Administration of Biological Safety Programs

Learning Objectives:

- Understand the safety, security, and funding agency requirements for research involving biological hazards including recombinant/synthetic DNA, select agents and toxins, and dual use research of concern.

- Understand how Biological Safety/Compliance Programs can be implemented and overseen at research institutions.
Overview

- Introduction to biological safety in research
- Risk assessment and biological safety levels
- Regulatory and funding agency requirements
- Elements of Biological Safety Programs
- Institutional responsibilities and considerations for successful programs
- When things go wrong
- Questions
University of Washington

Funding and Research

- $1.4 billion in federal research funds (2016)
- Three main campus locations and additional off campus research:
  - Seattle (main campus)
- Two medical centers
- Large University
  - 28,910 faculty and staff
  - Over 50,000 students (undergrad and graduate)
University of Washington Biological Safety Programs

- 1,813 of 4,100 (44%) labs have biohazards
- 539 of 970 (56%) lab Principal Investigators (PI) are registered with IBC
- 681 projects are registered with the IBC
- 387 IBC applications reviewed in 2016
  - 40% of applications involves animals
- Non-human primate research center, animal research, human gene transfer
- Select Agent Program and Biosafety level 3 (BSL-3)
  - Responsible Officials in EH&S-
    - Senior Director, Asst. Director, BSOs
Biological Safety

Biosafety is the maintenance of safe conditions in biological research to prevent harm to humans, animals, organisms, and the environment

- Appropriate facilities
- Appropriate equipment
- Using safe methods
- Proper training
- Safe working conditions
Biological Hazards

- Pathogenic agents (bacteria, rickettsia, fungi, viruses, protozoa, parasites, prions, and select agents)
- Human and non-human primate blood, tissue, body fluid, and cell culture
- Recombinant DNA molecules, organisms, vectors (e.g., plasmids, viral vectors), and viruses containing recombinant DNA molecules
- Recombinant or synthetically derived nucleic acid, including those that are chemically or otherwise modified analogs of nucleotides (e.g., morpholinos)
- Plants, animals or derived waste which contain or may contain pathogenic hazards (including xenotransplantation tissue)
Research Involving Biohazards

- Vaccine development and medical treatment for infectious diseases
- Gene transfer and therapy in biomedical research, heart repair, genetic disorders, cancer treatment
- Modified plants/trees for bioremediation
- Biohazards used in lab, in animals including non-human primates, human research participants
Regulations, Policies, Guidelines

- National Institutes of Health (NIH)
- Centers for Disease Control and Prevention (CDC)
- Animal and Plant Health Inspection Service (APHIS)
- Occupational Safety and Health Administration
- Federal Department of Transportation (DOT)
- World Health Organization (WHO)
- Public Health Agencies
- American Biological Safety Association (ABSA-international)
- AAALAC (Assn. for Assessment and Accreditation of Laboratory Animal Care)
- BMBL (Biosafety in Microbiological and Biomedical laboratories)
- And many more...
Risk Assessment and Biological Safety Levels (BSL)

High Risk

- Dangerous and exotic agents that pose a high risk of life-threatening disease
- Aerosol-transmitted
- No vaccines or treatments available
- **Examples:** Ebola, Smallpox, Marburg virus

BSL-4

- Indigenous or exotic agents that may cause serious or potentially lethal disease
- Inhalation route of exposure (aerosol-transmitted)
- **Examples:** *Yersinia pestis* (plague), tuberculosis, SARS coronavirus, *Bacillus anthracis*

BSL-3

- Agents that pose moderate hazards to personnel and the environment
- Majority of bio laboratories are BSL-2
- **Examples:** Human Blood, *Salmonella*, *Staphylococcus aureus*, Rabies virus

BSL-2

Low Risk

- Well-characterized agents not known to cause disease in humans
- Minimal potential hazard to laboratory personnel and the environment
- **Examples:** non-pathogenic *E. coli*, *Bacillus subtilis*

BSL-1
BSL-2 Laboratory

- Aerosol containment
- Negatively pressurized rooms
- Non-porous surfaces
- Handwashing sinks
- Emergency washing facility
- Biohazard door sign
- Training
- Sharps safety
- Decontamination of waste
- Occupational health medical
- Contained transport of materials
- Lab coat, gloves, eye protection
BSL-3 Laboratory

- BSL2+
- Dedicated HEPA exhaust
- Directional airflow with monitoring
- Wall/floor openings sealed
- Procedures contained in biological safety cabinet
- Minimal sharps use
- Decontaminate before leaving facility
- Medical management program
- Laboratory separated from general traffic and accessed through an anteroom
- Autoclave within the facility
- Hands-free sink
Select Agent Laboratory

Biological agents or toxins that have been declared by the USG to have “potential to pose a severe threat to public health and safety”

- BSL-3+ Biosecurity requirements
- Designated Responsible Officials
- Department of Justice background checks
- Initial and annual suitability assessments (trustworthy reliable)
- Three barriers to access agents
- Extensive medical management
- Information security
- Inventory control of agents, alarms
- Drills
- Inactivation
- Agent specific requirements (e.g., showering out)
- Federal oversight and inspection
Biological Hazard Laboratories

- https://www.youtube.com/watch?v=-1di7g4Hm1s
How Do You Know Your Research Involves Biohazards?

- Grant and contract application system
  - Ask targeted questions
- Outreach and communication
  - Through committees, emails lists
  - Survey and lab monitoring programs
  - National Biosafety Month
- Institutional review and approval
  - Including other institutional committees
Biological Safety Integrated in Project Lifecycle
Elements of Biological Safety Programs

- Institutional support and engagement
- Roles and responsibilities
- Risk assessment
- Procedures for biohazard control (engineering controls, safe work practices, protective equipment)
- Decontamination and waste management
- Worker health medical management
- Packaging, shipping, transport
- Spill and emergency procedures, reporting, and response
- Written policies and procedures
- Training and outreach
- Laboratory inspections
- Compliance monitoring and program review
1. Investigator submits application
2. EH&S/IBC risk assessment
3. Laboratory site-visit
4. Document review
5. Training and procedure verification
6. Occupational health review
7. Coordination with other regulatory departments/committees (e.g., animal welfare)
8. Institutional Biosafety Committee (IBC) review and vote
10. Re-review for changes, 3-year renewal
Medical Management

- Medical exams and clearance
- Vaccines, serum testing (as needed)
- Symptom awareness, monitoring, and reporting
- Coordination with medical centers and public health
- Medical treatment plans for each agent on shared website
- What if someone cannot be medically cleared?
<table>
<thead>
<tr>
<th><strong>Biosafety Plan</strong></th>
<th><strong>Burkholderia Pseudomallei (bacteria)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Disease Cause</strong></td>
<td>Melioidosis (also called Whitemore’s disease)</td>
</tr>
<tr>
<td><strong>Route of Infection</strong></td>
<td>Inhalation of aerosols, ingestion of contaminated material, direct contact with non-intact skin. Outside of the lab, this bacteria is found in soil and water tropical climates such as Southeast Asia and northern Australia</td>
</tr>
<tr>
<td><strong>Infectious Dose</strong></td>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Incubation Period</strong></td>
<td>Median is 9 days (range 1 - 21 days). Reactivation of previously asymptomatic disease can occur after months or years</td>
</tr>
</tbody>
</table>
| **Symptoms of Exposure** | - Localized: nodules, fever, general body aches
- Pulmonary: mild to severe pneumonia, high fever
- Acute bloodstream infections: may occur with underlying illness such as HIV, renal failure or diabetes
- Disseminated infection: abscesses are common in liver, spleen, lung, and prostate |
**Medical Management**

---

**EXPOSURE RESPONSE**  
for biological, chemical, or radiological exposures

**CALL 911 FOR ANY LIFE THREATENING EMERGENCY**

1. **PERFORM FIRST AID**

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needlestick, sharps injury, puncture wound, or animal bite/scratch</td>
<td>Wash exposed area thoroughly for 15 minutes with warm water and Sudsy soap.</td>
</tr>
<tr>
<td>Eye exposure</td>
<td>Use eye wash to flush eyes for 15 minutes while holding eyes open.</td>
</tr>
<tr>
<td>Skin exposure</td>
<td>Use nearest safety shower for 15 minutes. Stay under the shower and remove clothing. Use a clean lab coat or spare clothing to cover.</td>
</tr>
<tr>
<td>Inhalation</td>
<td>Move out of contaminated area and get help.</td>
</tr>
</tbody>
</table>

2. **GET MEDICAL HELP**

   **For chemical or radiological exposure or emergency:**
   - Call 911 and follow the instructions given.
   - Provide information about exposure including chemical name, dose, route, time since exposure, and Safety Data Sheet (SDS).

   **For biological and all other exposures:**
   - During business hours (Monday thru Friday 8 a.m. to 5 p.m.):
     - Call the Employee Health Center at **206.685.1026**.
     - Harborview sites call **206.744.3081**.
   - If Employee Health Center is closed:
     - Call 911 and follow the instructions given.

   Notify your supervisor. Secure the area before leaving.

3. **REPORT THE INCIDENT**

   **In the event of hospitalization, fatality, or radiological or recombinant DNA exposure, notify EHS immediately after first aid and getting help:**
   - During business hours (Monday thru Friday 8 a.m. to 5 p.m.):
     - Call the EH&S main phone line at **206.543.7262**.
   - Outside of business hours:
     - Call **206.685.UWPD (8973)** to reach EH&S staff on call.

   **All incidents and near misses:**
   - Submit a report via the UW Online Accident Report (OARS) within 24 hours at [https://oars.earhs.washington.edu](https://oars.earhs.washington.edu)

---

**ENGLISH HEALTH & SAFETY**  
**UNIVERSITY OF WASHINGTON**

---

**SRA International**  
**2017 Annual Meeting**  
**Vancouver, Canada | October 14-16**

---

**www.ehs.washington.edu**
Institutional Biosafety Committees

- Local review and oversight of research utilizing recombinant or synthetic nucleic acid molecules
- Ensure research conducted at or sponsored by the institution is in compliance with the *NIH Guidelines*
- Responsibilities need not be restricted to recombinant or synthetic nucleic acid molecule research
Institutional Biosafety Committees

- In a nutshell, what must IBCs review?
  - Review research for conformity with the *NIH Guidelines*
  - Potential risk to environment, personal, and public health
    - Containment levels per *NIH Guidelines*
    - Adequacy of facilities, SOPs, PI, and lab personnel training
    - Institutional and investigator compliance;
    - Set containment levels for experiments
      Review periodically institutional compliance with *NIH Guidelines*
  - Adopt emergency plans covering spills, contamination, other accidents
Institutional Biosafety Committees

- **Membership**
  - At least five individuals
  - Appropriate recombinant and synthetic nucleic acid expertise collectively
  - Plant and animal experts, biosafety officer as appropriate
  - At least two members not affiliated with the Institution

- **Expertise**
  - Expertise in assessment of risk to environment and public health
  - Knowledge of institutional commitments and policies, applicable law, professional standards, community attitudes, and environment
  - Biological safety and physical containment
  - Laboratory technical staff (recommended)
Institutional Biosafety Committees (IBC)

- Institutional Biosafety Committee (IBC)
- Institutional Animal Care and Use Committee (IACUC)
- Institutional Review Board (IRB)
Public trust is critical to continued scientific progress

- IBCs are an increasing component for public trust in recombinant DNA research

Current issues:
- Public Trust: Lapses in oversight in federal labs
- Changes in leadership at NIH and CDC
- Public concern and negative media attention

Gain of function research, emerging technologies (CRISPR), dual use research of concern, inventory, biosecurity, biosafety stewardship
Select Agent Program (USA)

- Overseen by the CDC and APHIS Select Agent Program
- 66 regulated select agents and toxins- “potential to pose a severe threat to public health and safety”
- 291 Institutions registered
- 1995- US microbiologist convicted of mail and wire fraud after misrepresenting the reasons for purchasing three vials of Yersinia pestis (the bacterium that causes plague)
- Since 2003 (the beginning of the program in its current regulatory form):
  - No confirmed thefts of a select agent or toxin from a registered entity
  - No deaths among laboratory workers
  - No reported cases of illness or death in the general public due to work with these agents in regulated laboratories
Select Agent Program: Suitability Assessment Programs

- Tier 1 Agents: Suitability assessment clearance required prior to work in select agent areas (initial and annual, ongoing)
  - Focusing on behaviors of concern
- Initial: Background check, reference check, training
- Suitability approval granted by Human Resources and Responsible Official
- Suitability Assessment team
- What if an individual is not cleared?
Select Agent Program: Enhanced Medical Management

ENVIRONMENTAL HEALTH & SAFETY
UNIVERSITY of WASHINGTON

UW Select Agent & BSL-3 Program

Symptom Development Procedures

Symptom development is temperature > 100.4°F (38°C), and/or symptoms consistent with infection from research agents. If you experience symptoms:

1) Seek evaluation by medical provider
   • Business Hours (M-F/ 8 a.m.- 5 p.m.): Employee Health Center – 206 [redacted]
   • Outside Business Hours: UW Medical Center Paging Operator – 206 [redacted]
   ✓ Identify yourself as UW Select Agent/BSL-3 worker. Request to speak to the Campus Health Physician. Be prepared to provide your name and phone #.
   ✓ If no response from physician within 30 minutes, go to the Harborview Medical Center Emergency Department (ED). If absolutely not possible, go to the nearest ED. Present this card at ED.

2) Notify EH&S Responsible Official (RO)/ARO
   • Business Hours (M-F/ 8 a.m.- 5 p.m.): 206 [redacted]
   • Outside Business Hours: Call UWPD dispatch 206 [redacted] ask for EH&S staff on call

***ED/CLINIC STAFF: IMMEDIATELY ISOLATE AND PROVIDE PATIENT WITH A MASK WHILE AWAITING TREATMENT. CONTACT UW MEDICAL CENTER PAGING OPERATOR AS SOON AS POSSIBLE***

Rev: April 2016
Dual Use Research of Concern (DURC)

- US Government Policy Effective 2015
- Research conducted for legitimate purposes that generates knowledge, information, technologies, and/or products that can be utilized both for benevolent and harmful purposes:
  - Applies to subset of Select Agents and toxins
  - Establish and implement policies and practices for identification and oversight of DURC
  - Provide education and training on DURC
  - Ensure appropriate research review for DURC potential
    - Assess the potential risks and benefits associated with DURC
    - Develop, and monitor compliance with risk mitigation plans
  - Report to US government funding agencies as required
Select Agent Program Support

Research Schools
* Principal Investigator
  * Lab Staff
  * Research Programs
  * Facility Management

Environmental Health & Safety/Biosafety Office
* Regulations
* Safety & Compliance
* Oversight

Risk Services
Human Resources
Labor Relations

Facilities
* General Maintenance
  * HVAC
  * Facility Security

Occupational Health & Medicine
* Pre-screening
* Medical Assessment
* Post exposure

Biosecurity and First Responders
* Seattle Police
  * Firefighters
  * FBI

Public Health
* UW Medicine
  * Seattle and King County
  * Washington State

Select Agent Program Support
External Support/Stakeholders

- Local fire department
- Police department
- Public health agencies
- Medical centers
- General Public
- Animals and agriculture
- Environment
2015: Tulane University

- Two primates diagnosed with Melioidosis (Whitmore's Disease), a bacterial illness of animals and humans more commonly diagnosed in tropical areas and not found in North America.
- Bacteria that sickened the non-human primates was identical to the one being used in the Tulane research center.
- Lapses in the appropriate use of personal protective equipment; specifically, the correct use of outer wear to prevent contamination of clothing beneath them, which could have led to the bacteria clinging to inner garments and getting carried out of the select agent lab where research was being conducted with the bacteria on mice.
- Research suspended. University revamped biosafety program and procedures.

[https://www.cdc.gov/media/releases/2015/s0313-burkholderia-pseudomallei.html](https://www.cdc.gov/media/releases/2015/s0313-burkholderia-pseudomallei.html)
When Things Go Wrong

- 2014: Safety lapses in federal labs at the CDC
  - Anthrax vials not inactivated properly
  - 75 people potentially exposed
  - No one infected
  - Increased public scrutiny
  - Enhanced regulatory oversight for all high containment labs
2008: Texas A&M University in College Station has agreed to pay a $1-million fine for lapses in biosafety procedures. The failures resulted in lab workers becoming exposed to high risk pathogens.

- CDC shut down all biodefence-related research at the university after the violations
- A&M stepped up safety procedures and training for lab workers
When Things Go Wrong

- 2001 Foot and Mouth Disease Outbreak, United Kingdom
  - A case was confirmed in cattle on a Surrey farm.
  - It was traced to a faulty drainage pipe at a nearby research facility where the virus was being used in the manufacture of animal vaccines.
  - 2,000 cases confirmed
  - 6 million sheep, cattle, pigs slaughtered
  - Billions of dollars lost
When Things Go Wrong
Laboratory Acquired Illnesses

- Majority of LAIs not connected to a known lab exposure
- Many LAIs go unreported
- Exposure Pathways: break through the skin (needlestick), ingestion, inhalation, mucous membrane contact
- Emphasize safety procedures to prevent cross contamination

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. of cases of infection</th>
<th>Relative risk of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shigella species</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>Brucella species</td>
<td>7</td>
<td>8012.5</td>
</tr>
<tr>
<td>Salmonella species</td>
<td>6</td>
<td>0.08</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>6</td>
<td>NA</td>
</tr>
<tr>
<td>MRSA</td>
<td>5</td>
<td>NA</td>
</tr>
<tr>
<td>Neisseria meningitidis</td>
<td>4</td>
<td>40.8</td>
</tr>
<tr>
<td>Escherichia coli O157:H7</td>
<td>2</td>
<td>8.6</td>
</tr>
<tr>
<td>Coccioides species</td>
<td>2</td>
<td>1.1</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>1</td>
<td>0.03</td>
</tr>
</tbody>
</table>


From: Laboratory-Acquired Infections
Clin Infect Dis | © 2009 by the Infectious Diseases Society of America
When Things Go Wrong

- Compromise safety, security, public trust
- Compromise institutional reputation
- Loss in funding and other financial losses
Takeaways

- Our role is to help facilitate science safely and in compliance with the regulations
- Know the regulations that apply to your biological research
- Must have institutional support, engagement, and funding to support effective biosafety programs
- Ensure you have biosafety technical expertise to implement programs
- Continually monitor program effectiveness
- Partner with administrative/research oversight departments, research departments, institutional committees, biosafety/EH&S office – It takes a village
Questions?

Katia Harb
Asst. Director for Research & Occupational Safety, Alternate Responsible Official, Select Agent Program
Environmental Health and Safety Department
University of Washington, USA
Kharb@uw.edu