International
BIOLOGICAL THREAT REDUCTION

Risk Assessment

Sandia National Laboratories

Laboratory Biosecurity and Biosafety Workshop

Pune, India

3 May 2006

www.biosecurity.sandia.gov

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under contract DE-AC04-94AL85000.

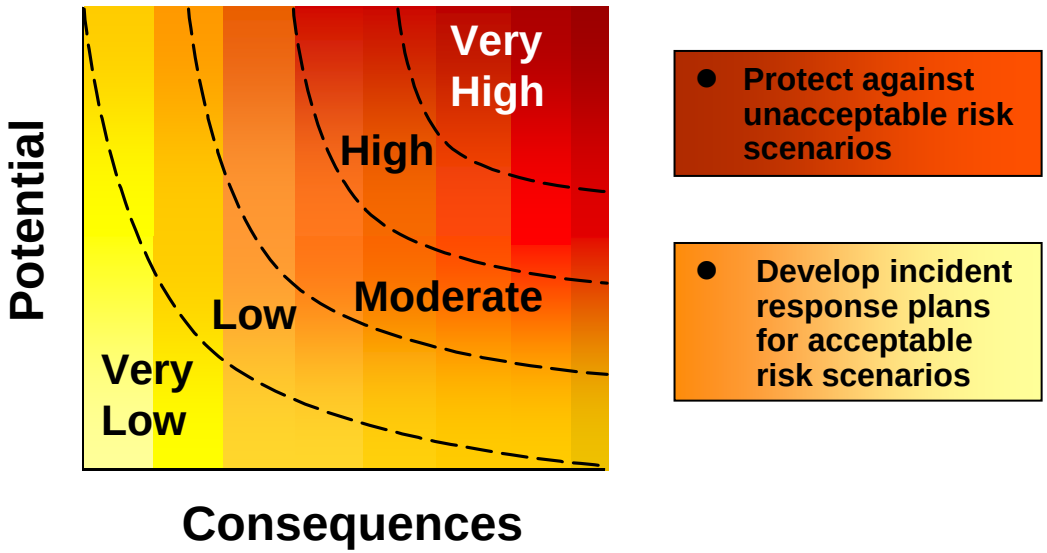
Sandia National Laboratories

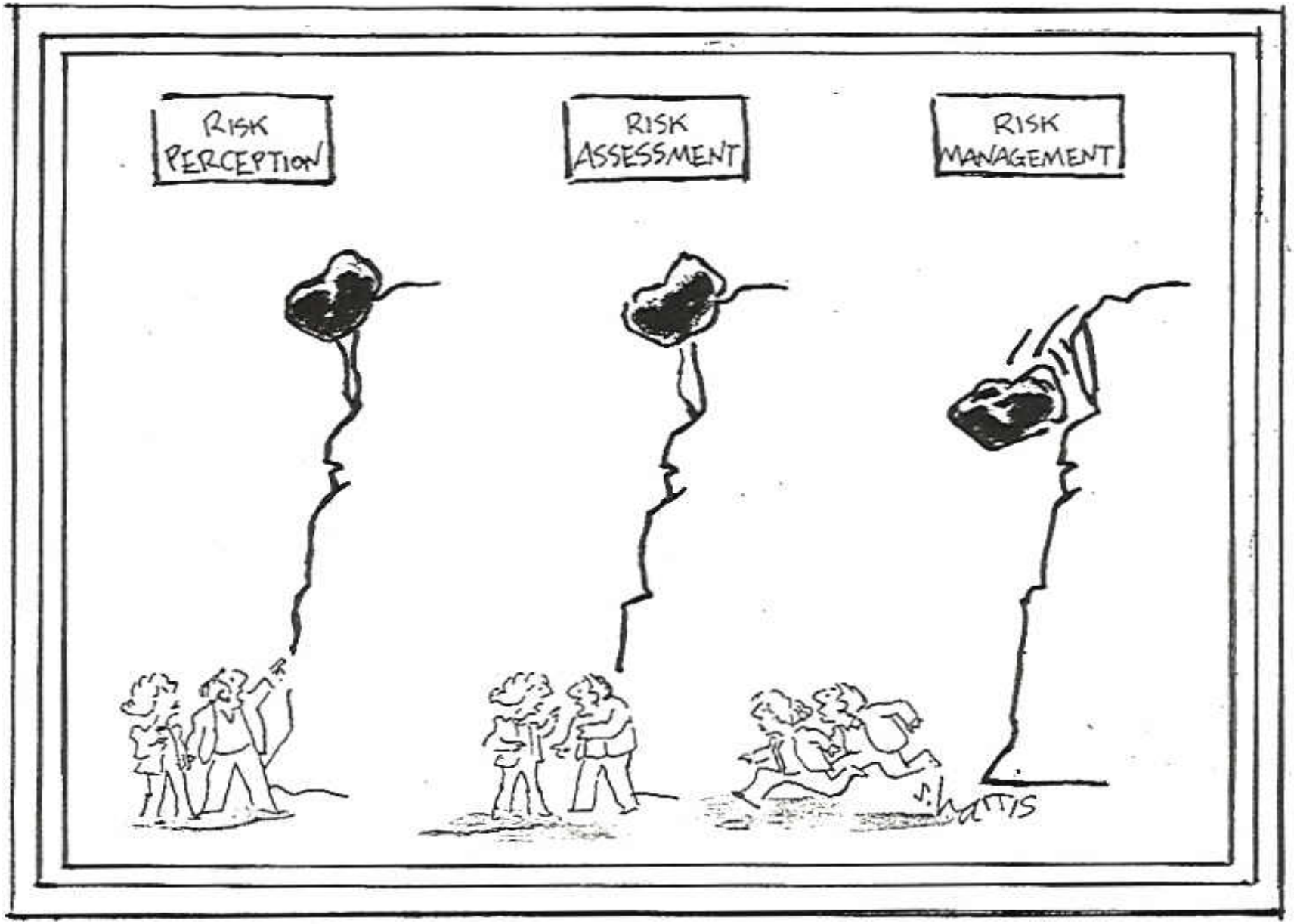
Risk

- 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

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




RISK PERCEPTION
RISK ASSESSMENT
RISK MANAGEMENT
J. HATTIS

Risk Perception in Laboratories

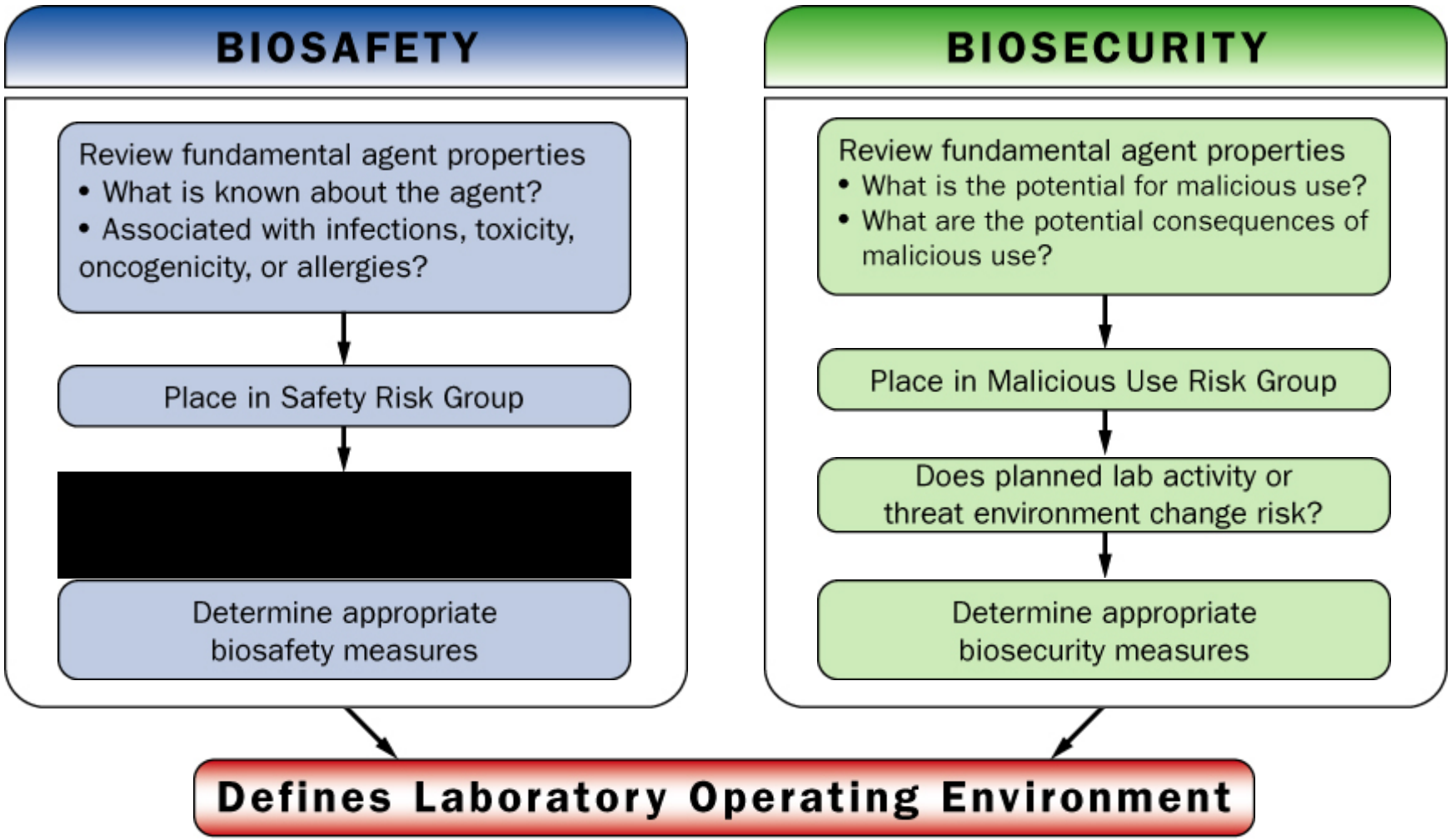
Biosafety risks: laboratory-acquired infections

- 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

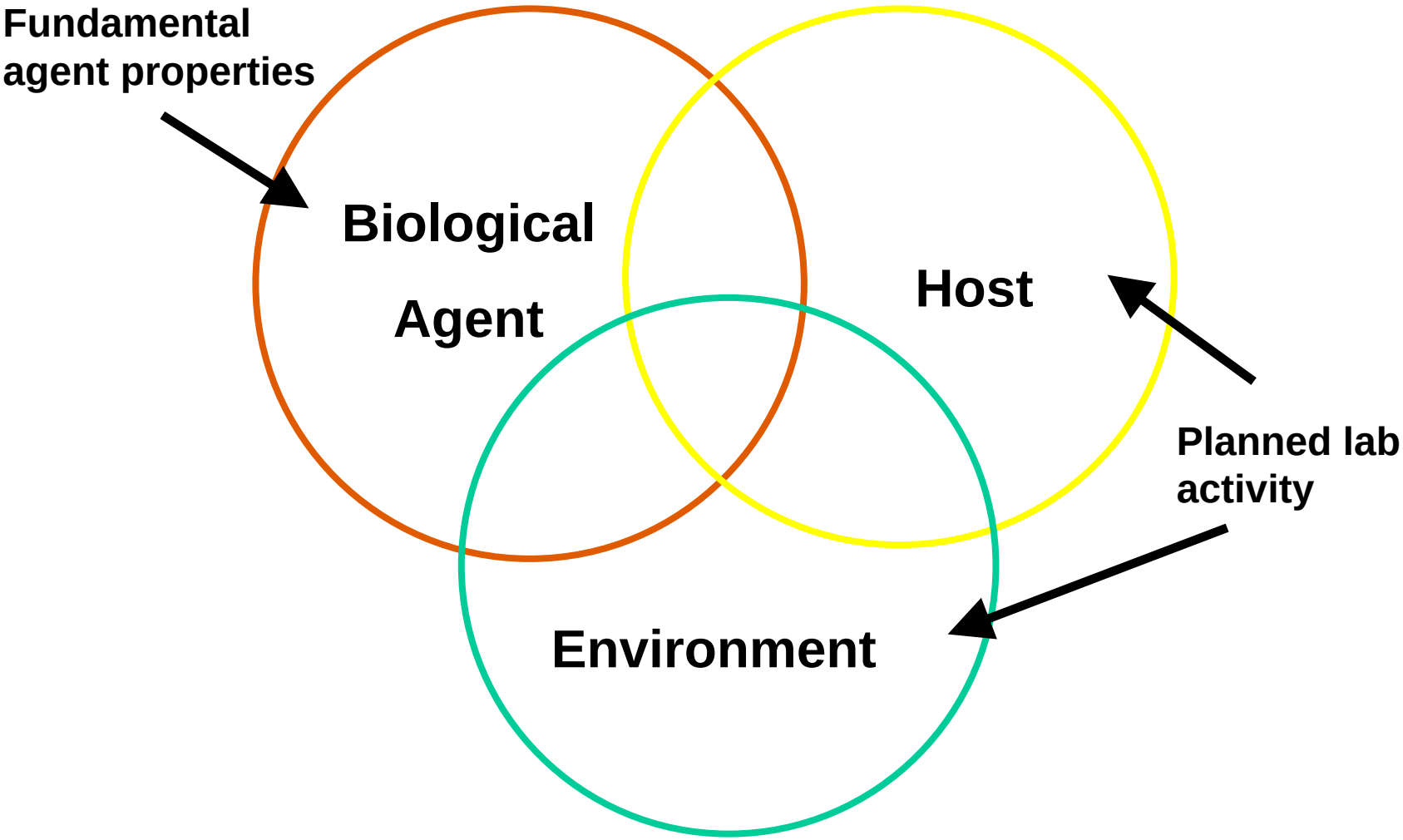


Risk Assessment

- **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

Safety Risk Group Examples

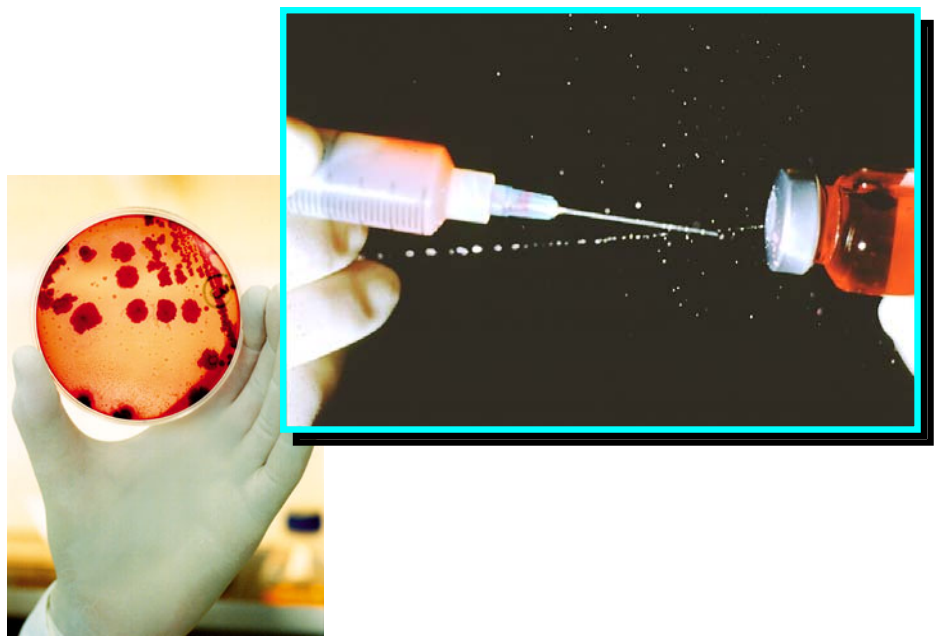
- **Risk Group 1**
  - ***Bacillus subtilis***
    - Ubiquitous bacterium found in water, soil, air
    - Not considered pathogenic or toxigenic to humans, animals, or plants
  - ***Escherichia coli* K-12**
    - E. coli is normal inhabitant of colon of almost all mammals
    - K-12 is debilitated strain – 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

Safety Risk Group Examples

- **Risk Group 3**
  - ***Mycobacterium tuberculosis***
    - Proven hazard to laboratory workers (3x higher rate of infection)
    - Low aerosol infectious dose (ID_{50} < 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)

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**

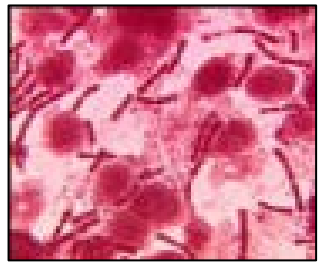


Biosafety Risk Assessment: Elements That May Modify Risk

- 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

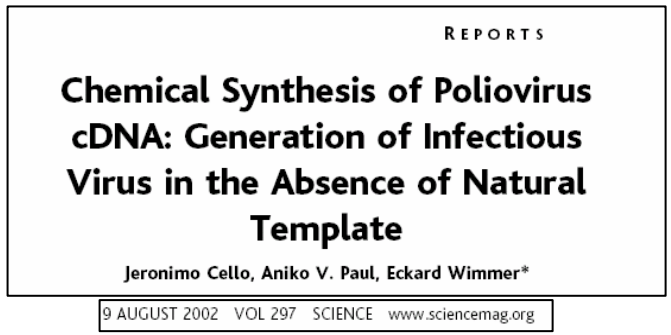
Biosecurity Risk Assessment

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



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

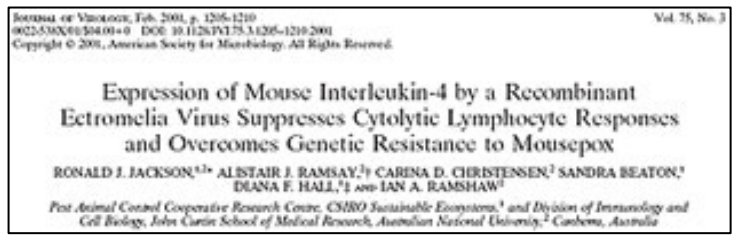


REPORTS

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



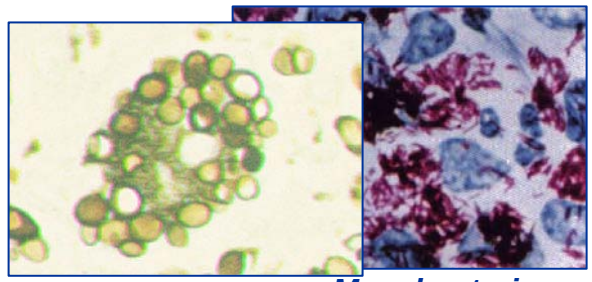
Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox

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

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

Malicious Use Risk Group Examples



Coccidioides immitis

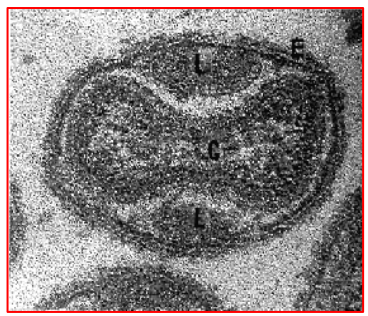
Mycobacterium leprae

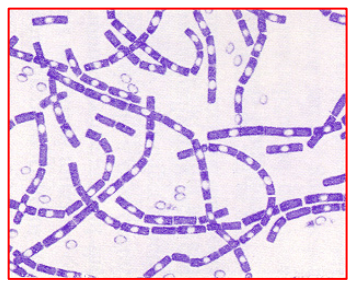
- **Nonpathogenic**
  - ***Bacillus cereus, Lactobacillus acidophilus*, Saccharomyces cerevisiae**
- **Low Malicious Use Risk (LMUR)**
  - ***Mycobacterium leprae***
    - **Consequences: Not highly virulent, not highly contagious, completely curable**
    - **Weaponization potential: Production is a significant 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**
    - **Weaponization potential: Requires technical skills to handle safely, easy to procure virulent strain, easy to grow**

Malicious Use Risk Group Examples

- **High Malicious Use Risk (HMUR)**
  - ***Bacillus anthracis***
    - **Consequences: High fatality rate, not contagious, early diagnosis is difficult**
    - **Weaponization potential: 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**
    - **Weaponization potential: History of weaponization, very stable, difficult to obtain**


Patient's leg covered in smallpox


Variola major

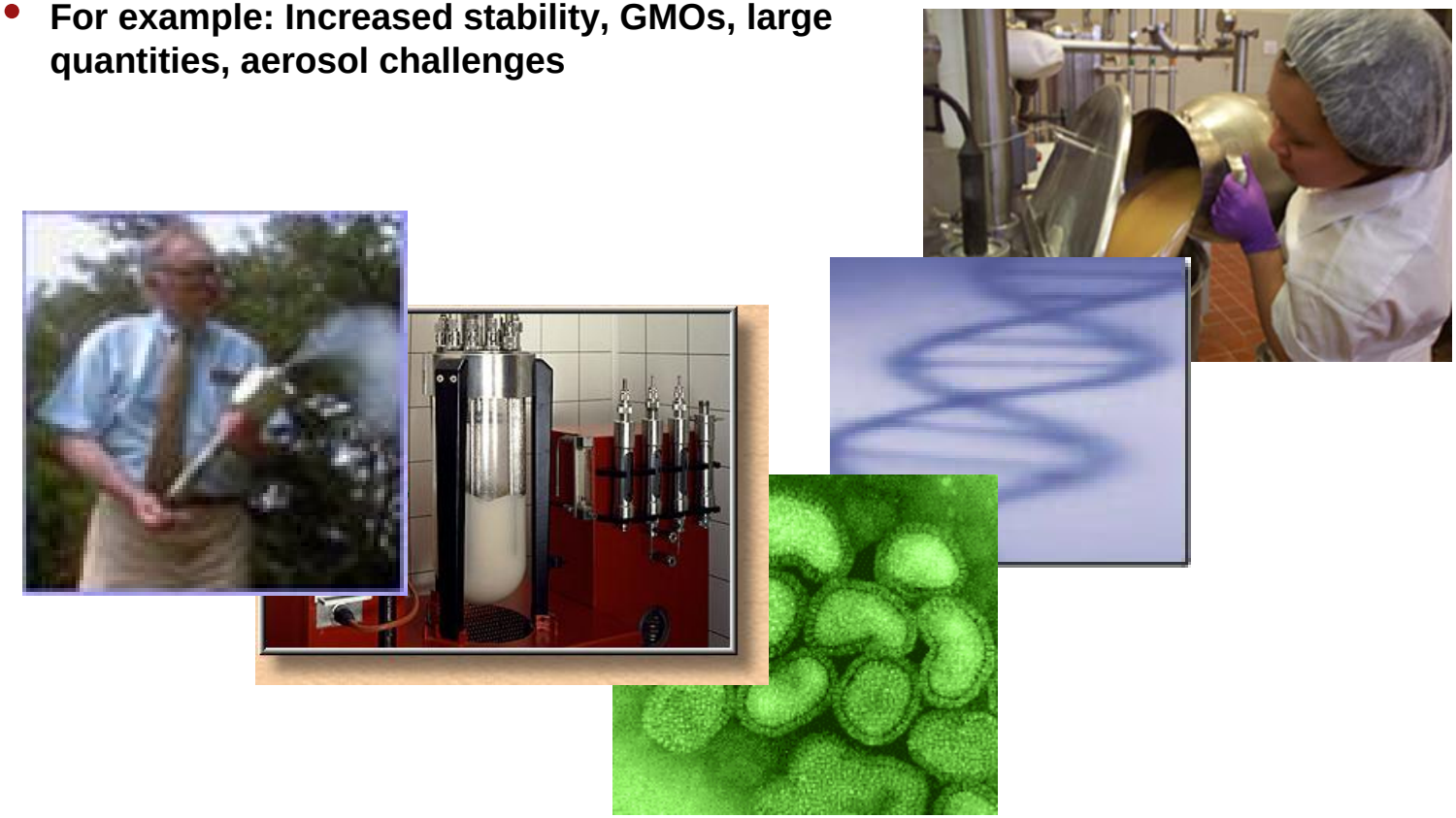

Bacillus anthracis

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**

Biosecurity Risk Assessment: Elements That May Modify Risk

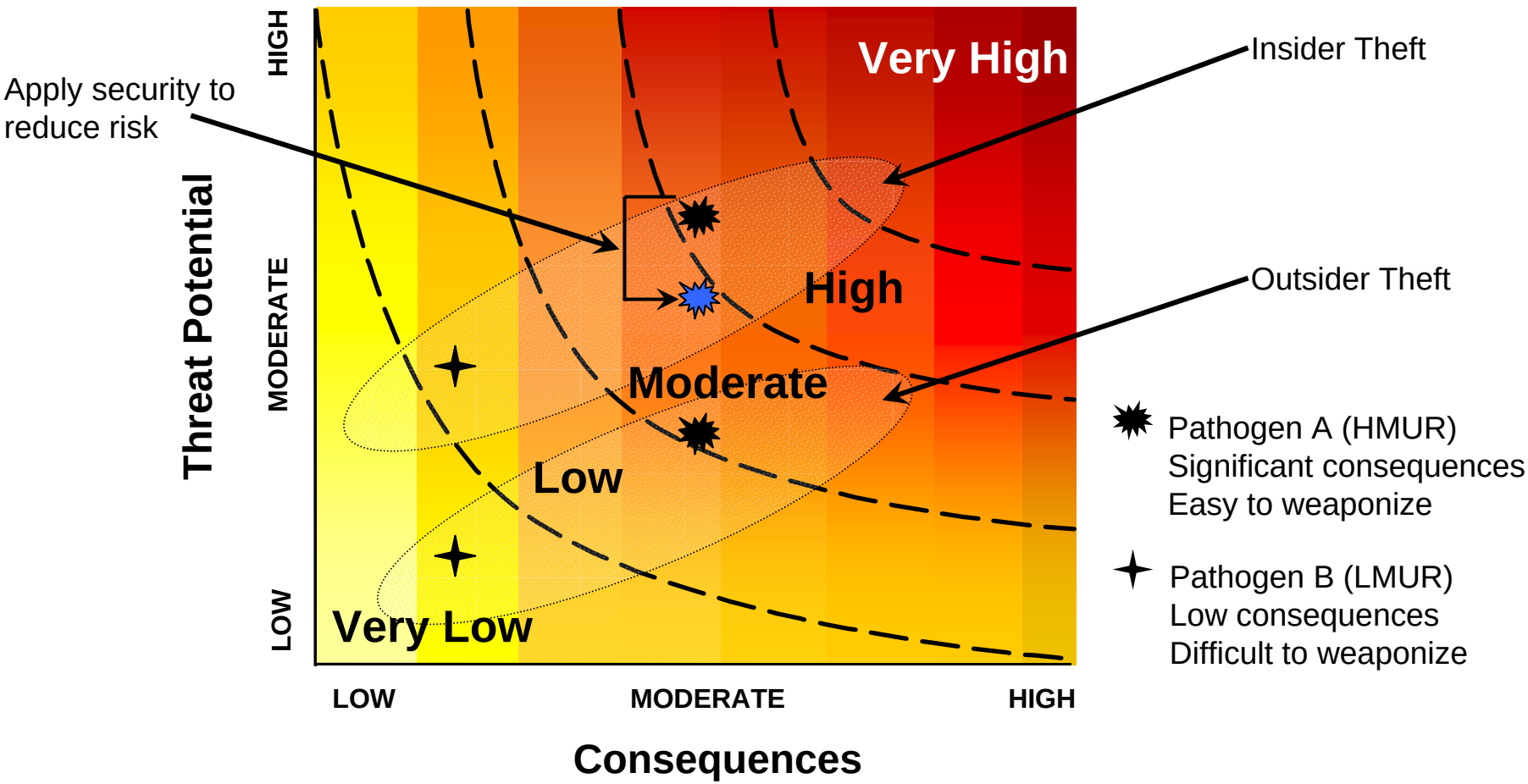
- **Consider lab experiment**
  - **Does planned experiment produce an agent with higher weaponization potential or higher potential consequences?**
    - **For example: Increased stability, GMOs, large quantities, aerosol challenges**



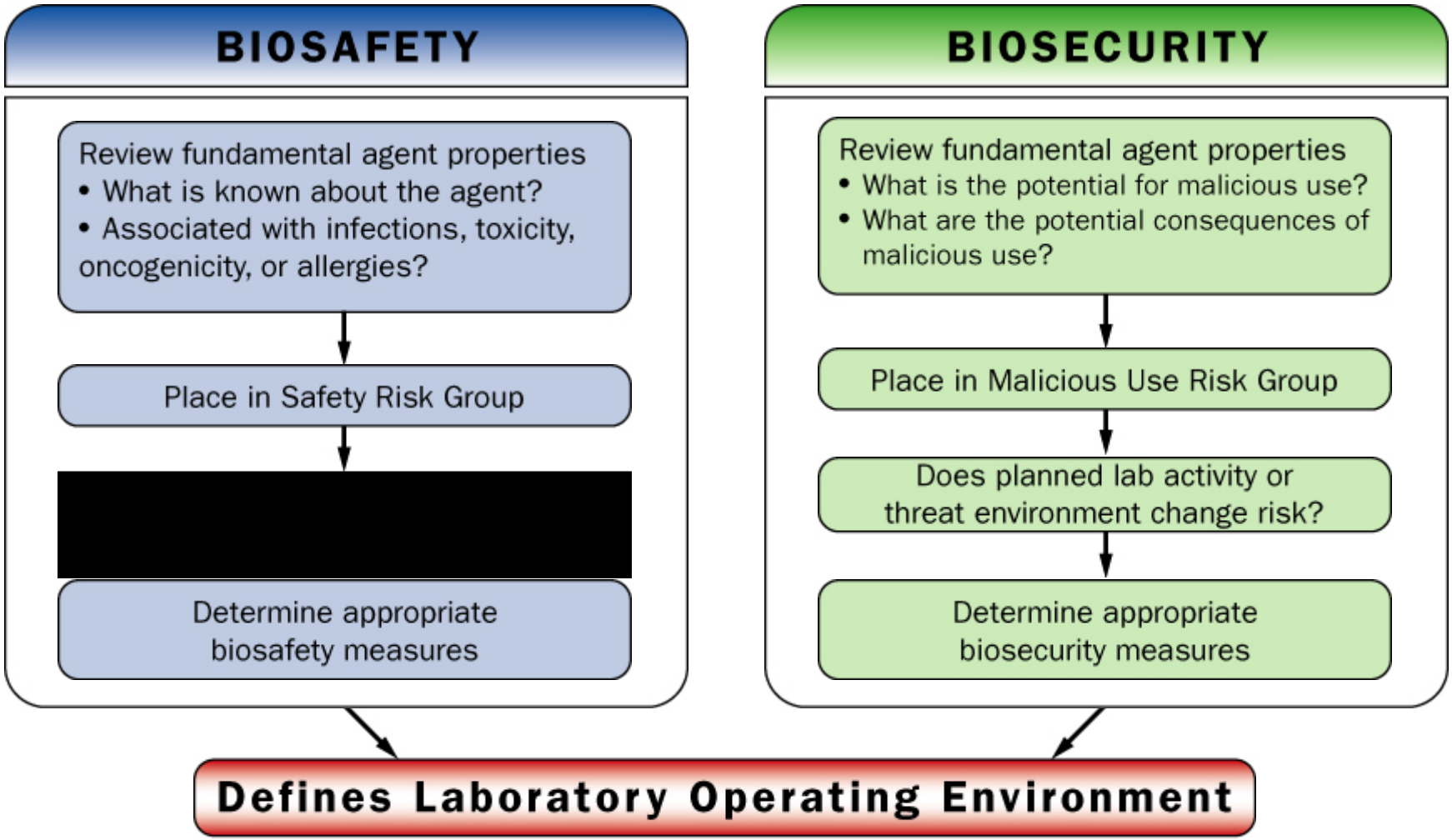
Biosecurity Risk Assessment: Elements That May Modify Risk

- **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

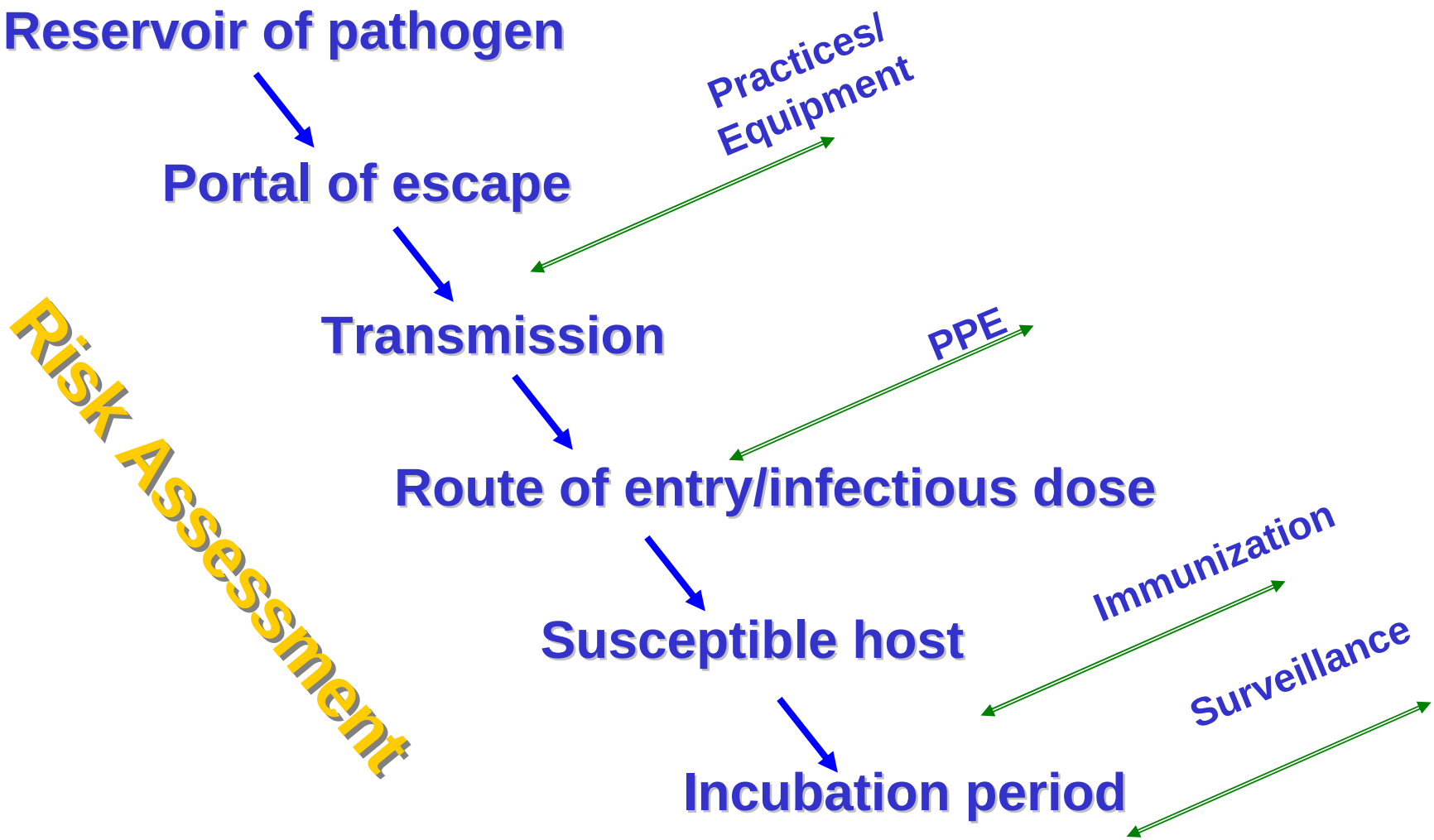
Biosecurity Risk: Insider vs. Outsider Threat



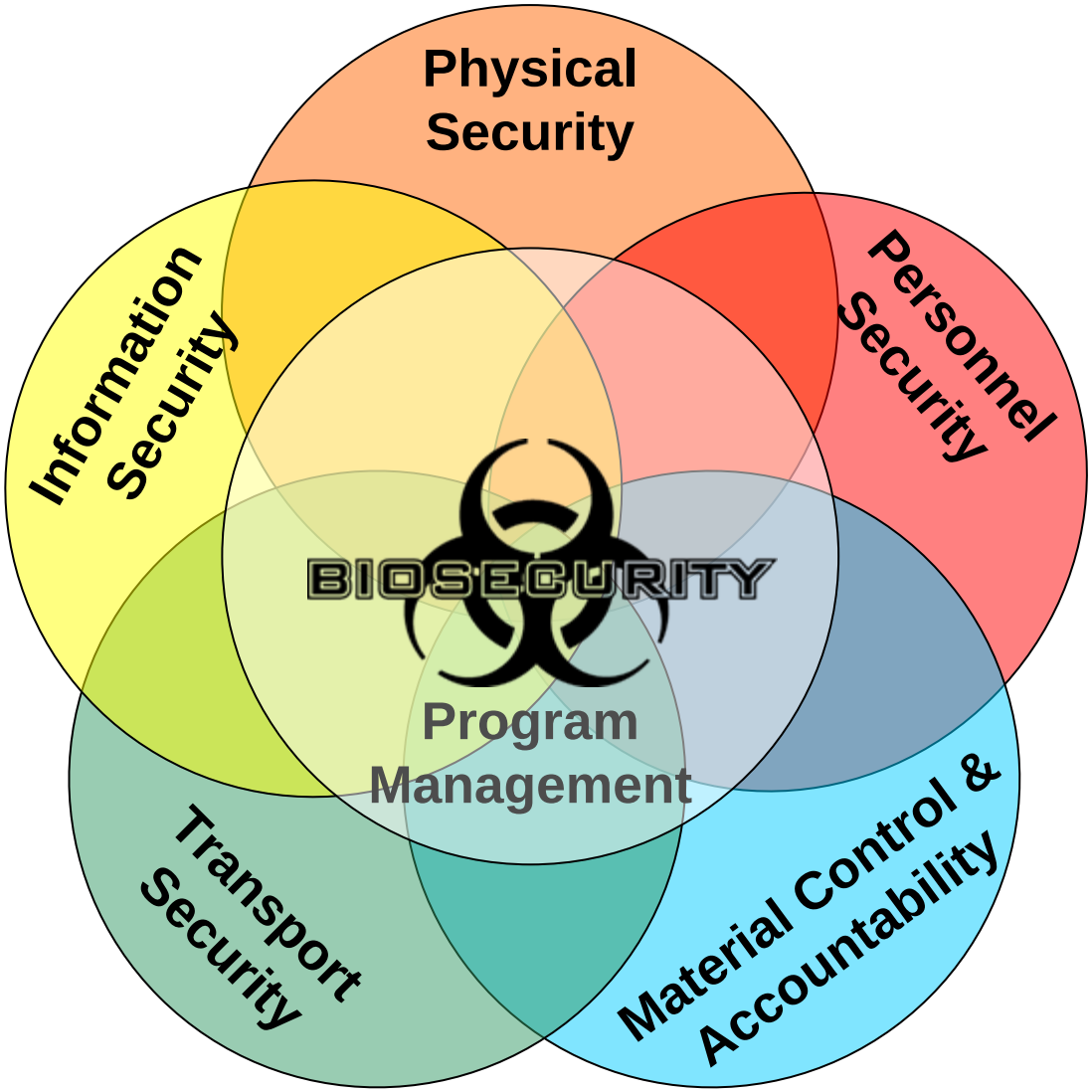
Integrated Biosafety and Biosecurity



Risk Management: Implementation of Biosafety



Risk Management: Implementation of Biosecurity



Conclusions

- Need to integrate biosafety and biosecurity considerations into decisions about laboratory operations
- 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
- Parallels exist between safety and security risk assessment processes