# Risk Assessment

*Risk Assessment for Laboratory Biosecurity and Biosafety*
*Nashville, TN*
*6 October 2007*

www.biosecurity.sandia.gov

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Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000.

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# Risk

- **Is a function of the likelihood an adverse event will occur**
- **Laboratory work with pathogens will always involve some level of safety and security risk**
  - Distinguish between "acceptable" and "unacceptable" risks
  - Cannot protect against every conceivable adverse event
- **Resources for risk mitigation are not infinite**
  - Existing resources should be used efficiently

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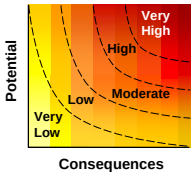
# Biosecurity and Biosafety Based on Risk Management

- **Most biological materials occur in nature and can be isolated from nature**
- **Critical not to compromise legitimate bioscience operations**
  - Systems should be designed to address unique situations
- **Management must distinguish between "acceptable" and "unacceptable" risks**
  - Ensure that protection and the cost is proportional to the risk




- Protect against unacceptable risk scenarios
- Develop incident response plans for acceptable risk scenarios

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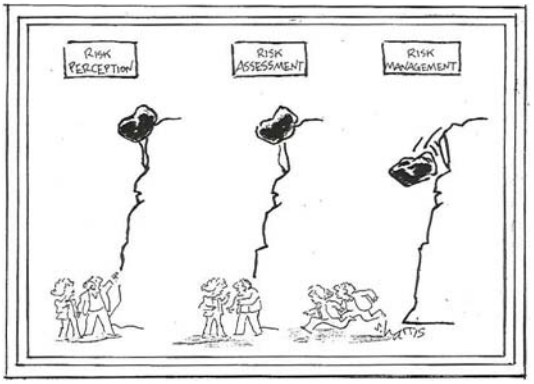



## Risk Perception in Laboratories

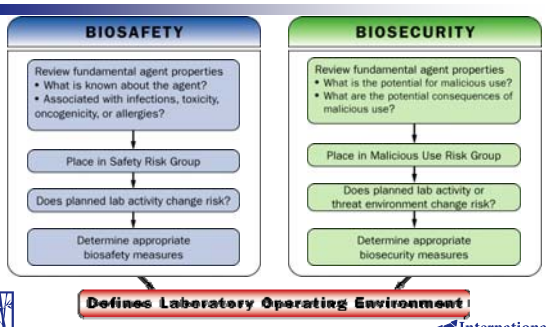
**Biosafety risks: laboratory-acquired infections**

- **History of lab-acquired infections**
  - Often attributed to carelessness or poor technique
  - Relatively few cases can be attributed to direct accident (mouth pipetting and sharps injuries)
  - Exposure to airborne pathogens generally presumed to be most plausible cause
  - Brucellosis is most common
- **Sporadic infections in community as a result**
  - 1973 and 1978—England had 3 secondary cases of smallpox
  - 1950—2 cases of Q fever in household of scientist
  - 1990—1 documented case of Monkey B virus from animal handler to wife
  - SARS—including 3 generations (9 cases)

**Biosecurity risks: laboratories as sources of material for malicious use**

- **Bioterrorism has emerged as a threat to international security**
  - 1984 Rajneeshee religious cult attacks
  - 1990s Aum Shinrikyo attempts
  - 2001 Anthrax attacks in the US
- **Examples of illicit acquisition**
  - 1990s—Aum Shinrikyo ordered *Clostridium botulinum* from a pharmaceutical company
  - 1995—Larry Wayne Harris, a white-supremacist, ordered 3 vials of *Yersinia pestis* from the ATCC
  - 1995—Laboratory technician Diane Thompson removed *Shigella dysenteriae* Type 2 from hospital's collection and infected co-workers

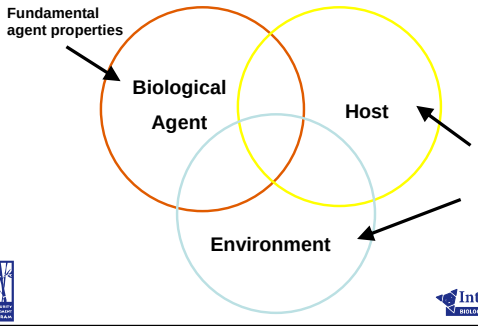
## Risk Assessment: Integrated Biosafety and Biosecurity



## Risk Assessment

- **Enables the professional (e.g. biosafety officer, responsible official) to:**
  - Become familiar with the proposed work activities (procedures, equipment, personnel)
  - Be a knowledgeable and credible partner with the investigator to develop a safe and secure environment for the work
- **Review all activities associated with infectious materials**
  - Proposed work activities
  - Personnel
  - Storage
  - Transfer and transport
  - Destruction

## Biosafety Risk Assessment




## Biosafety Risk Assessment: Safety Risk Group Evaluation

- **What is known about the agent?**
  - Pathogenicity – ability to cause disease
  - Virulence – degree of pathogenicity
  - Host range – restricted or broad, human, animals, plants
  - Communicability – are there reports of epidemics? Of laboratory infections?
  - Transmission – means (e.g. direct contact, vector borne) and routes (e.g. ingestion, inhalation)
  - Environmental stability – e.g. resistance to disinfection
- **Additional agent factors:**
  - Toxicity
  - Is the agent associated with cancer (e.g. Hepatitis B virus associated with liver cancer)?
  - Does the agent or by-products induce allergic reactions (e.g. Penicillin)?

## Biosafety Risk Assessment: Safety Risk Groups

- **Risk Group 1**
  - No or low individual and community risk
  - Unlikely to cause human or animal disease
- **Risk Group 2**
  - Moderate individual risk, low community risk
  - Can cause disease but unlikely to be a serious hazard. Lab exposures may cause serious infection, but effective treatment and preventative measures are available and risk of spread of infection is limited
- **Risk Group 3**
  - High individual risk, low community risk
  - Usually causes serious human or animal disease but does not ordinarily spread. Effective treatment and preventative measures are available.
- **Risk Group 4**
  - High individual and community risk
  - Usually causes serious human or animal disease and can be readily transmitted. Effective treatment and preventative measures are not usually available

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## Safety Risk Group Examples

- **Risk Group 1**
  - *Bacillus subtilis*
    - Ubiquitous bacterium found in water, soil, air
    - Not considered pathogenic or toxigenic to humans, animals, or plants
  - *Escherichia coli* K-12
    - *E. coli* is normal inhabitant of colon of almost all mammals
    - K-12 is debilitated strain – does not normally colonize human intestine
    - History of safe commercial use
- **Risk Group 2**
  - Measles virus
    - Pathogenicity: acute disease, fatality <0.5% - 25%
    - Host range: Humans
    - Transmission: primarily droplet spread
    - Vaccine available
  - Hepatitis B virus
    - Pathogenicity: asymptomatic and symptomatic infections, long-term fatality = 2-3%, 95% of adult infections self-limiting
    - Host range: Humans (chimpanzees are susceptible
    - Vaccine available

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## Safety Risk Group Examples

- **Risk Group 3**
  - *Mycobacterium tuberculosis*
    - Proven hazard to laboratory workers (3x higher rate of infection)
    - Low aerosol infectious dose (ID50 < 10 bacilli)
    - Host range: Primarily humans, cattle, primates, other animals (rodents)
  - St. Louis encephalitis virus
    - Pathogenicity: Fatality rate of 2-22%, 30-50% of severe cases have prolonged convalescence
    - Host range: Humans, wild birds, other mammals
    - Supportive care is only treatment
- **Risk Group 4**
  - Ebola virus
    - Pathogenicity: Sudden onset, 50 – 90 % fatality
    - Host range: Humans, monkeys, chimpanzees, domestic guinea pigs
    - BSL4 laboratory recommended even for clinical work (Public Health Agency of Canada)

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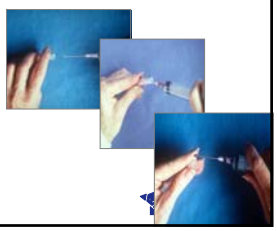
## Biosafety Risk Assessment: Elements That May Modify Risk

- **Does the environment or activity change the risk?**
  - Lab vs. field studies
  - Animal studies?
  - Procedures
    - Does planned experiment have the potential to generate aerosols?
  - Equipment
    - Needles
    - Centrifuges
    - Homogenizers
    - Pipettes



## Biosafety Risk Assessment: Elements That May Modify Risk

- **Are their host factors that change the risk?**
  - Deficiencies in host defenses
    - Pre-existing medical conditions – for example:
      - Asplenia, eczema
  - Reproductive hazards
    - Pregnancy, teratogens, mutagens – for example:
      - Rubella, *Toxoplasma*, *Chlamydia*
  - Allergies
    - Foreign proteins, vaccine constituents, antimicrobial therapies – for example:
      - Animal dander, egg proteins, latex
  - Immunization status
    - Immunization against workplace pathogens but …
      - Not always the answer (vaccine efficacy, safety issues)
  - Behavioral elements
    - Education, training, experience, motivation, attentiveness

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## Regional Perspective in the Biosafety Risk Assessment

- **Additional national or local considerations may influence the risk assessment**
  - History and epidemiology of the disease in country
  - Presence of reservoir(s) — ecology
  - Proximity to other potential disease foci in nearby countries
- **Examine training of personnel in country in microbiology, public health, veterinary sciences**
- **Determine available laboratory and scientific infrastructure**
- **Determine the economic realities**

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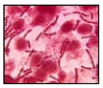
## Biosecurity Risk Assessment



1. **Evaluate assets (agent assessment)**
2. **Evaluate lab activity**
3. **Evaluate threat environment**

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## Biosecurity Risk Assessment: Malicious Use Risk Group Evaluation

- **Assess value of the agents from an adversary's perspective**
  - **Consequences**
    - Population
      - Transmissibility
      - Mortality
      - Morbidity
    - Economic
    - Psychological
  - **Task Complexity**
    - Acquisition
      - Natural
      - Laboratory
      - Synthetic biology
    - Production
      - R&D
      - Covert production
      - Ease of storage
    - Dissemination
      - Route of infection (e.g. aerosol, ingestion)
      - Environmental hardiness

Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template

Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox

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## Biosecurity Risk Assessment: Malicious Use Risk Groups

- **Nonpathogenic**
  - Malicious use would have insignificant or no consequences
- **Low**
  - Difficult to deploy, and/or
  - Malicious use would have few consequences
- **Moderate**
  - Relatively difficult to deploy, and
  - Malicious use would have localized consequences with low to moderate casualties and/or economic damage, and potentially cause pervasive anxiety
- **High**
  - Not particularly difficult to deploy, and
  - Malicious use could have national or international consequences, causing moderate to high casualties and/or economic damage, and the potential to cause mass panic and significant social disruption
- **Extreme**
  - Would normally be classified as highly attractive, except that they are not found in nature (eradicated)
  - Could include genetically engineered agents, if they would otherwise be classified as highly attractive

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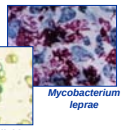
## Malicious Use Risk Group Examples

- **Nonpathogenic**
  - *Bacillus cereus, Lactobacillus acidophilus, Saccharomyces cerevisiae*
- **Low Malicious Use Risk (LMUR)**
  - *Mycobacterium leprae*
    - Consequences: Not highly virulent, not highly contagious, completely curable
    - Task Complexity: Production is a challenge, not environmentally hardy
- **Moderate Malicious Use Risk (MMUR)**
  - *Coccidioides immitis*
    - Consequences: Not contagious, 5-10 out of every 1000 infected develop life-threatening infection
    - Task Complexity: Requires technical skills to handle safely, easy to procure virulent strain, easy to grow



*Mycobacterium leprae*

*Coccidioides immitis*

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## Malicious Use Risk Group Examples

- **High Malicious Use Risk (HMUR)**
  - *Bacillus anthracis*
    - Consequences: High fatality rate, not contagious, early diagnosis is difficult
    - Task Complexity: History of malicious use, wide endemic area (but many less virulent strains), very stable, easy to grow and produce spores
- **Extreme Malicious Use Risk (EMUR)**
  - Variola major virus
    - Consequences: High fatality rate, contagious, few vaccinated
    - Task Complexity: History of weaponization, very stable, difficult to obtain

*Variola major*

*Bacillus anthracis*

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## Biosecurity Risk Assessment: Other Assets at Biological Facilities

- **Security Information or Systems**
  - May be targeted to facilitate gaining access to dangerous biological materials
- **Other Facility Assets**
  - May be targeted by political extremists, disgruntled employees, etc.
  - May include:
    - High containment laboratories
    - Animals

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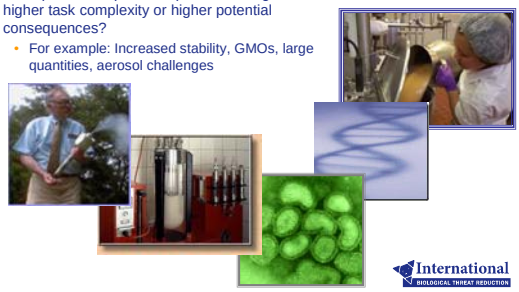
## Biosecurity Risk Assessment: Elements That May Modify Risk

- **Consider lab experiment**
  - Does planned experiment produce an agent with higher task complexity or higher potential consequences?
    - For example: Increased stability, GMOs, large quantities, aerosol challenges



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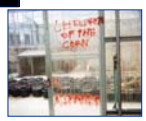
## Biosecurity Risk Assessment: Elements That May Modify Risk

- **Adversary Classes**
  - Terrorist
  - Extremist
  - Criminal

- **Insiders**
  - Authorized access to the facility, dangerous pathogens, and/or restricted information
  - Distinguish Insiders by level of authorized access
    - Site
    - Building
    - Asset
  - Facility management, site security, and local law enforcement interviews



- **Outsiders**
  - No authorized access
  - Local law enforcement, site security, and intelligence community interviews

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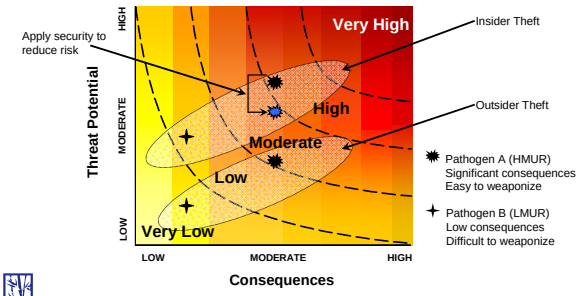
## Biosecurity Risk: Insider vs. Outsider Threat

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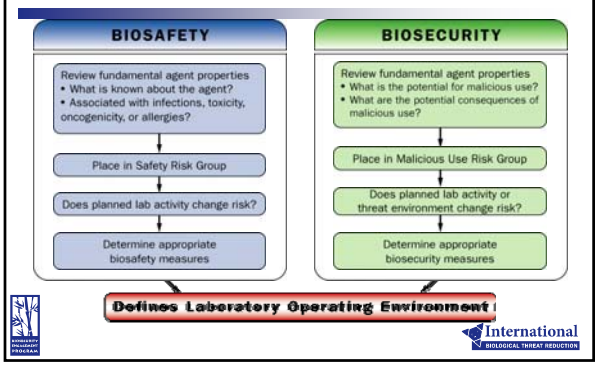
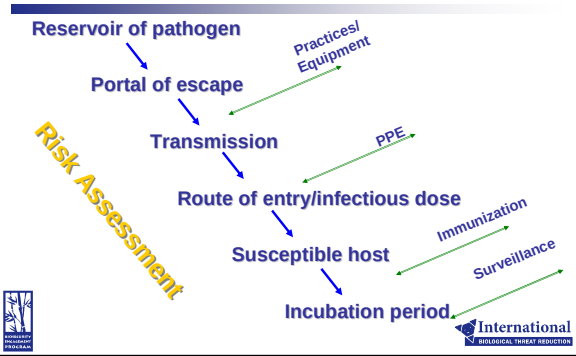
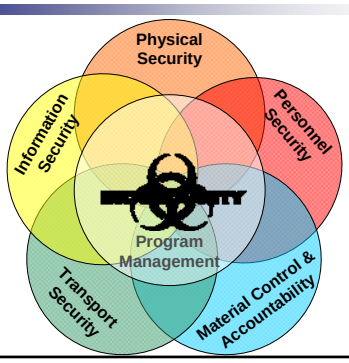
## Risk Assessment: Integrated Biosafety and Biosecurity




## Risk Management: Implementation of Biosafety




## Components of Laboratory Biosecurity



## Conclusions

- **Need to integrate biosafety and biosecurity considerations into decisions about laboratory operations**
- **Parallels exist between safety and security risk assessment processes**
- **Biological facility risk assessment provides an opportunity to concentrate resources on the highest risks**
  - Tiered system of protection based on risk assessment and risk management methodologies
- **Appropriate risk mitigation depends on the risk assessment**

**It depends!**