

Regulatory and Bio-safety requirements for Select Biological Agents

Biosafety Principles

- Risk Assessment and Hazard Identification
- Biological Containment
- Concentration and enclosure
- Exposure Minimization
- Physical Containment
- Hazard minimization

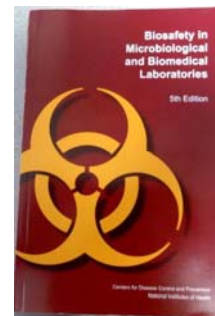
Ways to Minimize Exposure

- Engineering Controls: use of available technology and devices to isolate hazards from the worker
 - e.g. Biosafety cabinets (BSC), safer needle devices, puncture resistant sharps containers
- Administrative Controls: monitor compliance, provide accessibility of control methods, investigate exposures to prevent future occurrences
- Work Practice Controls: manner in which task is performed to reduce exposure
 - wash hands after removal of gloves, disposal of needles without recapping, no lab coats outside of lab
- PPE: specialized clothing or equipment used to protect workers from exposure
 - lab coats, gloves, face shields, eye protection, fluid resistant aprons, head and foot coverings

3

Lab Safety/ Biosafety Standards

- Biosafety Levels (BSL)
- Risk Assessment
- Proper Engineering, Work Practice Controls
- Risk Classification of Microorganisms, including bacteria, viruses, parasites, fungi, and rickettsia
- Other special practices



4

Principles of Containment Lab Function

“Containment”: describes safe methods for managing infectious materials in the laboratory environment or where they are being handled/maintained.

- Purpose of containment: reduce or eliminate exposure of lab personnel, other persons, and the outside environment to hazardous agents
- Three elements of containment:
 - Lab practice and technique
 - Safety equipment (primary containment)
 - Facility design (secondary containment)

Biosafety Level 1 (BSL1)

- Work with well characterized agents not known to cause consistent disease and present minimal hazard to laboratory personnel
- Work on open bench tops with standard microbiological practices
- Requires biohazard label, disinfection, mechanical pipetting, and basic biosafety training
- Examples: *E.coli* Dh5 α , *Staphylococcus epidermidis*, *Bacillus cereus*

6

Biosafety Level 2 (BSL2)

- Builds upon BSL1 guidelines
- Work with agents posing moderate hazard to laboratory workers and the environment
- Differs from BSL1:
 - Restricted access to labs
 - Lab personnel have specific training in handling pathogens
 - All procedures conducted in a BSC
 - Some immunizations may be required/ recommended
- Examples: HIV, Influenza virus, hepatitis B

7

Biosafety Level 3 (BSL3)

- Builds upon BSL2
- Work with indigenous or exotic agents that can cause serious or potentially lethal disease through respiratory route
- Differs from BSL2:
 - All manipulation in BSC
 - Special engineering and design features: ventilation system
 - Detailed training in pathogen handling, refresher trainings, etc
- Examples: *M. tuberculosis*, *B. anthracis*, SARS, avian influenza



8

Biosafety Level 4 (BSL4)

- Builds on BSL3
- Work with dangerous and exotic microorganisms that pose a high risk of aerosol-transmitted laboratory infections and life threatening disease for which no vaccines or cure
- Cabinet lab or Suit lab
- Examples: Smallpox , Ebola



Primary Containment: Safety Equipment

- Biological Safety Cabinets
- Closed containers
 - Safety cups on centrifuges
- Personal Protective Equipment (ppe)
 - Respirator (N95 or PAPR)
 - Tyvek coveralls
 - Shoe covers
 - Double gloves
 - Optional: goggles, head covers

Secondary Containment: Facility Design

- Special ventilation system
 - Unidirectional airflow
 - No recirculation of exhaust
 - HEPA filtered exhaust air
 - Audible pressure alarms
- Controlled access to facility
- Airlocks in entrance

Engineering Controls

- Biological Safety Cabinet (Class II)
- Chemical disinfectant traps
- Sharps containers & “safe needle” devices
- Centrifuge safety devices
- Specimen transport containers
- Vacuum line filters
- Replace glass with plastic where possible
 - Pasteur pipettes, capillary tubes coated

11



Personal Protective Equipment (PPE)



- Anything that is used to protect a person from exposure
 - Latex or Nitrile gloves
 - Goggles
 - Mouth barriers
 - Aprons
 - Respirators
 - Face shields
 - Others?



Laboratory Practice and Technique

- User requirements
 - Written/Hands-On Examination
 - Baseline serum/TB skin test, other vaccinations when required
 - Submit protocols for approval
 - Previous experience with tissue culture and pathogenic organisms
- Manipulations in Biological Safety Cabinets
 - Decrease aerosol production
 - Sterile technique
- Training Requirements
 - Biohazard
 - Radioactivity
 - Laboratory Safety
 - Bloodborne Pathogens

International Legislation

Chemical and Biological Weapons Control Act of 1991

- Response to major weapons programs in the 1980's which included chemical and biological weapons
- Established:
 - Elaborate system of economic sanctions and export controls in an effort to curb proliferation
 - Created broad array of economic and diplomatic sanctions to use against countries that use biological weapons in violation of international law
 - Sanctions on international companies

Amended Export Administration Act of 1979

- Enacted to prevent US companies and individuals from exporting any goods or technologies that would "directly and substantially assist" a govt. in developing or delivering a biological weapon to certain prohibited countries

Federal Legislation

- Biological Weapons Act of 1989
- The Anti-terrorism and Effective Death Penalty Act of 1996, Section 511 (Public Law 104-132)
- Bio-terrorism Enforcement Act of 2001
- Public Health Security and Bio-terrorism Prevention and Preparedness Act of 2002
- USA PATRIOT ACT 2002

Biological Weapons Act of 1989

- Passed in order to implement BWC Article IV and protect nation against Bio-terrorism attacks
- Key provisions:
 - Defines knowing development, manufacture, transfer, or possession as a crime
 - Defines "biological agent"
 - Provides that violator can be imprisoned for any term of years, including life
 - Fed. Govt. given broad civil and investigational powers to prevent development, production or stockpiling of bioweapons
 - Authorizes govt. to obtain civil injunction to prevent work not for peaceful purposes
 - Implement two part strategy to ensure criminal prohibitions not interfere with legitimate research

The Anti-terrorism and Effective Death Penalty Act of 1996, Section 511 (Public Law 104-132)

- Passed in wake of OKC bombing, to provide govt. with tools in war against domestic terrorism
- Expanded governments' power under the BWA
 - Broadened criminal provisions to reach anyone who "threatens" or "attempts" to develop bioweapon
 - Broadened provisions to include those who use recombinant technology to create new pathogens, or more virulent strains of existing pathogens
 - Establish new regulatory framework for controlling use of hazardous biological agents
 - CDC to establish and maintain
 - Create select agent list (42CFR)
 - Regulating Use and transfer

Categories of Select Agents

•Category A

- Easily disseminated or transmitted person to person
- High mortality, potential for major public health impact
- Might cause public panic and social disruption
- Requires special attention for public health preparedness

•Category B

- Moderately easy to disseminate
- Moderate morbidity and low mortality
- Requires specific enhancements of CDC diagnostic capacity and disease surveillance

•Category C

- Availability
- Ease of production and dissemination
- Potential for high morbidity and mortality. Can cause major health impact

CDC list of restricted agents

Category A:

*Bacillus anthracis***
Clostridium botulinum
*Yersinia pestis***
Variola major
*Francisella tularensis***
viral hemorrhagic fevers

Category B:

Coxiella burnetii (Q fever)
*Burkholderia mallei***
Ricin toxin
epsilon toxin from
Clostridium perfringens
Staphylococcus enterotoxin B

Category C:

Nipah virus
hantaviruses
tickborne hemorrhagic fever viruses
tickborne encephalitis viruses
yellow fever
multi drug resistant *Mycobacterium tuberculosis***

Bio-terrorism Enforcement Act of 2001

- Amends Anti-terrorism and Effective Death Penalty Act of 1996
- Provisions for person who possess agents without registration
- Restricts certain persons from possessing agents

Public Health Security and Bioterrorism Prevention and Preparedness Act of 2002

- National preparedness for Biological terrorism and other Public Health emergencies
- Enhance controls on dangerous biological agents/toxins
 - Regulatory control of certain biological agents and toxins
 - Regulation of transfers of listed biological agents and toxins
 - Possession and Use
 - Registration and Traceability Mechanisms
 - Inspections
 - Security requirements for registered persons
- Amendments to the federal food, drug and cosmetic act
- Drinking water security and safety

Final Rule 42CFR73

- CDC/USDA select agent rule "revised"
- Additional requirements to use, possess, transfer
 - Detailed Facility registration; Responsible Official
 - Incident Response Plan
 - Inventory records, Lab notebook records
 - Security Risk Assessments: FBI/ DOJ Fingerprinting
 - Security Plan
 - Permits for transfer
 - Inspections
 - Training requirements

*** Revisions to Select Agent Rule proposed in October 2011. Tiering of select agents, personnel reliability, increase security measures

USA PATRIOT ACT 2002

(Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism)

- Enhance domestic security against terrorism
- Enhance surveillance procedures
- Prohibits possession by restricted persons

New Jersey State Legislation

- SR 1225:

- Establishes a biological agent registry in the DHSS

- New Jersey domestic security preparedness Act

- Establish a taskforce responsible for the statewide coordination and supervision of all activities related to domestic preparedness for a terrorist act

Institutional regulations

- Select Agent Registration
- Institutional Bio-Safety Committee
- Institutional Animal Care and Use Committee
- Institutional Review Board
- OSHA policies: Lab Safety, Chemical Hygiene, Respirator Use

Institutional Biosafety Committee

- Reviews the safety of all protocols involving:
 - rDNA
 - Creation of transgenic animals
 - Cross- breeding of two transgenic rodent lines
 - Pathogens (Bsl2 and higher)
 - Human / Non-human Primate cell lines (including those from ATCC)
 - Human, Non/ human primate blood, fluids or tissues
 - Select agents (bioterrorism)
- IBC must approve before IACUC or IRB will approve protocols

27

Shipping of Select Agents

All agents shipped according to:

- US DOT regulations 49CFR171-180
- IATA Dangerous Goods Regulations
- US PHS Regulations 42CFR72

IMPORTATION OR TRANSFER AUTHORIZED BY
PHS Permit No. _____
Expiration Date _____

TO:

DO NOT OPEN IN TRANSIT
BIOMEDICAL MATERIALS
ETIOLOGICAL AGENTS OR VECTORS

NOTICE TO CARRIER: If inspection or arrival in U.S. reveals evidence of leakage or leakage, immediately notify the nearest Centers for Disease Control and Prevention (CDC), Atlanta, Georgia 30333 - Telephone 404-639-5011.

**Enforcement of Regulations:
Inspections**

- Inspections from CDC, DoD, DOT, USDA, and UMDNJ
- Inspectors observe:
 - Airflow system
 - Personal protective equipment
 - Standard Operating Procedures
 - Equipment
 - Spill and emergency procedures
 - 9CFR, 32CFR, 42CFR, CDC/NIH BMBL