



Basics of Biosafety & Good Laboratory Practice

21st October 2024

Regional Training Workshop on Rabies Diagnosis for South-East Asia, NIMHANS, Bangalore, 21-25 October 2024

Overview

- Biosafety vs Biosecurity
- Fundamentals of Good Laboratory Practice (GLP)
- Rabies specific biosafety / GLP aspects



Basics of Biosafety

Working Safely with Biological Materials

Safety is always Team Work

Key Definitions

- **Biohazard / Biological agent** : An agent of biological origin that has the capacity to produce deleterious effects on humans, i.e. microorganisms, toxins and allergens derived from those organisms; and allergens and toxins derived from higher plants and animals.
- **Biosafety**: Reduce or eliminate accidental exposure of individuals and the environment to potentially hazardous biological agents. Protect people from dangerous pathogens and limit lab access while work is in progress
- **Biosecurity**: The protection of pathogens, toxins, and sensitive information from loss theft and subsequent misuse. Main aim is to limit access of infectious pathogens beyond designated people.

WHO Classification of Biological agents

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.

**Source: Laboratory Biosafety Manual, WHO, 3rd Edition, 2004¹²*

What are the risks in a laboratory?

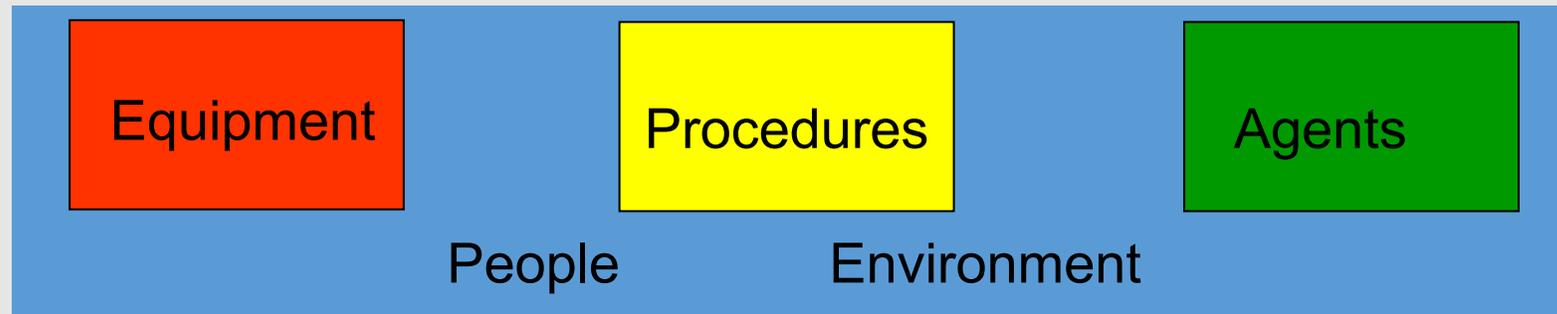
- Chemicals
- Radiation
- Fire
- Electrical
- Physical



Steps in building a biosafety plan for the laboratory

Step 1: Risk Assessment

The most important step in any Risk Assessment - risks can only be controlled if they are identified



- Each step is analyzed for potential inherent risks
- Decision on the relevance of any particular risk come later in the risk assessment processes

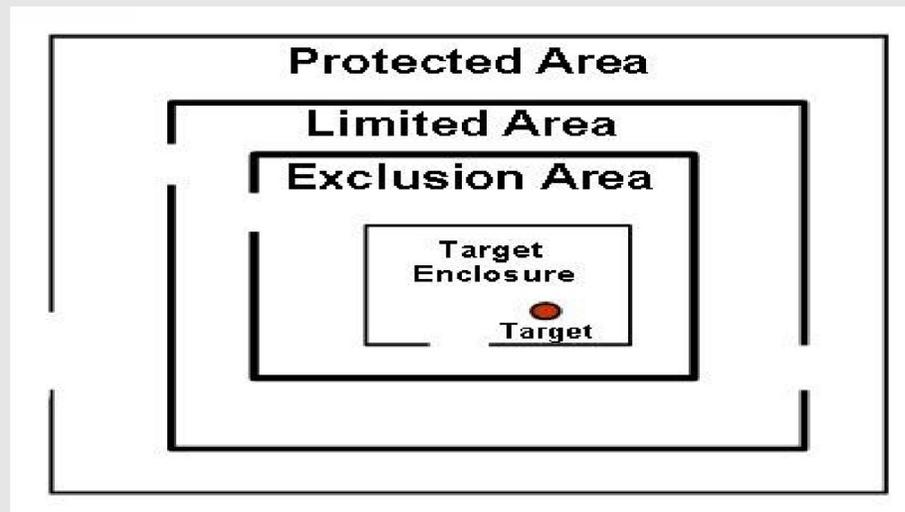
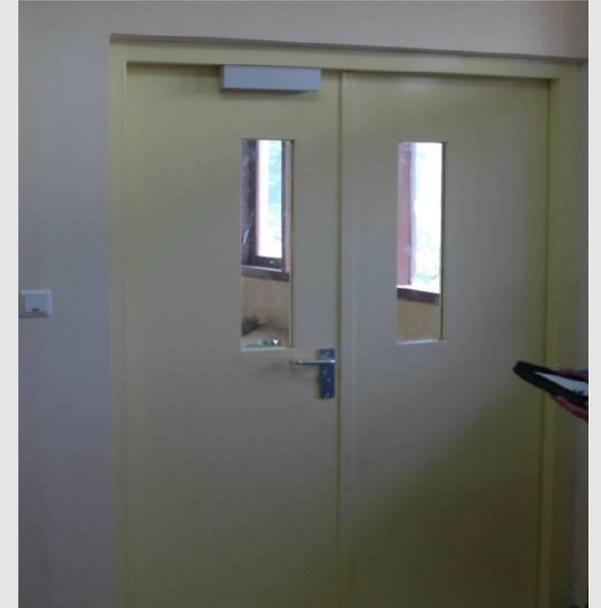
Step 2: Risk Reduction

1. Administrative Controls
2. Engineering Controls
3. Work Practice Controls
4. Personal Protective Equipment
5. Active Training and Surveillance

Administrative Control

1. Delegate safety responsibilities & oversight (Safety Committee)
2. Provide appropriate resources (Staffing & Funding)
3. Ensure implementation (Written safety manual, Laboratory personnel training)
4. Regulatory compliance (National & Local)
5. Physical security
6. Material Control and Accountability
7. Information security
8. Transport Security

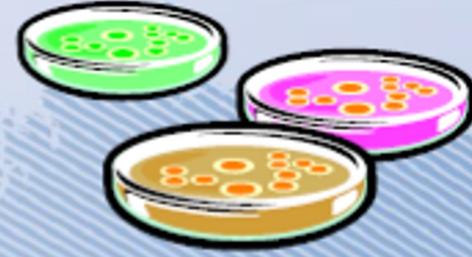
Physical security



Material Control & Accountability

Material Control & Accountability

What information should we keep track of?



Agent	Quantity	Form	Detail	Scope
Which agents?	Any amount of a replicating organism can be significant.	Repository Stocks, Working Samples, yes...	Materials as Items	Laboratory Strains? Wild-type?
Only viable organisms? Whole org. or just DNA?	For toxins, must define a threshold amount.	What about: In host? Contamination?	Each vial as a separate inventory record?	Clinical Samples?



Transport Security

Chain of Custody (CoC)

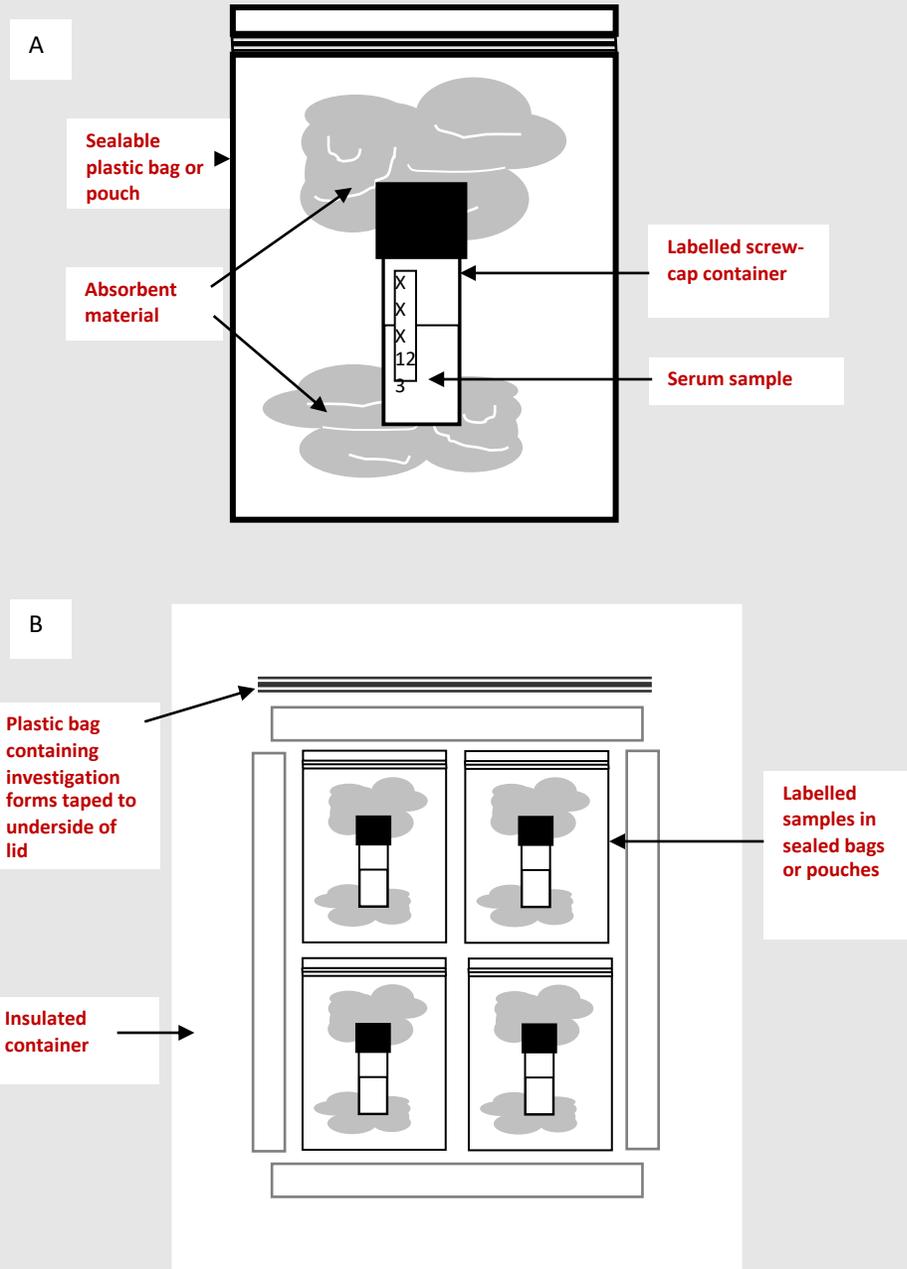
- All individuals who have control of sample
- Description of material being moved
- Contact information for a responsible person
- Time/date signatures of every person who assumes control

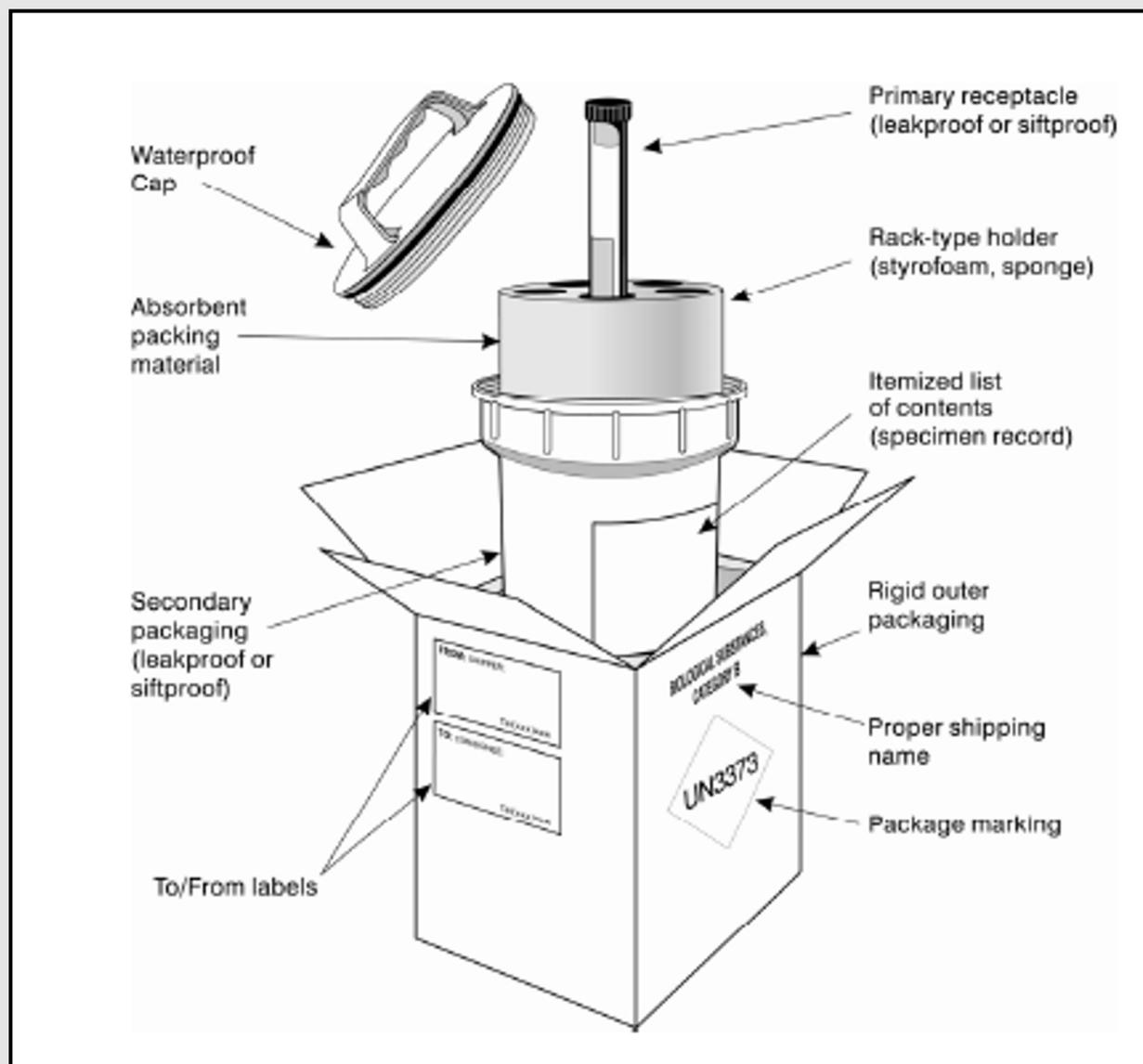


Preparing samples for Shipping Infectious Material

Key Points

- **Ensure Primary container is:**
 - Sample container
 - Leak-proof
 - **EXTERNALLY** threaded screw cap
 - Labelled appropriately
 - Wrapped in absorbent material
 - Sealed individually with Ziplock bag
- **Secondary Container**
 - Can enclose multiple primary containers
 - Leak proof
 - Meets IATA pressure test
- **Outer packing**
 - Secondary container
 - Protects contents from temperature changes and physical damage
 - Vaccine box or similar can be used
 - Labelled appropriately
 - Specimen information documents must be enclosed in separate Ziplock





Information Security

- **Information Security** may not be the most obvious area of biosecurity, but a failure here could have very severe consequences in terms of securing pathogens and toxins.
- **Protect information that is too sensitive for public distribution**
 - Label information as restricted
 - Limit distribution
 - Restrict methods of communication
 - Implement network and desktop security



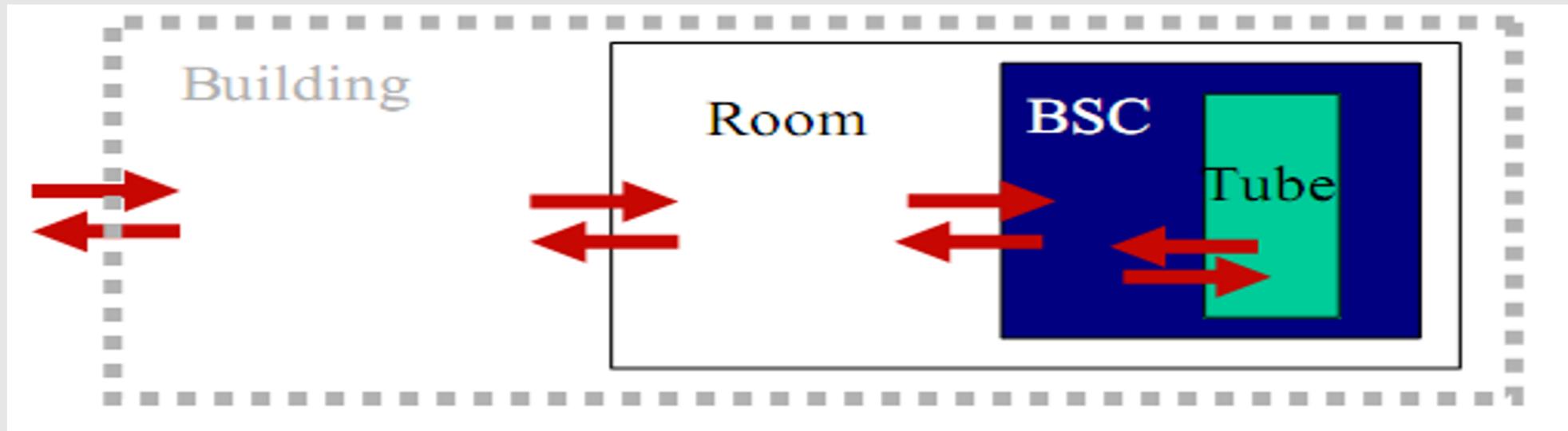
Engineering Control : Facility Design

- Restricted access
- Eyewash station
- Sink for handwashing
- Ventilation systems
- Floors
- Bench tops
- Walls, ceilings, and furniture

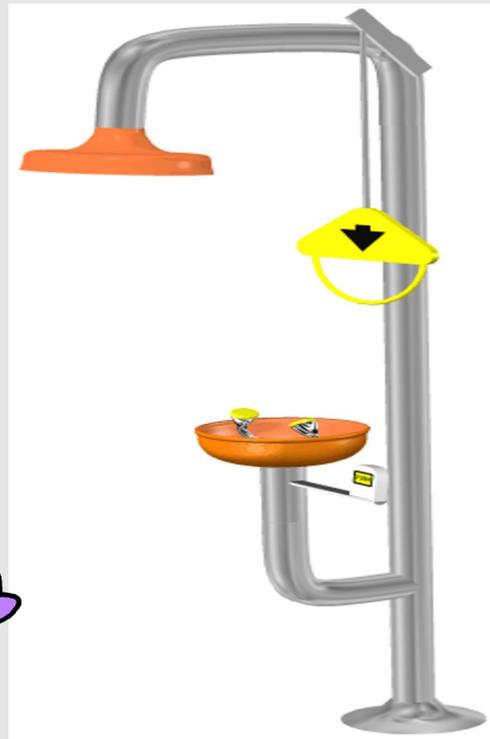


Engineering Controls

- **Primary barriers** – contain the agent at the source
- **Secondary barriers** – contain the agent within the room or facility in case an agent escapes from the primary barriers



Engineering Controls Safety Equipment



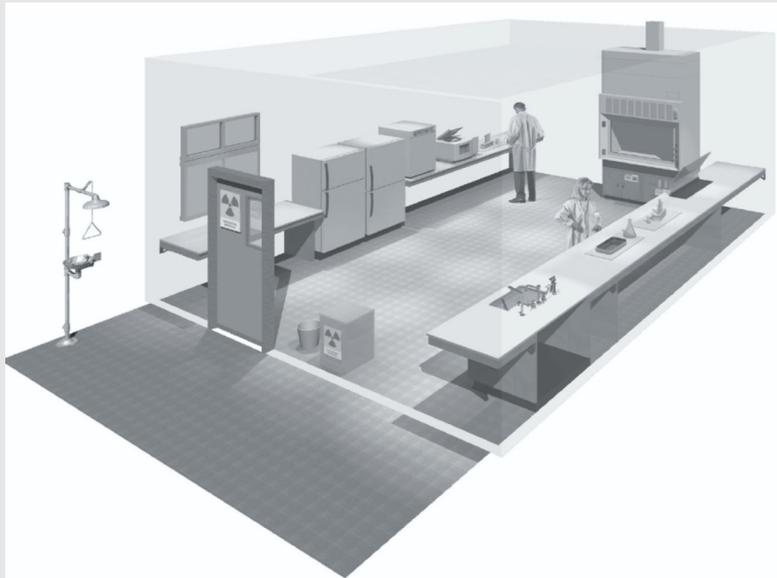
- First Aid and Medical treatment
- Emergency Equipment
- Showers, Eyewash Stations
- Safety Data Sheet

Biosafety Levels 1- 4 provide:

- Increasing levels of personnel & environmental protection & appropriate guidelines for:
 - Laboratory Practices and Techniques
 - Standard Practices and Special Practices
 - Knowledge of supervisor and personnel
 - Lab specific SOPs/Biosafety manual
 - Safety Equipment (Primary Barriers)
 - Laboratory Facilities (Secondary Barriers)
 - Buildings (Tertiary Barriers)
- Biosafety Level 1 labs - work with least dangerous agents, require minimal precautions
- Biosafety Level 2 lab - agents associated with human, animal, or plant disease
- Biosafety Level 3 lab -indigenous/exotic agents associated with human disease and with potential for aerosol transmission.
- Biosafety Level 4 labs - have most stringent methods as dealing with agents that are most dangerous to human health

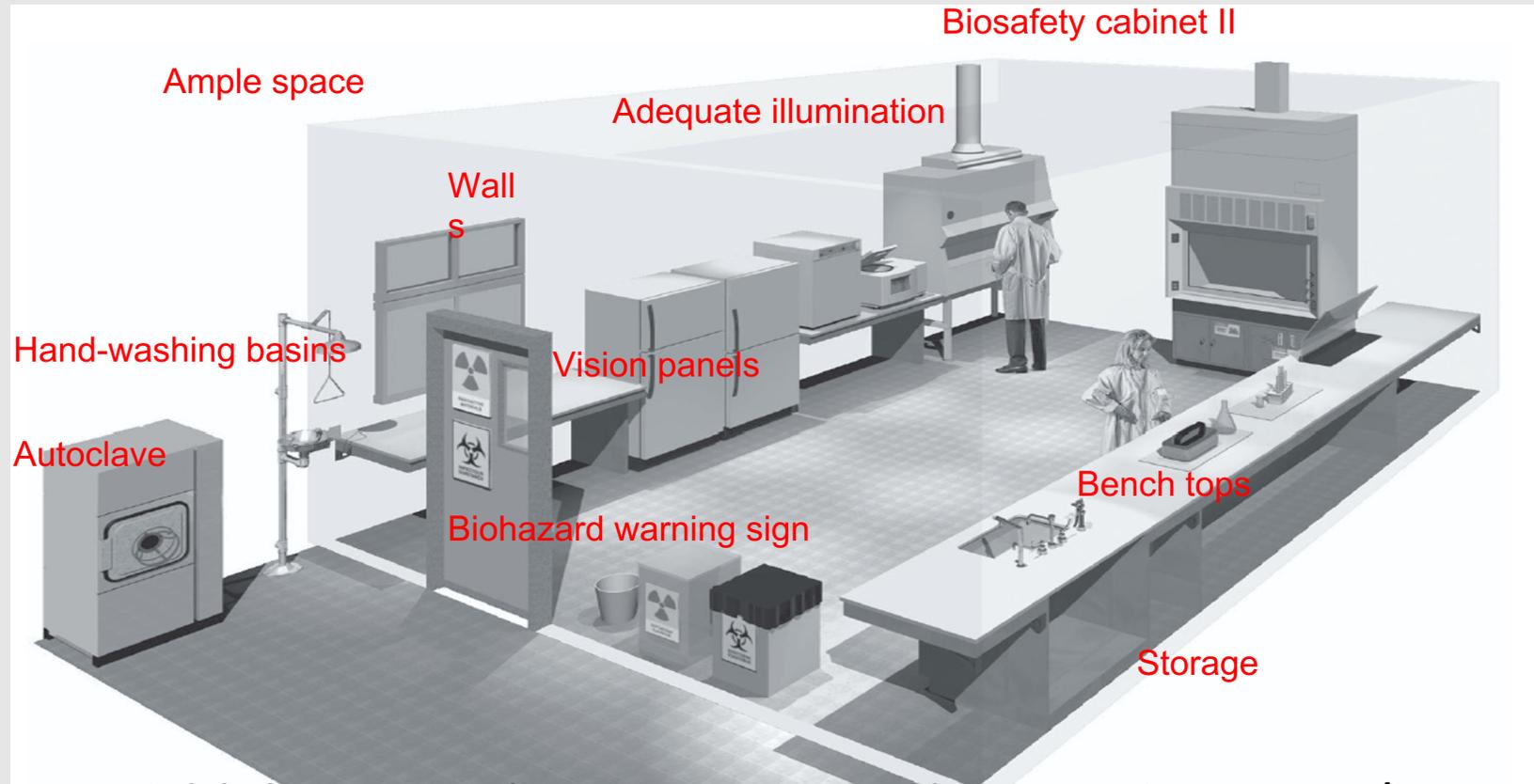
Biosafety Level 1

- Laboratories have doors.
- Sinks for hand washing.
- Work surfaces can be easily cleaned & decontaminated.
- Windows have screens.



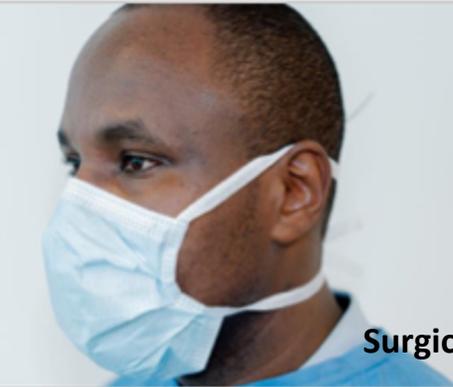
- Restrict/limit access when working
- No eating, drinking, etc.
- No mouth pipetting
- Minimize splashes and aerosols
- Decontaminate wastes
- Decontaminate work surfaces daily
- Wear applicable PPE
- Wash hands often
- Maintain insect & rodent control
- Prevent Cross Contamination :Keep cultures covered, Flame instruments and containers, Use sterile media and equipment, Keep hands or face away from cultures

Biosafety Level 2 laboratory



- **Basic lab, but restricted access, containment during certain processes (i.e. aerosols, large volumes, etc.)**
- **Autoclave and Biological Safety Cabinet desired**
- **Use good laboratory practices, waste disposal, and aseptic techniques**
- **Extreme care should be taken with contaminated needles and sharp lab instruments**

Personal Protective Equipment



Surgical/medical masks



N95/Respirators



Face Shield



Gloves



Disposable Gown



Coveralls/body suit



Safety goggles

Training Employees

1. In proper use of PPE
1. Why PPE is necessary.
2. When PPE is necessary.
3. What PPE is necessary.
4. How to properly put on, take off, adjust and wear the PPE.
5. The limitations of the PPE.
6. Proper care, maintenance, useful life and disposal of PPE.

Surveillance and Training

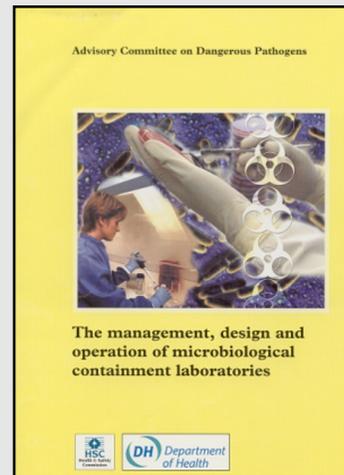
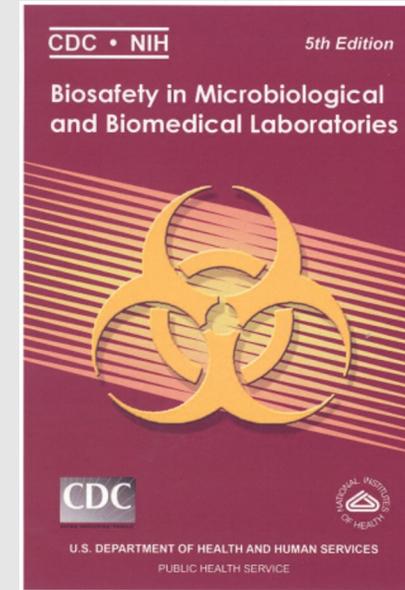
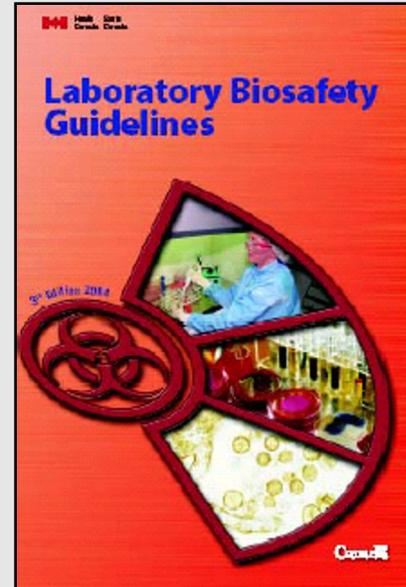
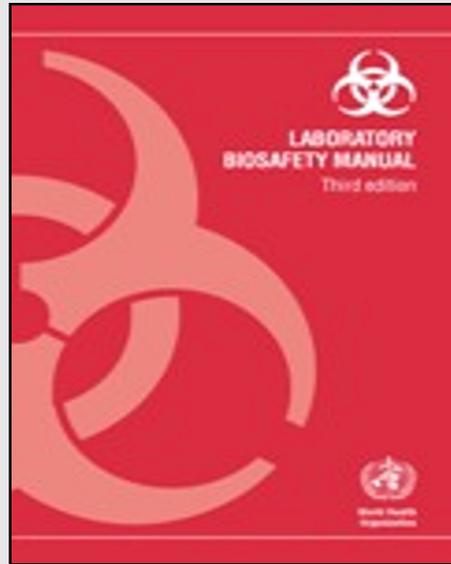
Hospital Infection Control Committee

- Committee with people from diverse specialties
- Policies and Procedures
- Induction training and Refresher training
- Surveillance of Hospital Acquired Infections
- Vaccination of staff
- Reporting of incidents / accidents

Institutional Biosafety Committee

- Periodic review of safety practices across the campus.
- Review of protocols

Standards for Biosafety



Good Laboratory Practice

What is Good Laboratory Practice ?

Defined as: *“...a quality system concerned with the organizational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.”*

History of GLP

-In the early 1970s, the FDA investigated a number of cases of poor practice in toxicology laboratories throughout the USA

- Results of this investigation in about 40 laboratories revealed many cases of poorly managed studies, insufficient training of personnel, and some cases of deliberate fraud

- In 1976, the FDA published a draft regulation on GLP

- After the consultation period, the final regulation was published in 1978

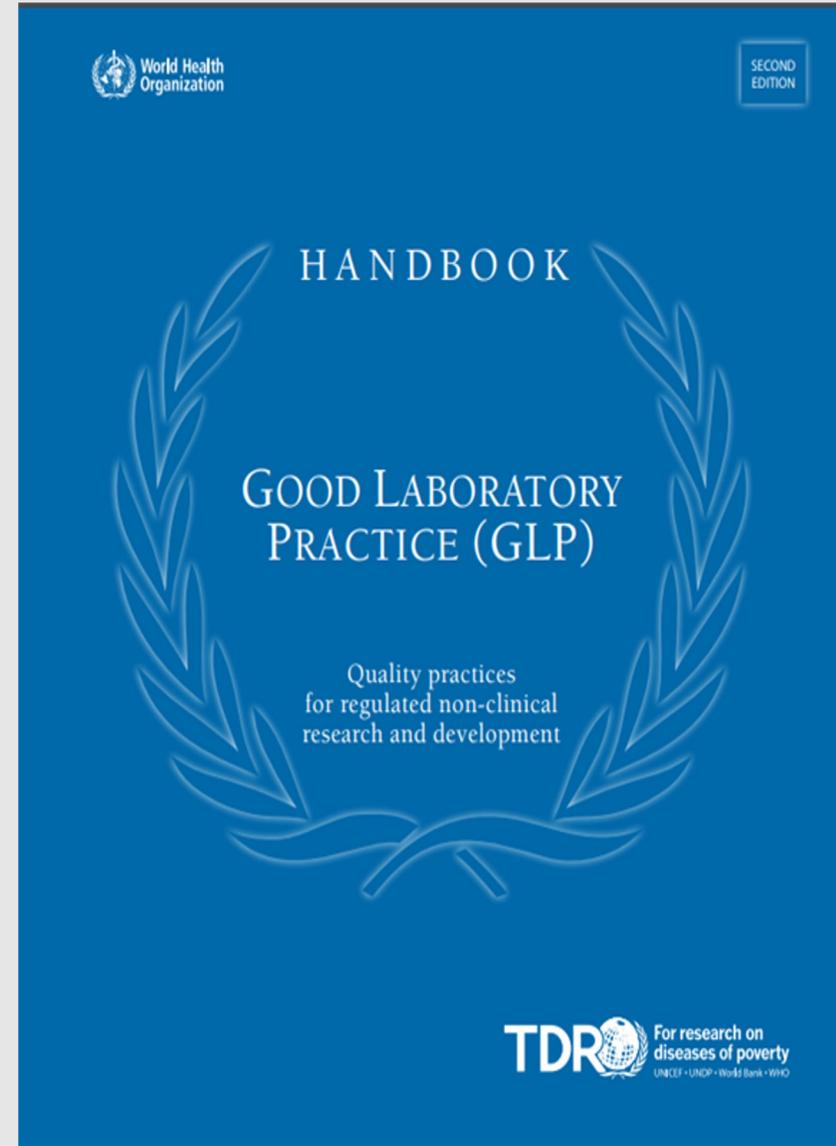
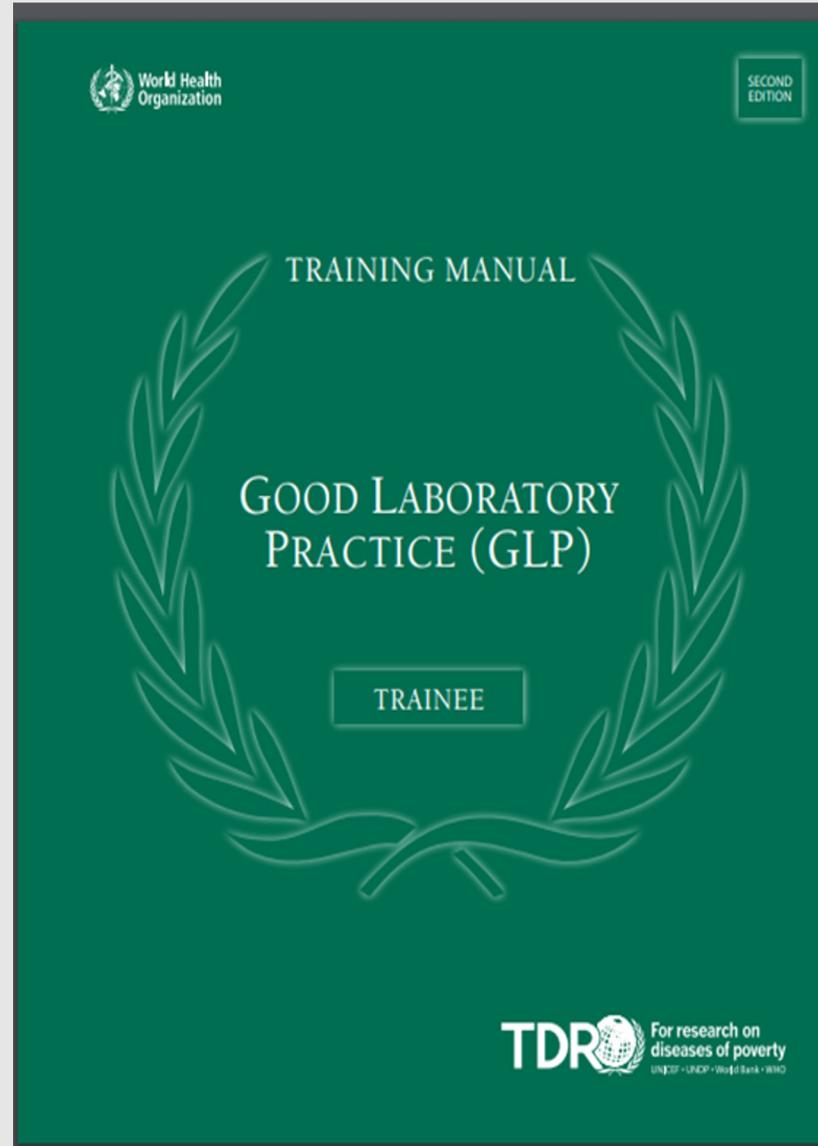
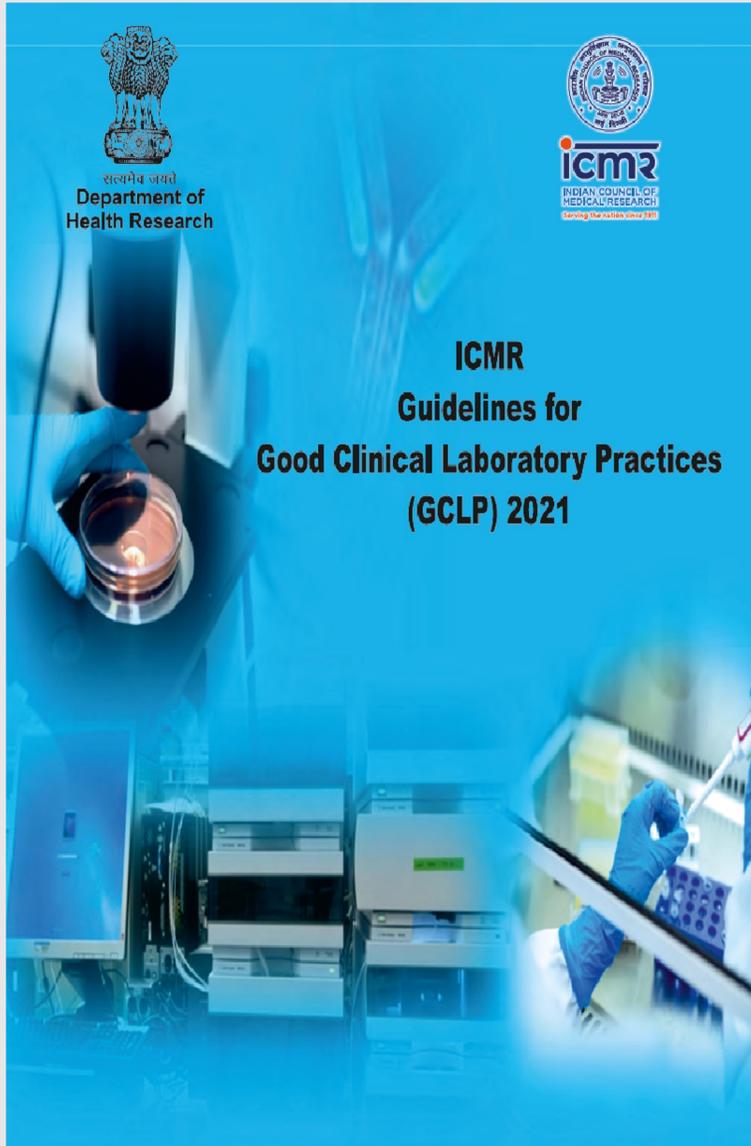
- This came into force in 1979

- Many countries introduced their own GLP Regulations

- The OECD produced GLP Principles in 1981.

These regulations have now become the international standard in the domain

Guidelines for Good Laboratory Practice



Scope / Utility of GLP

- Where is it applicable?
 - Who should follow GLP?
 - When is it applicable?
 - Who will enforce GLP?
- Where is it applicable: **All types and levels of laboratory**
 - Who should follow GLP: **All cadres of laboratory workforce**
 - When is it applicable: **Every moment of laboratory work**
 - Who will enforce GLP: **Internal and external agencies**

Fundamental pillars of GLP

- Infrastructure
- Personnel
- Documentation
- Equipment
- Reagents and Consumables
- Laboratory Safety
- Housekeeping

Infrastructure

- Identity of the laboratory
- Adequate space with good ventilation for laboratory activities
- Storage of reagents, specimens
- Biomedical waste management
- Partitions for incompatible activities
- Restricted access
- Safety with contingencies for Emergency
- Space for additional activity

Personnel

- Laboratory hierarchy must be defined
- Ideal qualifications with requisite experience
- Job description with in-house training (induction training, technical, safety, administrative, professional development training etc.)
- Ethics
- Evaluation of the training
- Competency assessment
- Vaccination

Documentation

- Paper based vs electronic
- Administrative and Technical (Pre-examination, examination and post-examination)
- Comprehensive and concurrent with activity
- Standard Operating procedures (SOP)
- Paper based: legible, secure and must be retained as per legal requirements
- Electronic data: access, restrictions, back-up, data privacy
- Training and retraining for better enforcement

Equipment

- Varied equipment both old and new
- Need based request / purchase of equipment
- New equipment : IQ , OP, PQ
- Manufacturer specifications
- SOP for equipment with dedicated trained manpower
- Maintenance : PM / AMC / CMC / BME
- Periodic Calibration
- Equipment Log Book
- Record keeping
- Condemnation

Pipettes

- Wide range
- Correct pipetting technique
- Daily maintenance / Trouble shooting
- Calibration

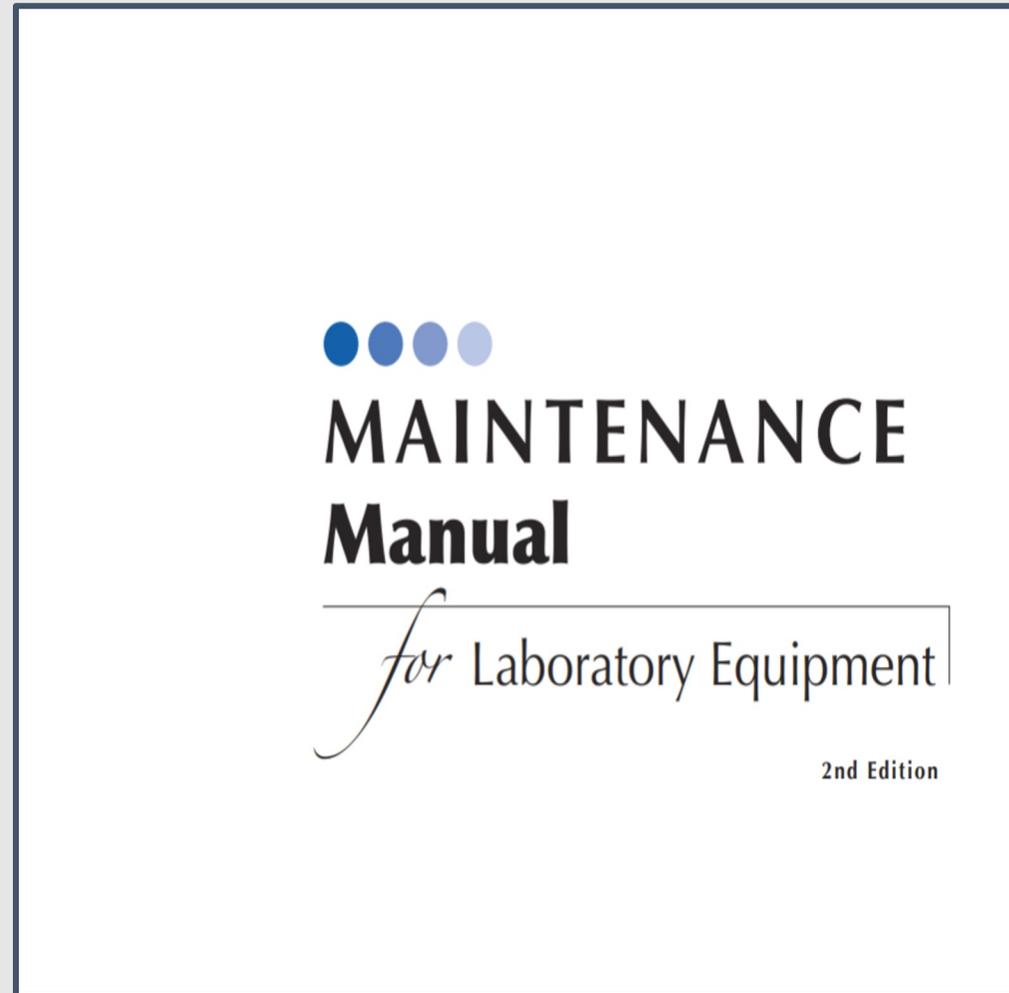


Centrifuge

- Various types with varied temperature specifications
- Flat surface
- Balance
- Check of leaks...and follow bio-medical waste management guidelines if there are any
- Maintenance



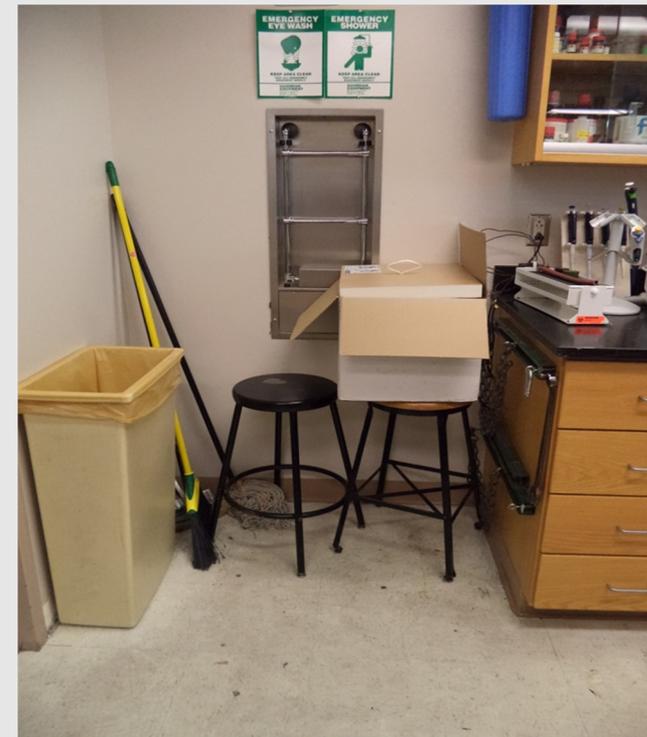
WHO guidelines for Laboratory equipment



Reagents and Consumables

- Basic requisite for uninterrupted services
- Fit for purpose....with focus on quality
- Verification
- Labelling and storage
- Disposal
- Log book
- Supply chain and lead time

Housekeeping



Laboratory Safety

- Awareness of institution specific safety policy and procedures ...safety manual
- Personal Protective equipment
- Biomedical waste management
- Vaccination
- Chemical safety
- Electrical Safety
- Risk Assessment and Risk mitigation plan

Rabies virus : Biosafety and GLP

Biosafety 2 practices adequate

- Mandatory PPE and pre-exposure rabies vaccination
- Training and periodic re-training

Biosafety 3

- Propagation of large quantities of virus
- Procedures that generate lot of aerosols
- Lyssaviruses with effectiveness of current prophylaxis unknown
- Use of pseudo viruses for neutralization

In summary

- Laboratory specific GLP and Biosafety Guidelines : policies , procedures, training of staff
- Local, Regional, National guidelines
- Enhance awareness
- Knowledge must be translated to day-day laboratory practice
- Periodic review of laboratory needs