or deliberate release of pathogens and toxins [12]. On the other hand, risk assessment is an essential part of a biosafety program, which collects information about the type of available organisms, their physical location, and also identification of staff who are responsible for the

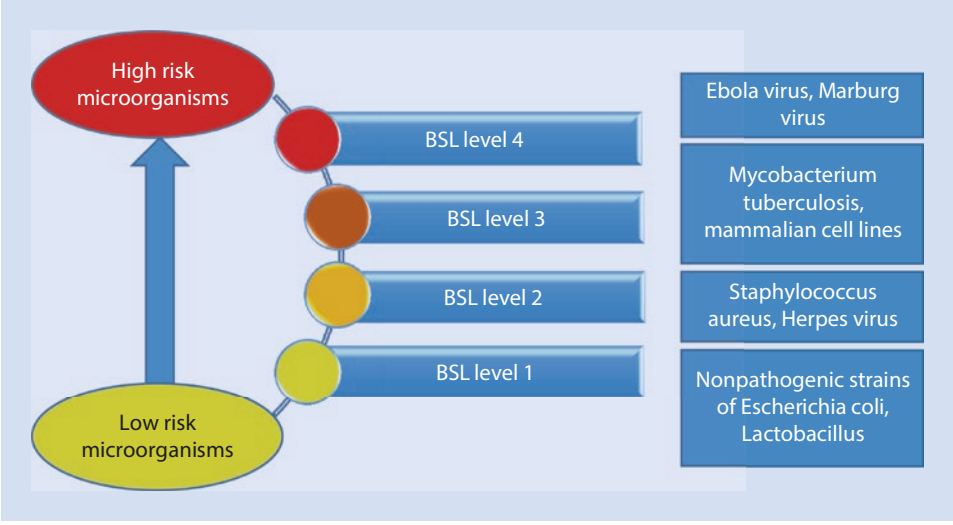

Fig. 3.1 Biosafety levels (BSL). Microorganisms classified by four risk groups and accordingly biosafety levels are divided into four classes. Biosafety level 1 refers to low-risk microorganisms such as Nonpathogenic strains of *Escherichia coli* and *Lactobacillus*, while biosafety level 4 refers to high-risk microorganisms such as *Ebola* and *Marburg* viruses. Additionally, biosafety levels 2 and 3 are located between 1 and 4 [7, 9]

maintenance of organisms [13]. Moreover, professional and ethical competency of all employees faced with dangerous pathogens that are permanently accessed to sensitive materials has a central role in laboratory biosafety programs. As a result, assessing competency of employees, training specific security issues, and complying accurate protection approach against pathogens are rational tools for promoting biosecurity in the laboratories [12]. Therefore, it is necessary to determine the biosafety level, type of microorganisms, available facilities, arrangements, skills, and procedures for performing a safe performance in laboratories [4, 14].

3.5 Good Microbiological Techniques

The aim of good microbiological techniques (GMT) is improving public health and also lifestyle. Each laboratory must take safety measures to eliminate or reduce potential hazards. GMT plays a pivotal role in laboratory safety and is based on the prevention of contamination [15].

Because of improper collecting, transferring, and handling of samples in laboratory, humans will be prone to risk of infections [16]. To prevent contamination in laboratories, some procedures should be considered as follows:

- *Transferring of Infectious Substances*: Transportation of infectious substances and materials should be done in accordance with national and international standards and rules. These rules describe how to properly use packaging materials and other transportation requirements to reduce potential damages and possible infections. For example, using a triple packaging system is essential for transporting potentially infectious substances [17].
- *Specimen Receipt*: A particular room for receiving a large number of specimens should be considered [18].
- *Opening Packages*: For opening packages, a disinfectant must be available and opened in biological safety cabinets (BSCs) [18].
- *Avoiding Ingestion of Infectious Agents and Contact with Skin and Eyes*: Personnel should wear disposable gloves during microbiological manipulations and avoid touching mouth and eyes; moreover, they should not eat and drink in the laboratory [16].
- *Disinfection and Sterilization*: Basic knowledge of disinfection and sterilization is essential for laboratory safety. As highly contaminated materials cannot be disinfected or sterilized quickly, it is important to know the principles of initial cleansing as disinfecting. In this regard, general rules apply to all known pathogens. Accordingly, specific conditions should be used to eliminate contamination depending on the type of testing, nature, and source of contaminations. As a result, preclearing materials are essential to provide suitable disinfection and sterilization. Some types of chemical germicides are used as disinfectant (Table 3.2) [7, 17].
- *Waste Disposal*: Contaminated materials should be removed from laboratory daily. Moreover, most instruments, laboratory clothes, and glassware should be reused or recycled. It is important that all infectious materials are decontaminated, incinerated, and autoclaved [19].

Table 3.2 Some examples of chemical germicides and their functions [7, 17]

Examples of chemical germicides	Function
Chlorine (sodium hypochlorite) (NaOCl)	Fast-acting oxidant, bleaching
Sodium dichloroisocyanurate (NaDCC)	Eliminating blood or other biohazardous liquids
Chloramines	Disinfecting water supplies
Chlorine dioxide (ClO_2)	Disinfecting, strong and fast-acting germicide, and oxidizer
Formaldehyde (HCHO)	Eliminating microorganisms and spores
Glutaraldehyde ($OHC(CH_2)_3CHO$)	Eliminating Lipid- and nonlipid-containing viruses, fungi, bacteria, and spores
Phenolic compounds	Eliminating vegetative bacteria and lipid-containing viruses, mycobacteria
Quaternary ammonium compounds	Eliminating vegetative bacteria and lipid-containing viruses
Ethanol (ethyl alcohol, C_2H_5OH) and 2-propanol (isopropyl alcohol, $(CH_3)_2CHOH$)	Eliminating fungi, vegetative bacteria, and lipid-containing viruses but not spores
Iodine and iodophors	Preoperative skin antiseptic and surgical scrub
Hydrogen peroxide (H_2O_2) and peracids	Disinfecting heat-sensitive medical devices

3.6 Laboratory Equipment

3.6.1 General Equipment

General laboratory equipment mainly include pipettes, centrifuges, freezers, incubators, hot plates, coolers, stirrers, water baths, bunsen burners, scales, fume hoods, and also microscopes [18, 20].

3.6.2 Safety Equipment

As aerosols are critical sources of contamination, their dispersion should be reduced. Harmful aerosols can be released by the most of laboratory activities such as mixing, blending, sonicating, grinding, shaking, and centrifuging [21]. Therefore, to achieve contamination control and personnel and product safety, it is seriously recommended that all procedures be performed in BSCs [22]. As a result, not only implementing safety equipment in laboratory is important but also laboratory operator should be trained to ensure safety of equipment regularly. Moreover, it is necessary to implement a system for monitoring equipment calibration [21].

3.6.2.1 Biological Safety Cabinets (BSCs)

BSCs are designed to protect personnel, laboratory environments, and materials against contamination by pathogens. BSCs are classified into three groups based on biosafety levels (Table 3.3) [7, 22].

3.6.2.2 Pipetting Aids, Homogenizers, Sonicators, and Specimen Containers

- Pipettes and pipetting aids [7]:
  - Pipetting by mouth is prohibited. Therefore, personnel must always use a pipetting aid.
  - All pipettes should have cotton caps to reduce contamination.

Table 3.3 The classification of biological safety cabinets [7]

Types of biological safety cabinets	Biosafety level	Airflow instructions	Protective function
Class I	1, 2, 3	Protective cabinet 0% circulated 100% exhausted HEPA* filter Hard duct	Staff, environment, risk groups 1 and 2 microorganisms
Class II	1, 2, 3	Vertical laminar flow Recirculating air cabinet HEPA filter	As class I plus products, chemicals and risk groups 3 and 4 microorganisms
Type A1		70% circulated 30% exhausted Exhaust to room or thimble connection	
Type A2		70% circulated 30% exhausted Exhaust to room or thimble connection	
Type B1		30% circulated 70% exhausted *Hard duct*	
Type B2		0% circulated 100% exhausted *Hard duct*	
Class III	1, 2, 3, 4	Enclosed glove box with two HEPA filters 0% circulated 100% exhausted Hard duct	As class II and III with complete isolation

*HEPA** high-efficiency particulate air

  - Never blow air into a fluid containing infectious agents, and do not mix infectious agents by blowing and suction.
  - Liquids should not be removed by force from the pipette [18, 20].
- Homogenizers and sonicators can reduce small pathogens from liquids and should be used in BSCs or be covered with shields during working [7].
- Specimen containers should be made by high resistance glass, metal, or plastic and should not leak when the cap is in place. No material should remain on the outer surface of the container. It is better to label the dishes properly before filling for easy identification and avoiding hazards [7, 18]. Moreover, specimen containers should be placed on secondary containers such as boxes and racks to prevent their spillage and leakage. Secondary metal or plastic containers should be autoclavable [18].

3.6.2.3 Personal Protective Equipment and Clothing

PPE are important to reduce high risks of contact with aerosols, accidental inoculations, and splashes. Some of the PPEs include the following [23, 24]:

- Laboratory coats and gowns: Laboratory coats protect personnel from workplace hazards such as chemical splashes, chemicals spills, or biological materials such as blood and tissue specimens. Therefore, long-sleeved and fully buttoned coats are better choices. On the other hand, personnel should not wear laboratory coats and gowns when they are outside the laboratory [23, 24].
- Gloves: Latex, vinyl, or nitrile gloves are used to protect against infectious agents, blood, and body fluids [23].
- Face protection devices: Eyes and face protection devices including safety spectacles, safety goggles, face shield, face respirators, and masks protect personnel from hazards that may cause serious injury on the face and eye. Safety goggles and face shield are the best choices to protect staff from chemical splashes, while safety spectacles are not suitable. Moreover, masks with filters are used for protecting against gases, toxic vapors, aerosols, and microorganisms [24].

3.7 Safety Against Fire, Electrocution, and Chemicals

Personnel in microbiological laboratories are exposed to hazardous chemicals as well as pathogenic microorganisms [25]. Therefore, they should be aware of the toxic effects of chemicals, exposure pathways, and potential hazards. Personnel may be exposed to dangerous chemicals through skin contact, needle sticks, ingestion, and inhalation [25]. On the other hand, personnel may face a variety of hazards such as fire, electricity, radiation, and noise. A summary of these hazards and relevant preventive actions is presented in Table 3.4 [26].

3.8 Biosafety Instruction

Risk assessment process is the basis of biosafety [7]. Risk assessment steps should be carried out by individuals who are well trained and those with the good knowledge of organisms, tools, methods, animal models, and equipment [13]. Accordingly, laboratory director or researcher is responsible for providing risk assessment equipment and facilities

Table 3.4 A summary of laboratory hazards, undesirable effects, and ways to prevent them [25, 26]

Types of laboratory hazards	Undesirable effects	Protective measures	Examples
Toxic chemicals	Seriously damaged in the respiratory system, blood, lungs, kidneys, liver, gastrointestinal system, other organs, and tissue. Carcinogenic or teratogenic and skin damage	Attention to chemical incompatibilities	Alkali metals such as cesium, sodium, potassium, and lithium with carbon dioxide, chlorinated hydrocarbons, and water
Explosive chemicals	Fire, skin damage	Attention to chemical incompatibilities	Azides with copper or lead, ethers that have aged and dried to crystals, perchloric acid, picric acid, and picrates
Chemical spills	Fire, seriously damaged in the respiratory system, lungs	Protective clothing such as heavy-duty rubber gloves, overshoes or rubber boots, respirators, chemical spill kits, scoops and dustpans, forceps (for picking up broken glass), mops, cloths and paper towels, buckets, soda ash sodium bicarbonate ($NaHCO_3$) for neutralizing corrosive chemicals and acids, sand to cover alkali spills, nonflammable detergent	Spilled materials and flammable spilled materials
Compressed and liquefied gases	Fire, skin damage	*Compressed gas cylinders and liquefied gas containers*: securely fixed, transported with their caps in place and supported on trolleys, stored in bulk in an appropriate facility at some distance from the laboratory. The area locked and appropriately identified. Should not be placed near radiators, open flames other heat sources, sparking electrical equipment, or in direct sunlight *Small and single-use gas cylinders*: Must not be incinerated	Compressed gas cylinders, liquefied gas containers, and small and single-use gas cylinders

Table 3.4 (continued)

Types of laboratory hazards	Undesirable effects	Protective measures	Examples
Fire hazards	Fire, skin damage	Close cooperation between local fire prevention officers and safety officers, training of laboratory staff in fire prevention, immediate action in case of fire, and using fire-fighting equipment	Electrical circuit overloading, poor and perished insulation on cables, open flames, deteriorated gas tubing, flammable or explosive materials, incompatible chemicals, and sparking equipment
Electrical hazards	Fire, electric shock	Installation of circuit breakers and earth-fault-interrupters in appropriate laboratory electrical circuits	eElectrical installations including earthing or grounding systems
Noise	Hearing problems	Engineering controls such as enclosures or barriers between noisy areas and other work areas or around noisy equipment considering hearing conservation and medical monitoring programs	Certain laser systems
Radiation	*Somatic effects*: leukemia, bone, lung, and skin cancers, minor skin damage, hair loss, blood deficiencies, gastrointestinal damage, and cataract formation *Hereditary effects*: chromosome damage or gene mutation, impaired fertility, menstrual changes in women, congenital malformations, mental impairment, and radiation-induced cancers	Minimizing the time of radiation exposure, maximizing the distance from the radiation source, shielding the radiation source, substituting the use of radionuclides with nonradiometric techniques	Ionizing radiation

in collaboration with safety and staff who are responsible for laboratory biosafety. Risk assessment measures should be reviewed regularly and revised as necessary. Revisions will be provided using scientific literatures and other relevant information sources [16].

3.8.1 Assessment of Microbiological Hazards

To identify microbiological hazards, microbiological risk assessment must be performed according to hazard identification, exposure assessment, hazard characterization, and risk characterization [27].

- *Hazard identification*: Hazard identification identifies chemical, biological, and physical agents which can cause an adverse effect on health which is related to the presence of a pathogen in food [27].
- *Exposure assessment*: Exposure assessment provides a qualitative or quantitative estimation of the intake of a microbiological hazard in a specific food or a range of foods [27].
- *Hazard characterization*: The main point in hazard characterization is the association between the amount of exposure to a chemical, biological, or physical agent and the adverse impact on health [13, 27].
- *Risk characterization*: Risk characterization is a combination of hazard identification, exposure assessment, and hazard characterization [27].

3.8.2 The Importance of Proper Documentation

Documentation plays a critical role in the quality system of laboratory which relies on the recording of vital information. Documents should be stored in laboratory and must be available to all laboratory staff. Policies and programs should be followed by biosafety officers. Therefore, every aspect of a new device or a new drug should be recorded, examined, revised, updated, submitted, and archived. In addition, the competency of all staff should be assessed, monitored, and recorded based on qualification and training programs and in relation with the responsibilities [28].

3.8.3 Standard Operating Procedures (SOPs)

SOP is a document which develops based on GLP program. Therefore, SOP content should comply with GLP rules [16]. According to the information obtained from risk assessment processes, biosafety levels, and testing facilities, SOPs are developed to provide the highest level of quality and safety during work [29].

3.8.4 Guidelines for Basic Laboratories: Biosafety Levels 1 and 2

WHO has recognized that biosafety in laboratory is one of the most important international issues. In 1983, WHO published the first edition of the laboratory biosafety manual. Then, codes of practice for safe exposure to microorganisms were developed, and coun-

tries were encouraged to enforce these regulations. Since 1983, many countries have applied specific recommendations to develop their codes of practice. Guidelines for basic laboratories (biosafety levels 1 and 2) can be generalized to implement in laboratories with any biological level (▶ Boxes 3.1 and 3.2) [7]. Also, guidelines for containment laboratories (biosafety level 3) and the maximum containment laboratories (biosafety level 4) are developed on the basis of guidelines for basic laboratories [30].

Box 3.1 Code of Practice for Basic Laboratories (Biosafety Levels 1 and 2)

- Only staff should enter the laboratory.
- It is necessary to install an international biohazard warning sign on the doors of the rooms with the risk of group 2 microorganisms or higher ones.
- Laboratory doors should always be closed.
- There should be special permission for staff to enter animal laboratory. On the other hand, any animal-specific projects are allowed to be entered.

Box 3.2 Guidelines for Design and Establishment of Basic Laboratories (Biosafety Levels 1 and 2)

1. Laboratory should have adequate light and avoid any reflection of stunning light and brightness.
2. Accumulation and congestion of laboratory equipment, outbreak of insects and rodents, formation of dust (particles), and working with high volume or high concentration of microorganisms should be reduced.
3. Laboratory should provide sufficient work area in a safe condition. Cleaning and maintenance should be done.
4. Floors, ceilings, and walls should be completely smooth, easy to clean, impervious to liquids and resistant to chemicals and disinfectants. Floors should not be slippery.
5. Some facilities outside the workplace should be provided to keep personal clothing, as well as eating and drinking.
6. Bench surfaces must be impervious to heat, resistant to water, disinfectants, acids, bases, and solvents.
7. In biosafety level 2, autoclave gas sterilizer and other related equipment should be accessible.

3.8.5 Guidelines for Containment Laboratories: Biosafety Level 3

Containment laboratories – biosafety level 3 – are designed to use for procedures involved in group 3 microorganisms or group 2 with a high concentration [7]. This type of laboratories requires more restricted guidelines and rules than basic ones (▶ Box 3.3 [9] and Box 3.4 [31]).

Box 3.3 Code of Practice for Containment Laboratories: Biosafety Level 3

- Laboratory protective clothing should cover the entire body, and the head and shoe covering should be considered.
- The biological risk sign should be installed on the main entrance door including information about safety requirements for entering into the laboratory, the biosafety level, and also the name of the laboratory supervisor.
- Working with infectious agents should be done in BSCs or other containment devices.
- It is necessary to use respiratory protective equipment.

Box 3.4 Guidelines for Design and Establishment of Containment Laboratories: Biosafety Level 3

Some additional and necessary equipment should be added to basic laboratories to provide a containment laboratory condition:

- A ventilation system should be installed in building. Therefore, air flow from the containment laboratory cannot be recirculated to other spaces within the facilities.
- High-efficiency particulate air (HEPA): Air should be recirculated and reconditioned with HEPA filters within the containment laboratory. Depending on the type of agents, air should be discharged via HEPA filters. When exhaust air is discharged to the outside of the building, it should be dispersed away from air intakes and occupied building.
- Heating ventilation and air conditioning (HVAC): HVAC systems should be installed in containment laboratory to prevent sustained positive pressure. Also, specific alarms should be installed to alert personnel to HVAC system failure.

3.8.6 Guidelines for Maximum Containment Laboratories: Biosafety Level 4

Maximum containment laboratories are designed as a workplace which is involved with group 4 microorganisms. Controlling of these laboratories should be supervised by national health authorities [32] (▶ Boxes 3.5 and 3.6 [7, 32]).

Box 3.5 Code of Practice for Maximum Containment Laboratories: Biosafety Level 4

- Two personnel should work in maximum containment laboratory (two-person rule). Accordingly, no one should work alone.
- It is required to change clothing and shoes completely before entering and upon exiting the laboratory.
- Personnel should be trained in case of emergency such as injury and illnesses and relevant disasters.
- In maximum containment laboratories, a method of communication between personnel should be established and also support personnel outside the laboratory for normal and emergency conditions.

Box 3.6 Guidelines for Design and Establishment of Maximum Containment Laboratories: Biosafety Level 4

Some additional and necessary equipment should be added to containment laboratories to provide maximum containment laboratory condition including primary containment, controlled access, controlled air system, disinfection of effluents, sterilization of waste and materials, airlock entry ports, containment drain, and emergency power.

3.8.7 Guidelines on Laboratory Animal Facilities

Personnel who use animals for laboratory practices and diagnostic purposes should be morally committed to take care of them and avoid any unnecessary harm. Accordingly, adequate food and water, as well as a hygienic and comfortable place, should be provided for animals. For security reasons, animal house should be a unit completely independent of the laboratory. If connected to the laboratory, it should be completely separated from the public parts of the laboratory with perfect disinfectant procedures [33]. Animal labo-

Table 3.5 Containment levels for laboratory animal facilities, methods, and safety equipment [7]

Risk group	1	2	3	4
Containment levels	ABSL*1	ABSL2	ABSL3	ABSL4
Laboratory safety equipment	Limited access, gloves, and protective clothing	ABSL1 methods+ hazard warning signs, biological cabinet Class I or II, disinfection of waste and shelves before washing	ABSL2 methods+ controlled access, biological cabinet, and special protective clothing	ABSL3 methods+ extremely limited access, changing clothes before arrival, biological cabinet class III or positive pressure suits, shower on exit
Cage processing methods	Do not need autoclave	Autoclave cages before washing, changing cages in BSC*	Autoclave wastes prior removing from the area	Autoclave wastes prior removing from the area

*ABSL** animal facility biosafety level, *BSC** biological safety cabinets

ratory equipment can be designated based on a risk assessment protocol, risk group microorganisms, and biosafety levels 1, 2, 3, and 4. A summary of methods and safety equipment used according to animal facility biosafety level (ABSL) can be seen in Table 3.5 [7].

3.8.8 Guidelines for Laboratory Commissioning

The aim of the laboratory commissioning is defining a regular process of monitoring and also collection and verification of documents to ensure that all of the structural components of a GLP-based laboratory are installed, inspected, tested, and approved correctly in accordance with the international or national standards. On the other hand, laboratories are dynamic and complex environments that can be adapted to healthcare needs [28]. All biomedical laboratories should be certified to ensure that they are on the correct way focusing on the following considerations [7]:

- Engineering controls are carried out properly and consistently as they are designed.
- Administrative controls are in accordance with the established protocols and are performed in a suitable site.
- PPE is provided based on established criteria to be suitable for the tasks.
- Materials and wastes are completely decontaminated. Proper waste management practices are carried out quickly.
- For the general safety of the laboratory, including chemical, electrical, and physical safety, there are well-defined procedures which are conducted properly.

Fig. 3.2 Safety checklist. Important points which should be considered in the safety checklist of GLP [7]. To ensure proper establishment, there should be answer to questions about laboratory premises; staff facilities and services; safety against fire, chemicals, and electrical hazards and also suitable heating, lighting, and ventilation system; and more importantly laboratory biosafety and biosecurity

3.9 Safety Checklist

A proper safety checklist helps director to assess the safety and security of the laboratory. Some important points which should be considered in safety checklist of GLP are indicated in Fig. 3.2.

3.10 Challenges and Future Perspectives

In recent years, following the advancement in technology and industrialization, biomedical sciences has being dramatically grown. Therefore, to avoid several challenges, appropriate codes of practice and protocols are needed. GLP standards are developed to direct

laboratories in a right manner. Accordingly, GLP has been popularized throughout the world. Few people can estimate contemporary challenges about GLP regulatory which is faced today [34]. The aim of GLP is not only decreasing the adverse events of biological products but also improving human health and safety of environment [3]. GLP is also a protocol for nonclinical laboratory researches which can help scientists to perform biomedical researches perfectly. There are several challenges such as issues surrounding record keeping. For example, their reliability and trustworthy especially due to limited access to electronic systems and internet are serious limitations. To overcome these challenges, environmental protection agency (EPA) implements standard requirements that are equipped to receive information electronically for data submission [34]. Other challenges include very old information which is not in accordance with GLP guidelines, heavy costs and regulatory burdens, insufficient staff, and inadequate technical training. Accordingly, there are some procedures that can enhance the quality of the research such as monitoring GLP compliance through regulatory inspections, optimization, and electronic records including signatures, electronic system, internet, etc. [35]. The most important procedure is optimization [36]. It is predictable that other novel methods based on using burgeoning technologies including nanotechnology, biocides, computer modeling, electronic data, and record keeping using the fastest supercomputer with the ability to perform 1000 trillion calculations per second will be developed in the near future [34, 36].

Take-Home Messages

- In 1983, the WHO has developed codes of practice for safe exposure to microorganisms and encouraged countries to enforce these regulations.
- Biosafety is a set of rules that are used to handle the hazards of living organisms and also isolate them in an enclosed laboratory. The base of biosafety is the risk assessment process.
- Risk assessment should be carried out by individuals who are well trained and those with the good knowledge of organisms, tools, methods, animal models, and equipment.
- GPL is a set of techniques that provide safety and quality in the laboratory and environment and also safety of personnel.
- GLP can be used as a practical standard to direct nonclinical laboratory researches.
- Microorganisms are classified into four risk groups based on their possibility of harm in humans, animals, and environments.
- Laboratory facilities are designed and classified based on biosafety levels 1, 2, 3, and 4.
- There are some procedures that can enhance the biosafety and quality control of the laboratories such as using electronic records, internet, optimization, etc.

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