International
BIOLOGICAL THREAT REDUCTION

Biological Risks and Risk Management: Lab Biosafety and Biosecurity

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National Training Seminar on Biosafety and Biosecurity, Pakistan, June 2007

www.BEPstate.net

www.biosecurity.sandia.gov

Sand No. 2006-2174C, 2007-1747P 2005-7121C, 2005-7122C, 2005-7039C
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BIOSECURITY ENGAGEMENT PROGRAM

Evolution of the Biological Threat

- The biological threat has evolved in concert with
  - Increasing emergence and re-emergence of highly infectious disease
  - Advance of biotechnology globally
  - Rise of transnational, asymmetric terrorism
- This recent "globalization" of the biological threat has broadened the availability of materials, technologies, and expertise needed to maliciously disseminate infectious disease

Mt. Merapi, Yogyakarta, Indonesia

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Infectious Disease

- Global outbreaks of emerging and re-emerging infectious disease present a growing threat to international security
- Most dangerous infectious diseases are often tropical diseases that emerge in developing countries
- Infectious diseases now spread across borders as never before
- Natural outbreaks represent unpredictable sources of dangerous pathogens for terrorists

SARS virus

FMD outbreak UK

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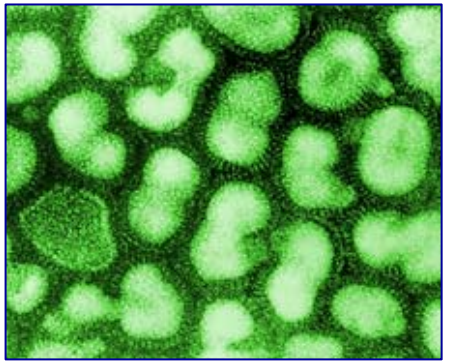
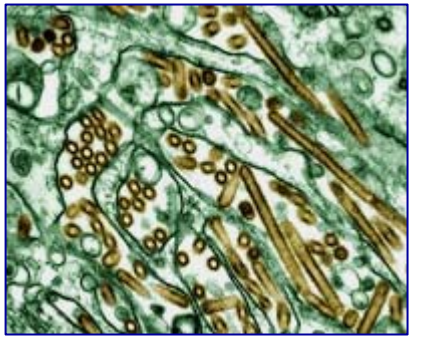
Highly Pathogenic Avian Influenza

- **H5N1 strain of highly pathogenic avian influenza first emerged in 1997 and has spread to 59 countries**
  - **Officially 306 people infected, and 185 fatalities**
  - **Has also infected other mammals**



Avian influenza virus

- **Sequencing of the 1918 pandemic influenza virus revealed that H5N1 is very similar *(Taubenberger 2005)***
  - **Unlike the strains of the 1958 and 1967 pandemics**



- **The virus is evolving**
  - **Strain in Turkey had mutations that made it more adaptable to humans than birds**
  - **Strain in Vietnam resistant to Tamiflu®**
  - **Confirmed human-to-human transmission in Indonesia**

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Biotechnology and the Life Sciences

- Rapid expansion of bioscience worldwide is perhaps the most significant influence on the biological threat
- Viable and virulent organisms are stored and used in more legitimate bioscience facilities across the globe than ever before
- Individuals with the expertise necessary to misuse biology can be found in nearly all areas of the life sciences internationally
- The tools necessary to develop and disseminate a low-grade biological weapon are ubiquitous

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Double-Edge Sword of Biotechnology

- **Genetic modification**
  - **2001 – IL-4 and mousepox (Australia)**
  - **2003 – IL-4 and mousepox (St. Louis)**
- **Chemical synthesis**
  - **2002 – polio virus (Stony Brook)**
  - **2003 – phi-X174 virus (Venter)**
  - **2005 – 1918 influenza virus (Taubenberger)**

- **Advance of biotechnology will ease**
  - **Acquisition barriers**
  - **Production barriers**
  - **Dissemination barriers**

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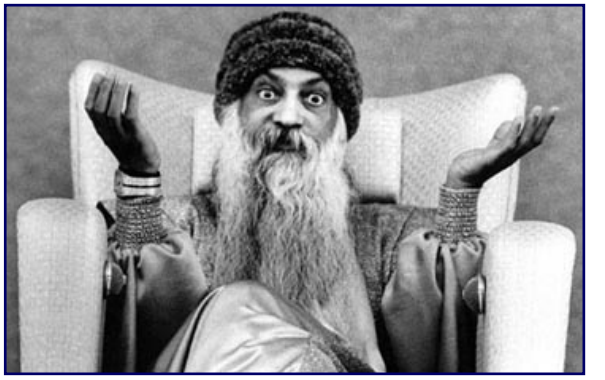
Origins of Bioterrorism

- In 1910, the Pancho Villa guerillas used shards of pottery and obsidian laced with botulinum toxin to attack federal sentries

- In 1952, the Kenyan Mau Mau separatist group used African milk brush toxin to poison steer

- In 1981, Dark Harvest, an environmental extremist group in the United Kingdom, delivered anthrax-contaminated soil to a political party conference

- In 1984, Rajneeshees cult contaminated restaurant salad bars in The Dalles, Oregon with salmonella bacteria



Bhagwan Shree Rajneesh

Gruinard Island, UK

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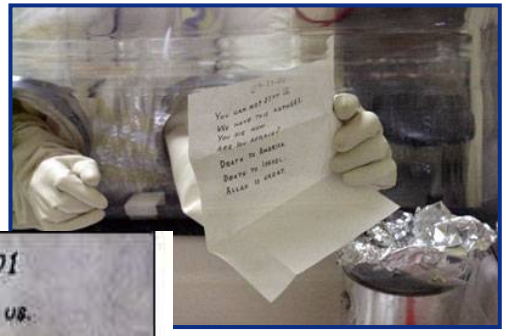
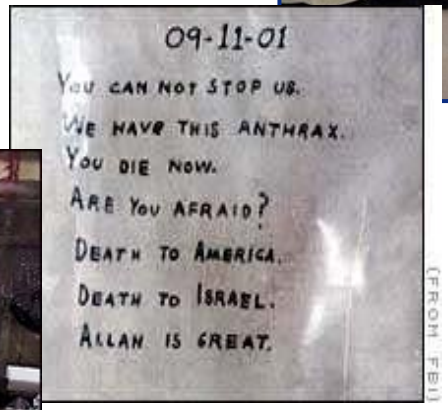
Escalation of Bioterrorism

Aerosolization of Bacillus anthracis and botulinum toxin by Aum Shinrikyo

- **Aum Shinrikyo – 1990s**
  - **Aerosolized and disseminated biological agents in Japan**
    - **Vaccine strain of *Bacillus anthracis***
    - **Inactive strain of *Clostridium botulinum***

- **US anthrax attacks – 2001**
  - **Highly refined: 4-7 letters contaminated over 60 different sites**
  - **Highly virulent: killed 5, injured 22**





Amerithrax

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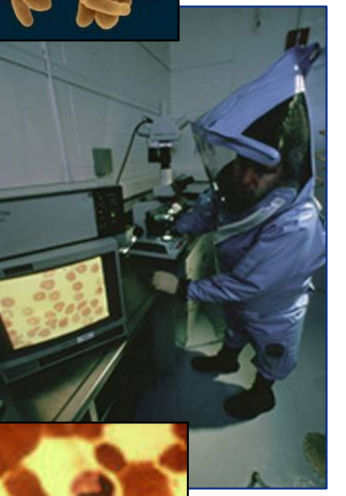
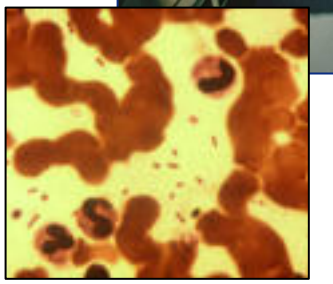
Laboratory Biosafety and Biosecurity

- **Laboratory biosafety**
  - **Objective: reduce or eliminate accidental exposure to or release of potentially hazardous agents**
- **Laboratory biosecurity**
  - **Objective: protect biological agents against theft by those who intend to cause harm**
- **Common strategy**
  - **Implement graded levels of protection based on a risk management methodology**
- **Control of certain biological materials is necessary, but *how* that is achieved must be carefully considered**
  - **Laboratory biosecurity and biosafety should be integrated systems that avoid compromising necessary infectious disease research and diagnostics**

Francisella tularensis





Yersinia pestis

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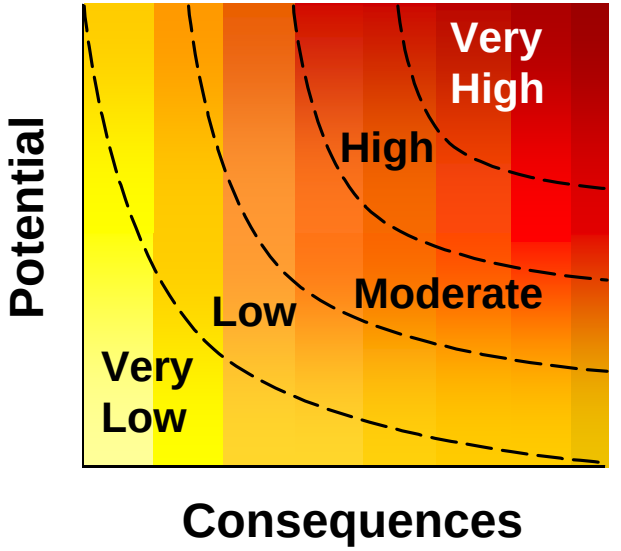
Strengthening Biological Risk Management

Vision for Integrated BioRisk Management:

- ✓ Increased focus on "awareness" to change current culture
- ✓ Clarify terminology
- ✓ Development of targeted "training strategies"
- ✓ Securing "commitment" from key stakeholders, including government officials, who must be on board
- ✓ Continue increasing "capacity" based on Regional/Country needs and establish accountability through development of Country "report cards"

Biosecurity and Biosafety Based on Risk Management

- Laboratory work with pathogens will always involve some level of safety and security risk
- 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
- Resources are not infinite; existing resources should be used efficiently
- 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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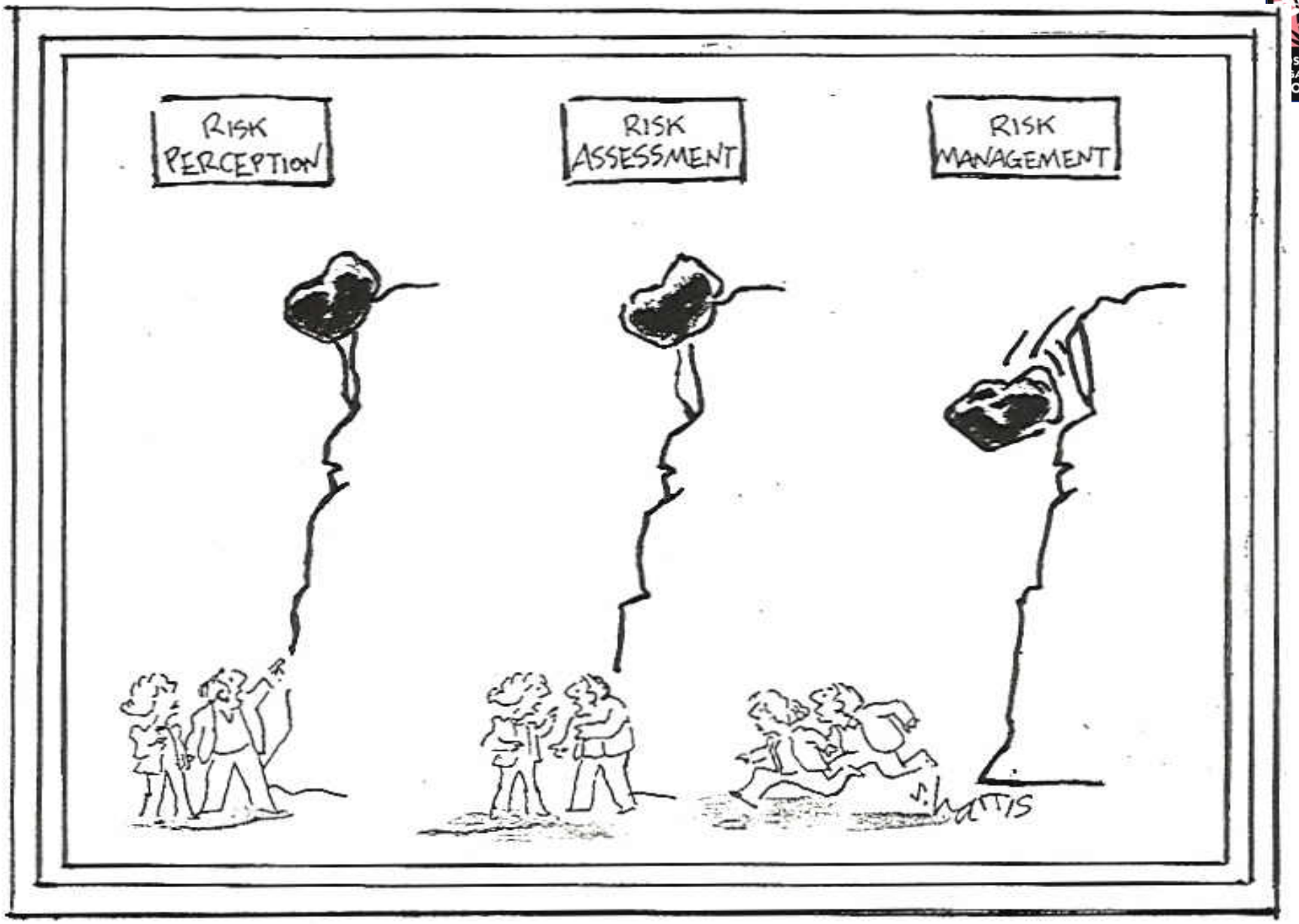

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Risk Perception in Laboratories

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

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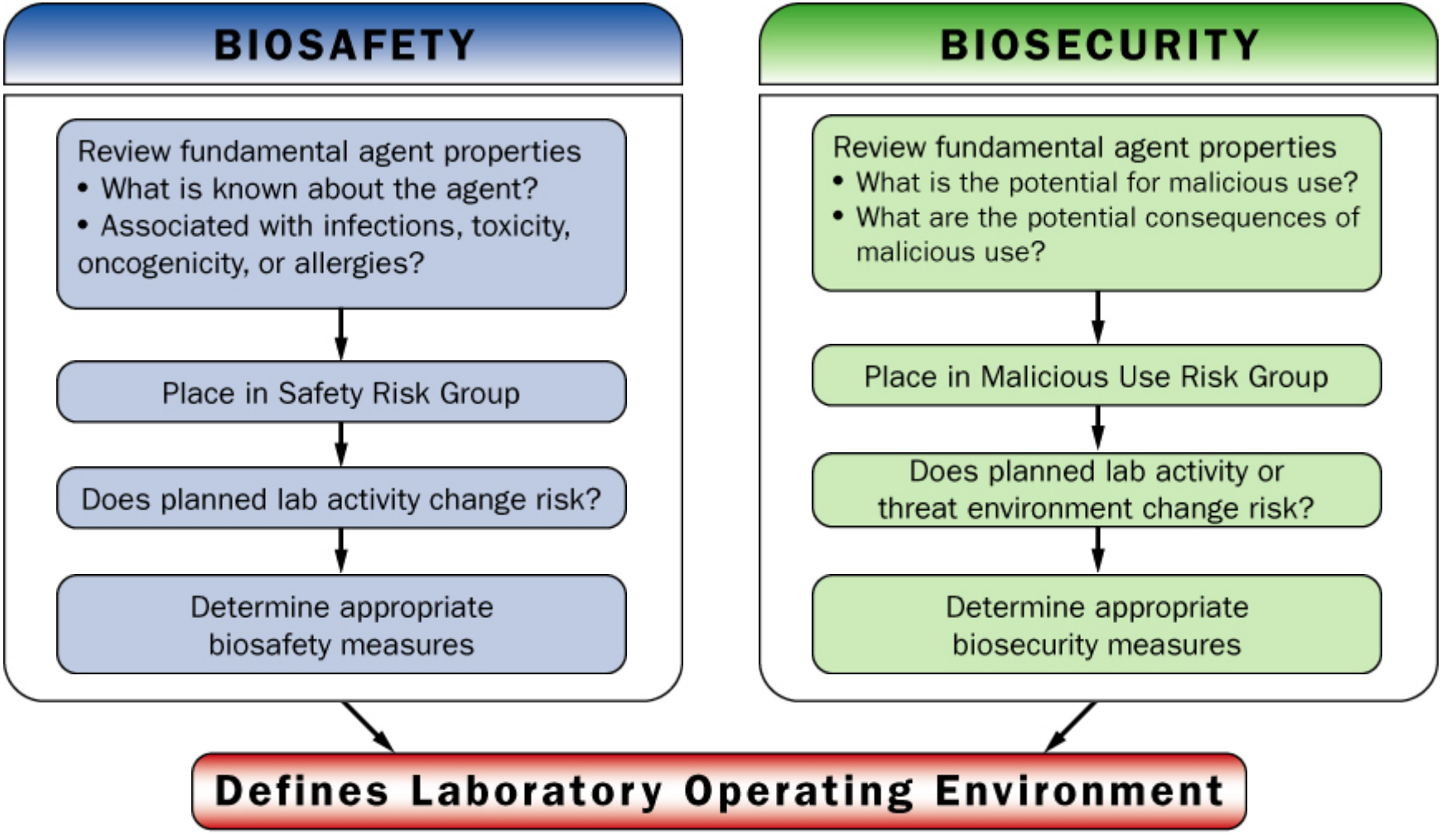
Risk Assessment: Integrated Biosafety and Biosecurity



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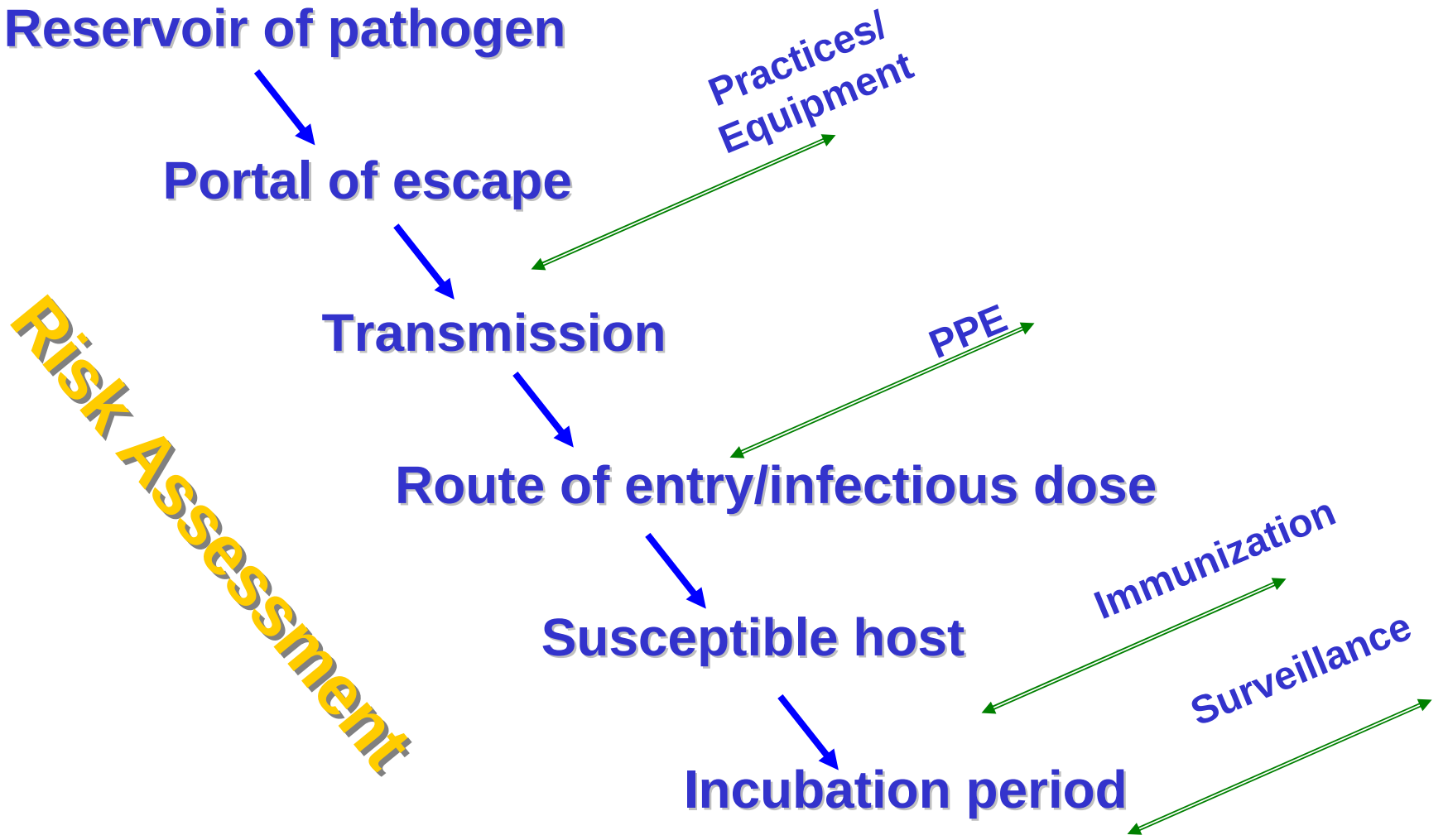
Risk Management: Implementation of Biosafety



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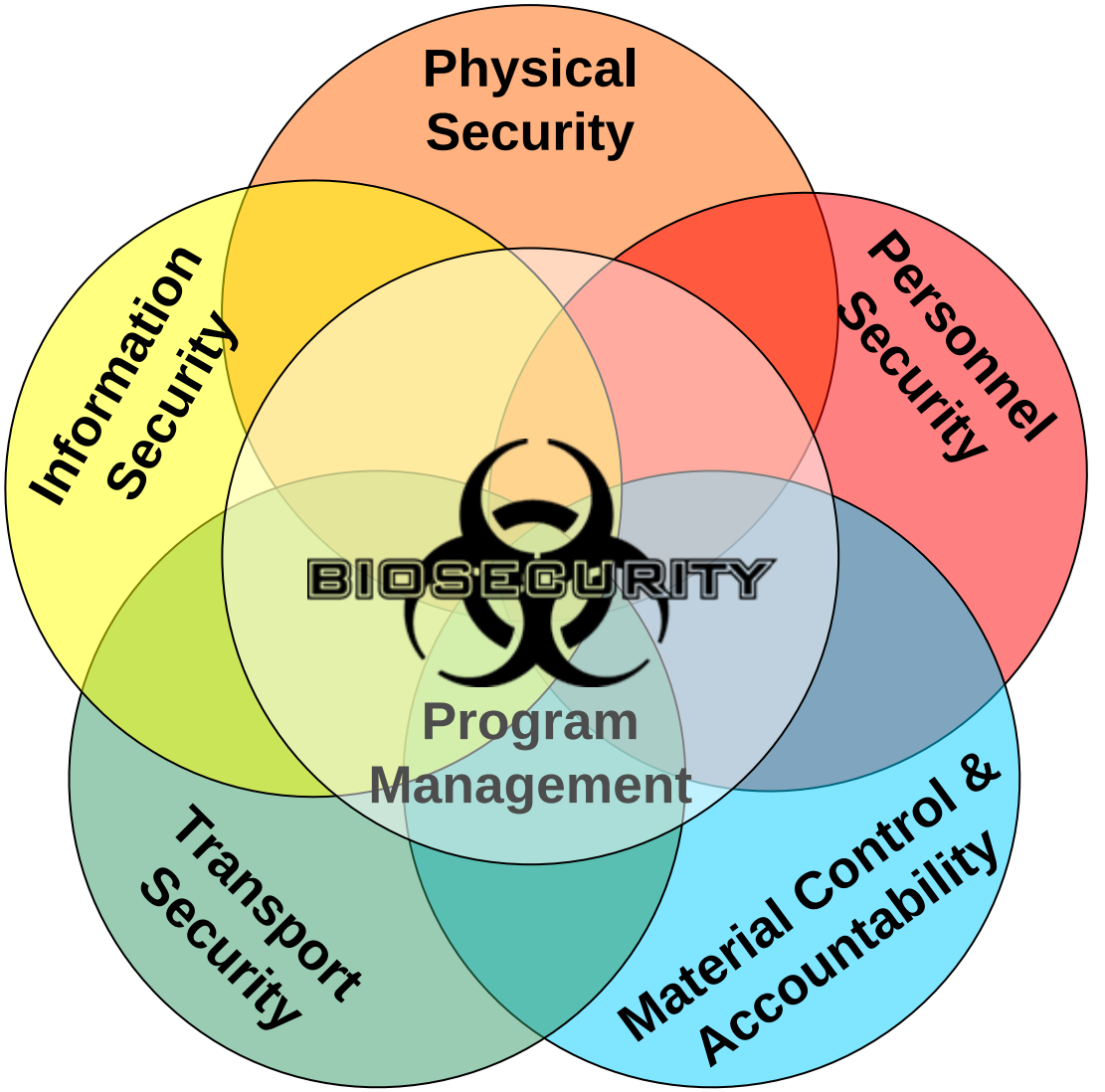
Risk Management: Implementation of Biosecurity



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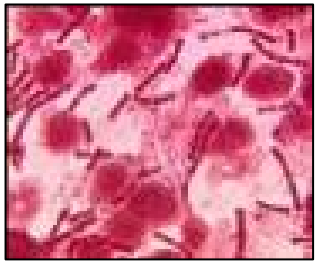
Biosecurity Risk Assessment



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**
  - **Weaponization potential**
    - **Acquisition**
      - Natural
      - Laboratory
      - Synthetic biology
    - **Production**
      - R&D
      - Covert production
      - Ease of storage
    - **Dissemination**
      - Route of infection (e.g. aerosol, ingestion)
      - Environmental hardiness

REPORTS

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

Jeronimo Cello, Aniko V. Paul, Eckard Wimmer*

9 AUGUST 2002 VOL 297 SCIENCE www.sciencemag.org

JOURNAL OF VIROLOGY, Feb. 2001, p. 1205–1210 Vol. 75, No. 3
0022-538X/01/$04.00+0 DOI: 10.1128/JVI.75.3.1205–1210.2001
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Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox

RONALD J. JACKSON,[1,2]* ALISTAIR J. RAMSAY,[2]† CARENA D. CHRISTENSEN,[2] SANDRA BEATON,[1] DIANA F. HALL,[1]‡ AND IAN A. RAMSHAW[2]

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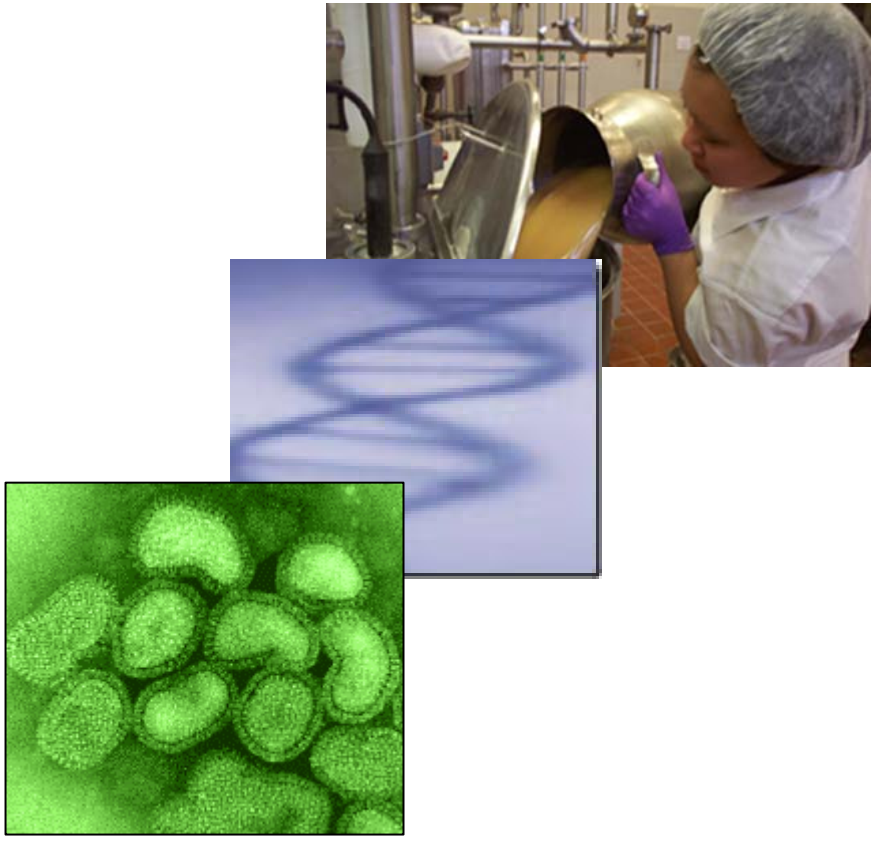
Biosecurity Risk Assessment: Elements That May Modify Risk

- **Consider lab experiments**
  - **Does planned experiment produce an agent with higher weaponization potential or higher potential consequences?**
    - **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 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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Laboratory Biosecurity System

- Biosecurity system components
  - Physical security
  - Personnel security
  - Material handling and control measures
  - Transport security
  - Information security
  - Program management practices
- Each component implemented based on results of risk assessment
- In general, biosecurity for
  - Moderate risk focuses on the insider
  - High risk focuses on both the insider and the outsider

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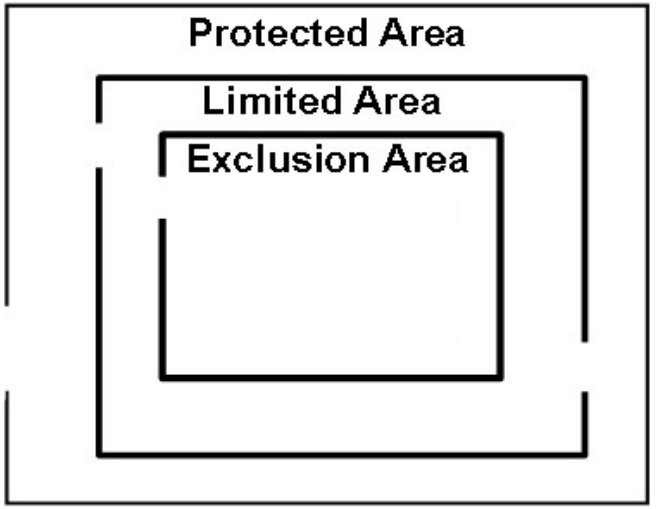
Physical Security: Concentric Layers of Security

- **Property Protection Areas**
  - **Low risk assets**
    - **Grounds**
    - **Public access offices**
    - **Warehouses**



- **Limited Areas**
  - **Moderate risk assets**
    - **Laboratories**
    - **Sensitive or administration offices**
    - **Hallways surrounding Exclusion Areas**

- **Exclusion Areas**
  - **High risk assets**
    - **High containment laboratories**
    - **Computer network hubs**

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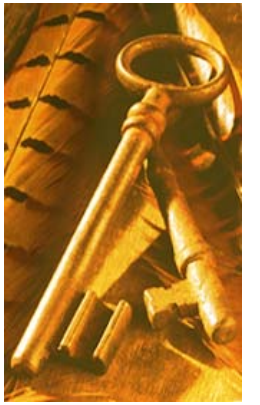
Physical Security: Access Controls

- Access control ensures that only authorized individuals are allowed into certain areas
  - Increasingly strict controls as you move toward higher risk assets
- Property Protection Areas: Fences
  - Mark the boundaries of your property
  - Announce your intention to protect the property
  - Elicit strong statement of intent from intruder
  - Terrain features can also serve this purpose
- Limited Areas
  - Unique item
  - Controlled possession
  - Electronic or physical key
- Exclusion Areas
  - Unique item
  - Unique knowledge
  - Controlled possession
  - Electronic key card <u>and</u> keypad or biometric device

  or
  - Controlled key <u>and</u> second individual to verify identity



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Physical Security: Intrusion Detection and Response

- Intrusion Detection
  - Guards
  - Electronic sensors
- Alarm Assessment
  - Validation of violation before response
  - Can be direct (guards) or remote (video)
- Response
  - On-Site Guard Force
    - Supports electronic systems
    - Patrols or guards perimeter and buildings
    - Summons and directs local law enforcement
  - Local law enforcement (police) support
    - Reinforces or substitutes for on-site guard force
    - Memorandum of understanding

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Personnel Security: Screening

- Conduct screening for authorized individuals
  - Degree of scrutiny commensurate with level of risk associated with the position
    - Need for unescorted access to restricted areas
    - Types of assets held in the restricted areas
    - Level of authority in association with high risk materials

- Mechanisms
  - Verify credentials
  - Check references
  - Criminal history
  - In-depth background investigation

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Personnel Security: Badges

- **Badges should be issued to those individuals authorized to be in restricted areas**

- **Badge return**
  - **Upon employee termination**
  - **Daily or at the conclusion of a limited term for visitors**

- **Report lost or stolen badges**

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Personnel Security: In-Processing and Out-Processing

- **In-Processing**
  - **Complete all required forms, safety training, security training and immunizations as applicable for work environment**

- **Out-Processing**
  - **Retrieve keys**
  - **Access changes or termination**
  - **Retrieve property**
  - **Deactivate computer and electronic access accounts**

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Personnel Security: Visitor Controls

- **Types**
  - **Personal Visitors**
    - **Family members**
  - **Casual Visitors**
    - **Tours, seminars**
    - **Equipment repair technicians**
  - **Working Visitors**
    - **Visiting researchers**
    - **Facility maintenance personnel**

- **Controls**
  - **All visitors should have a host at the facility**
  - **Visitors should be escorted in restricted areas**

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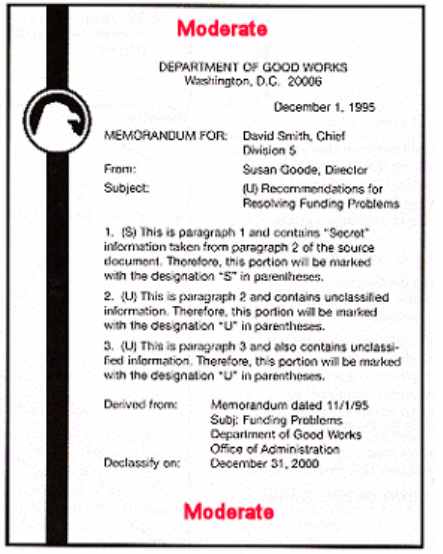
Information Security

- **Protect information that is too sensitive for public distribution**
  - **Label information as restricted**
  - **Limit distribution**
  - **A review and approval process aids in the identification of sensitivities**
  - **Restrict methods of communication**
  - **Implement network and desktop security**

- **Biosecurity-related sensitive information**
  - **Security of dangerous pathogens and toxins**
    - **Risk assessments**
    - **Security system design**
  - **Access authorizations**



Moderate

DEPARTMENT OF GOOD WORKS
Washington, D.C. 20006

December 1, 1995

MEMORANDUM FOR: David Smith, Chief
Division 5

From: Susan Goode, Director

Subject: (U) Recommendations for Resolving Funding Problems

1. (S) This is paragraph 1 and contains "Secret" information taken from paragraph 2 of the source document. Therefore, this portion will be marked with the designation "S" in parentheses.

2. (U) This is paragraph 2 and contains unclassified information. Therefore, this portion will be marked with the designation "U" in parentheses.

3. (U) This is paragraph 3 and also contains unclassified information. Therefore, this portion will be marked with the designation "U" in parentheses.

Derived from: Memorandum dated 11/1/95
Subj: Funding Problems
Department of Good Works
Office of Administration

Declassify on: December 31, 2000

Moderate

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Information Security: Communication and Network Security

- **Communication Security**
  - **Mail, email, or fax security is required**
  - **Limited discussions in open areas**
  - **Information should only be reproduced when needed and each copy must be controlled as the original**

- **Network Security**
  - **Firewalls**
  - **User authentication**
  - **Virus protection**
  - **Layered network access**
  - **Desktop security**
  - **Remote and wireless access controls**
    - **Encryption**
    - **Authentication**

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Material Control & Accountability: Objectives

- Ensure the complete and timely knowledge of:
  - What materials exist
  - Where the materials are located
  - Who is accountable for them
- Operating procedures associated with the materials
  - Location of storage and use
  - Identification
  - Inventory
- Documentation and reporting requirements
- Purpose is NOT to detect whether something is missing

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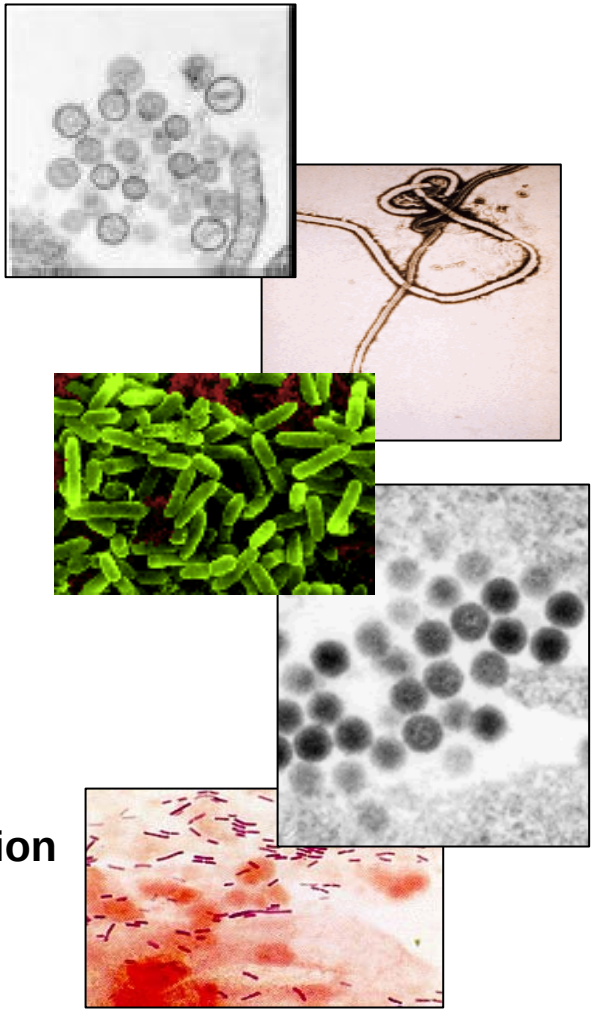
Material Control and Accountability

- Agent
  - What agents are high risk?
  - Viable? Whole organism or DNA?
- Quantity
  - Any amount can be significant
  - A threshold amount for toxins
- Form
  - Repository stocks, working samples, in host, contamination
- Detail—what level is adequate for MC&A?
  - Material as *items*
  - Each vial as a separate inventory record?
- When does MC&A start & stop?
  - Naturally occurring; clinical samples; disposition



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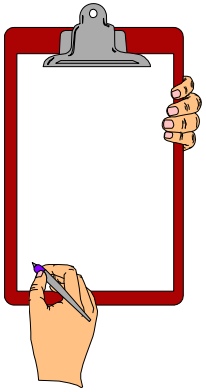
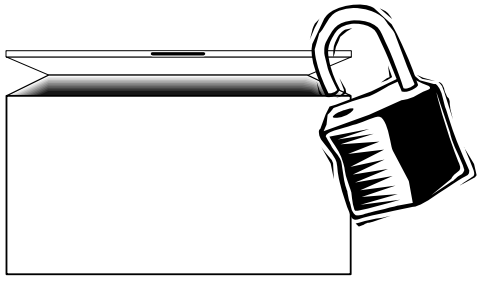
Material Control and Accountability

- **Control is either…**
  - **Engineered / Physical**
  - **Administrative**



- **Containment is part of material control**
  - **Containment Lab / Freezer / Ampoule**

- **Procedures are essential for material control**
  - **For both normal and abnormal conditions**



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Material Control and Accountability

- **All material should have an associated "accountable person"**
  - **The person best in a position to answer questions about the associated material**
  - **Not someone to blame!**
  - **Ensure that no material is "orphaned"**

- **Procedures should ensure accountability**
  - **Experimental work: laboratory procedures**
  - **Inventory: know what you have**
  - **Reporting: document routine MC&A practices**
  - **Audit/ assessment: is this working?**
    - Ensures effective *implementation* of MC&A
  - **Training: personnel understand requirements**

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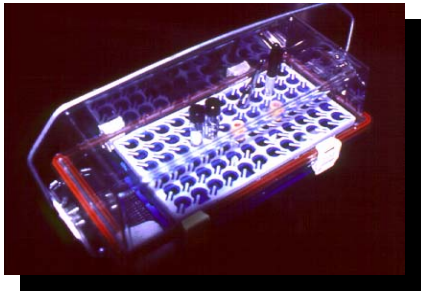
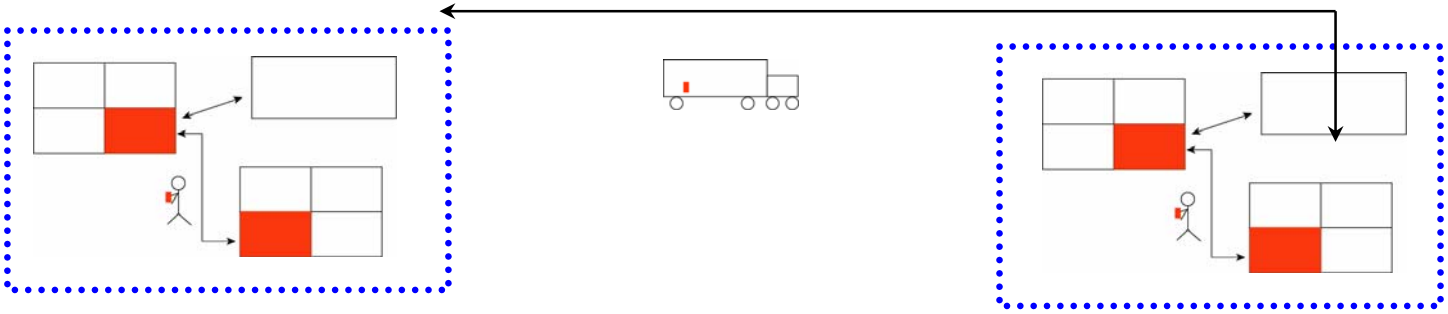
Transport Security: Internal Transport

- Movement of materials to and from restricted areas within a facility
- May involve personnel from
  - Labs
  - Shipping areas
  - Receiving areas
  - Disposal areas (e.g. autoclave and incinerator rooms)
- Move materials safely and securely
  - Standard Operating Procedures
  - Leak-proof containers
  - Pre-approval?
  - Tracking?





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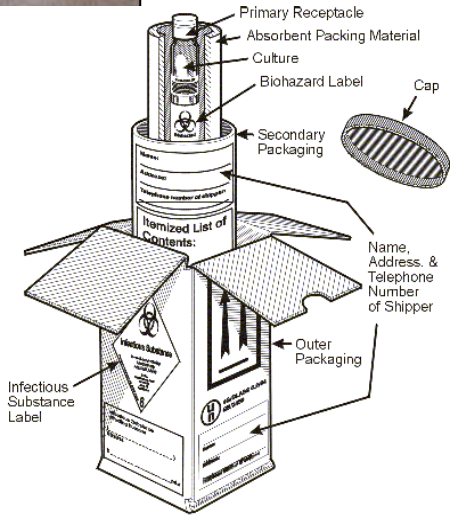
Transport Security: External Transport

- Movement of materials from one facility to another facility
- May involve commercial carriers
- Occur within a wide array of international and state regulations and standards
- Must be able to move frozen materials efficiently
- Need to be cost-effective
- International transport of infectious materials is regulated



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Transport Security: Facility Responsibilities

- **Personnel security**
  - **For people who have access to dangerous pathogens and toxins or information during transfers**
- **Establish chain of custody (tracking)**
  - **Record all individuals who have contact with the dangerous pathogens and toxins**
- **Provide physical security**
  - **For packages that need temporary storage**
- **Protect transport documentation**
- **Determine who is able to authorize, transport, and receive dangerous pathogens and toxins**

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Carrier Security

- Carriers should provide security by
  - Ensuring reliable and trustworthy people handle the package
  - Controlling access to transport facilities, docks, and vehicles
  - Tracking shipping progress
  - Providing ongoing security training for employees

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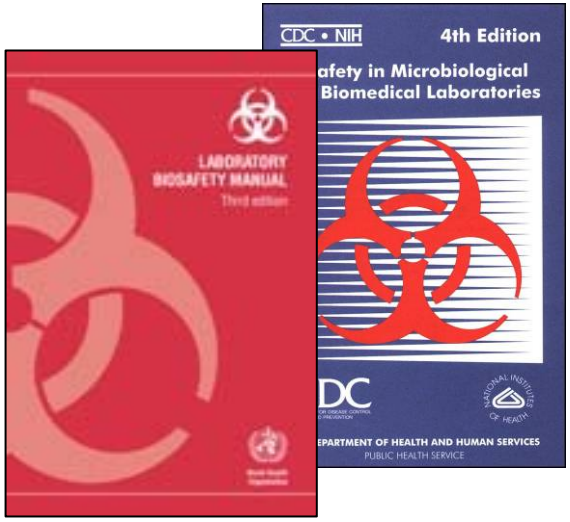
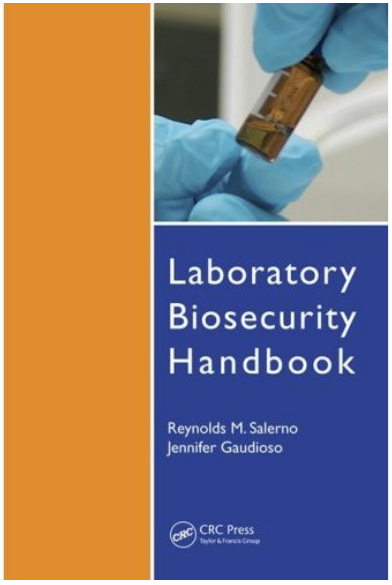
Laboratory Biosecurity Supports Laboratory Biosafety

- Laboratory biosecurity supports the laboratory biosafety agenda of preventing disease in people, animals, and plants and minimizing the risk of worker injury

- Safe and secure laboratories help
  - Ensure the containment of hazardous infectious substances in laboratories
  - Maintain citizens' confidence in the activities of the bioscience research community
  - Increase transparency to investors in the biomedical and biotechnology industries
  - Protect valuable research and commercial assets
  - Reduce the risks of crime and bioterrorism





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Similar Physical Aspects of Biosafety and Biosecurity

Biosafety

- Physical protection
  - Increasing levels of physical containment to prevent the accidental release of dangerous biological agents
    - BSL-1
    - BSL-2
    - BSL-3
    - BSL-4
  - Examples: negative air pressure, cabinets and hoods

Biosecurity

- Physical protection
  - Graded protection designed to secure dangerous biological agents from adversaries
    - Property Protection Area
    - Limited Area
    - Exclusion Area
  - Examples: access controls, intrusion detection

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Similar Procedural Aspects of Biosafety and Biosecurity

Biosafety

- Material control and accountability
  - Handling procedures to prevent accidental infection
  - Use of personal protective equipment
- Personnel reliability
  - Background checks to ensure proper credentials to handle dangerous organisms
  - Policies to prevent untrained individuals from working with materials that pose a biosafety risk

Biosecurity

- Material control and accountability
  - Basic inventory procedures to limit opportunities for illicit acquisition
  - Designation of laboratory workers responsible for specific material
- Personnel reliability
  - Background checks to ensure personnel are reliable and trustworthy
  - Procedures to remove unauthorized personnel from secure areas

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Similar Procedural Aspects of Biosafety and Biosecurity, cont.

Biosafety

- **Transport**
  - **Requirements to ensure the safe transport of materials within a lab**
  - **Federal and international regulations governing the transport of infectious substances outside the lab**

Biosecurity

- **Transport**
  - **Best practices to ensure the secure transport of materials both inter-facility and intra-facility**
  - **Chain of custody where appropriate**

Biosafety and Biosecurity share a variety of components

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Potential Conflicts between Biosafety and Biosecurity

- Emergency alarm – electronic locks
  - Safety – doors fail open
  - Security – doors fail secure
- Emergency egress
  - Safety – move people into the safest location as quickly as possible
  - Security – prevent people from moving into or through restricted areas
- Emergency response
  - Safety – provide emergency responders with locations of hazards and responsible individuals
  - Security – control distribution of sensitive information only to those with a need to know
- Signage
  - Safety – identify hazardous substances and responsible parties
  - Security – avoid identification of target materials or individuals with access
- Keys required inside laboratory areas
  - Safety – contamination concern
  - Security – multiple layers of access

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Thank You!

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