SAND2008-1141P

Biosafety Risk Assessment Project (Biosafety-RAM)

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Sandia National Laboratories
March 2008

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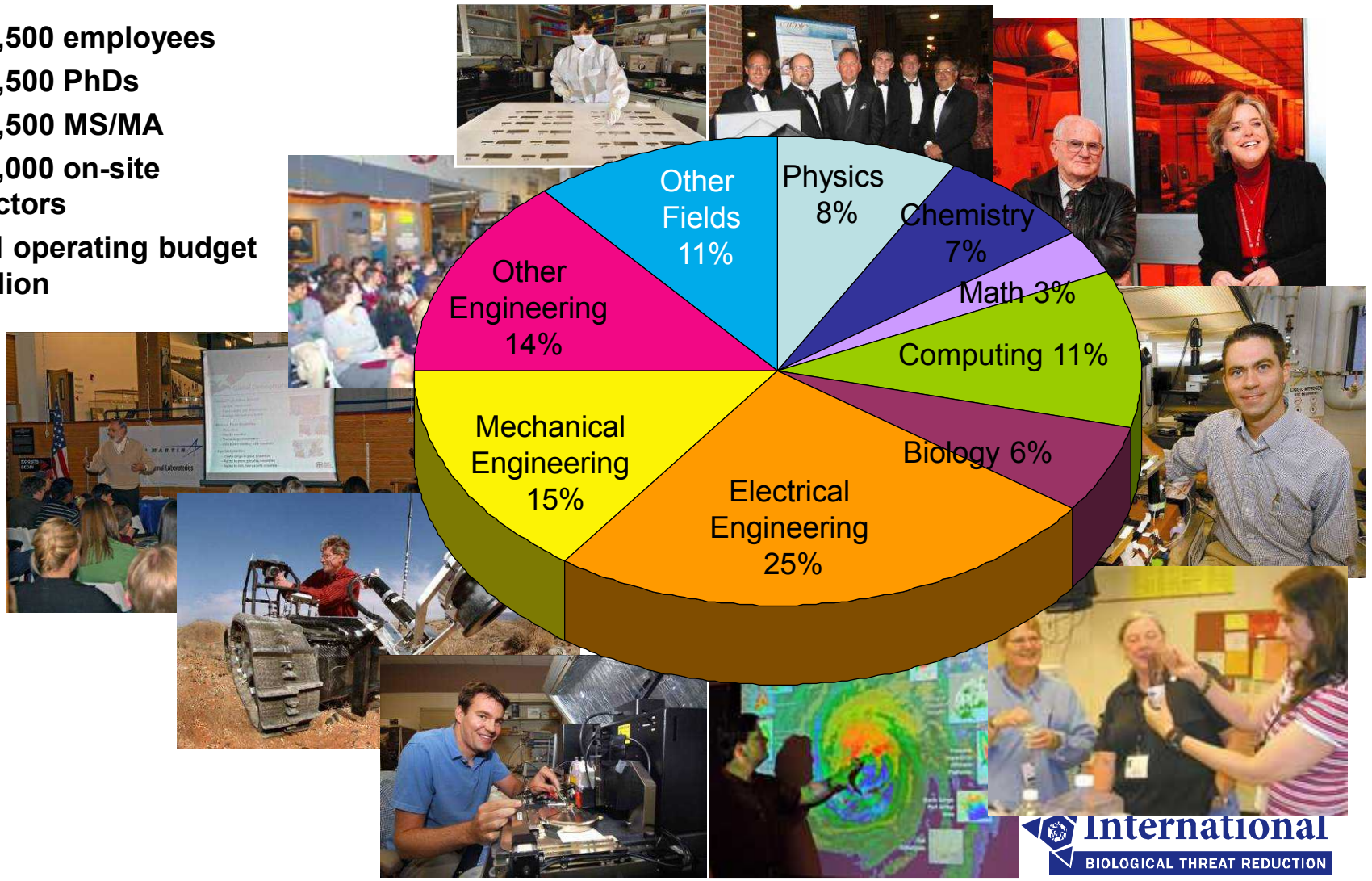
Sandia National Laboratories

Provides innovative, science-based, systems-engineering solutions to the most challenging national and international security problems

- **Over 8,500 employees**
- **Over 1,500 PhDs**
- **Over 2,500 MS/MA**
- **Over 1,000 on-site contractors**
- **Annual operating budget ~$2 billion**



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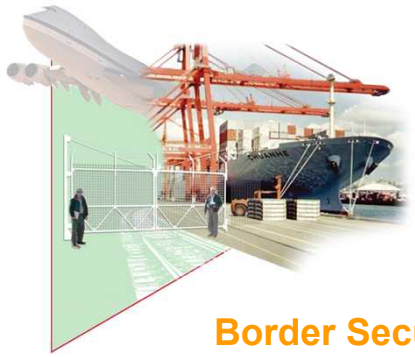
Sandia's Global Security Center

Reduces current and emerging proliferation and terrorism threats by creating sustainable system solutions through international cooperation

US/Russia Nuclear Security

Reducing the risk of theft or diversion of Russian nuclear weapons, materials, and related expertise

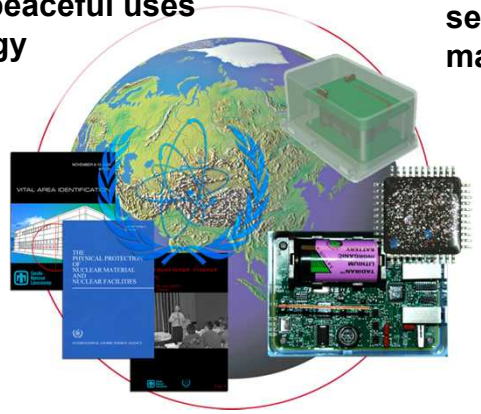


Border Security

Detecting, deterring, and interdicting nuclear smuggling across international borders

Nuclear Nonproliferation/ International Physical Security

Preventing the proliferation of weapons of mass destruction by enhancing International Safeguards, and promoting the peaceful uses of nuclear technology



Biological/Chemical Threat Reduction

Reducing biological and chemical threats globally by focusing on safety and security of legitimate materials

Regional Security

Developing technical solutions to regional security problems

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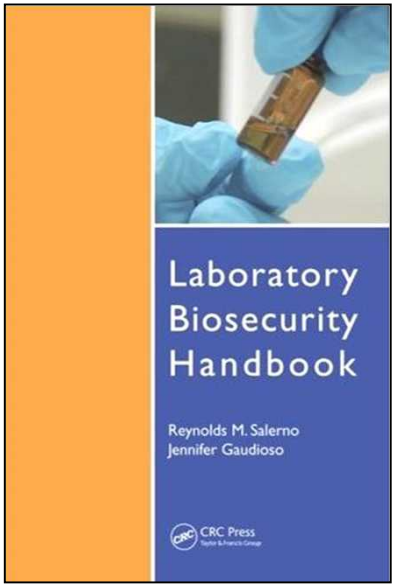
Sandia's International Biological Threat Reduction

- **IBTR's mission: To enhance United States and international security by reducing biological threats worldwide**

- **IBTR's highest goals**
  - Enhance safety, security, and containment of dangerous biological agents in bioscience facilities
  - Strengthen capacities to detect and control dangerous biological agents
  - Improve understanding and mitigation of biological threats



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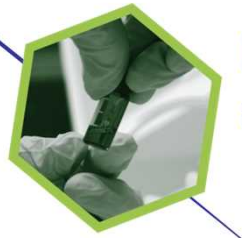
IBTR Technical Program Areas

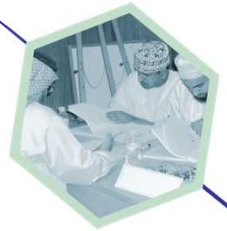
Extensive collaboration with US Government agencies

Laboratory Biosafety, Biosecurity, and Biocontainment

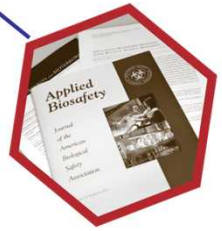


Infectious Disease Diagnostics and Control

Training and Workshops



Policy, Regulatory, and Guidelines Support



Assessments and Analysis

Extensive collaboration with international organizations

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT OECD

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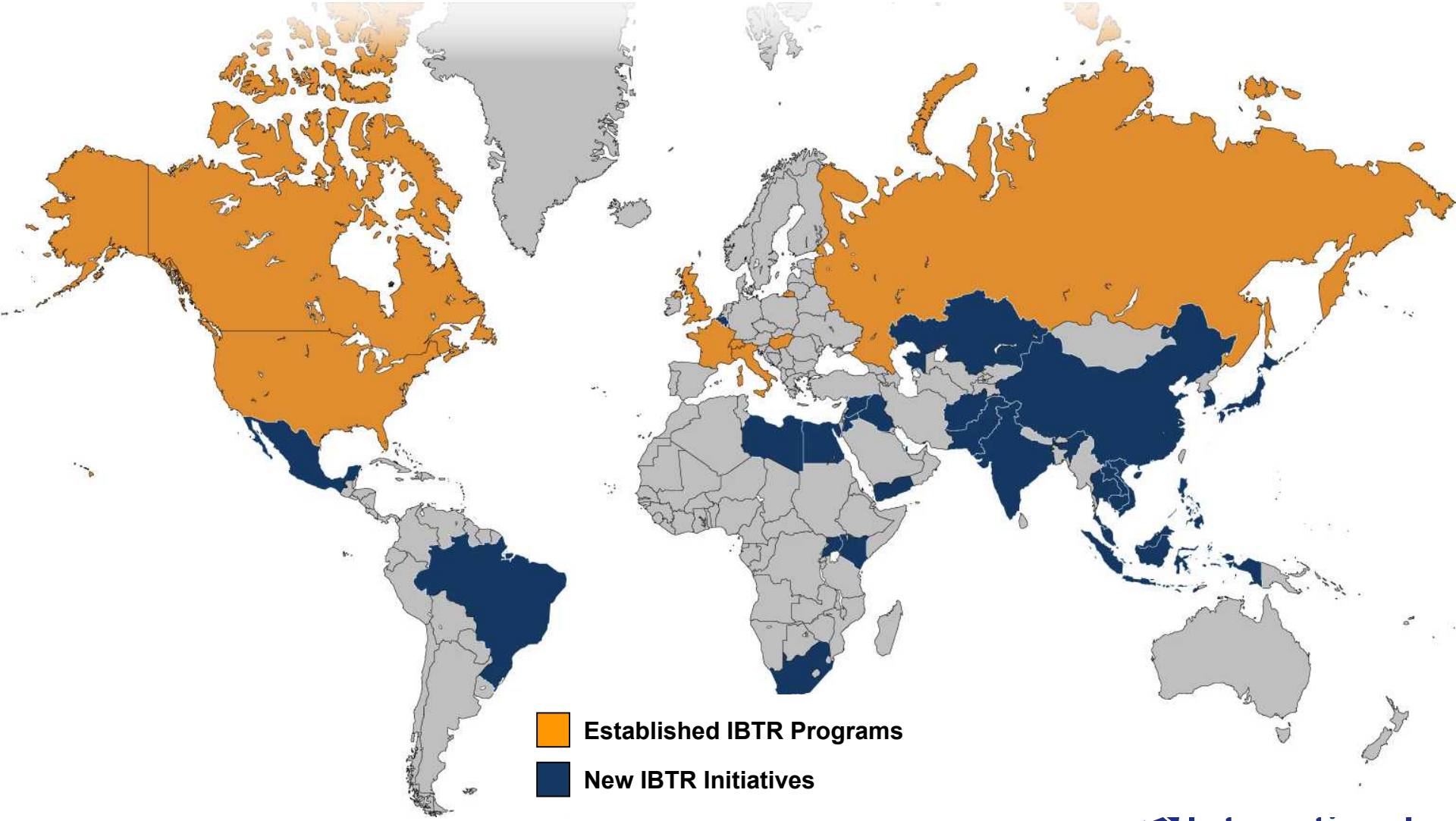
IBTR International Engagement To Date



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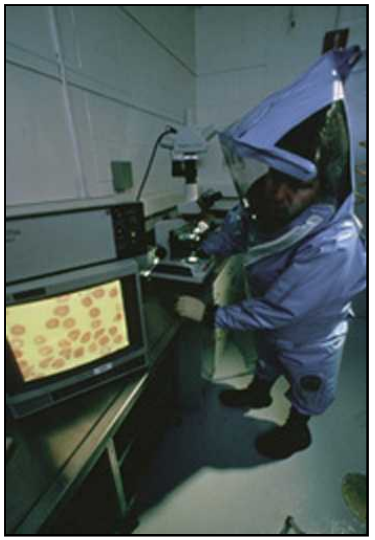
IBTR Risk Assessments – Rationale

- **Risk assessment is a fundamental element of our laboratory biosafety and biosecurity work – both domestically and internationally**
- **Risk is the likelihood an adverse event will occur**
  - A function of probability and consequences
- **Laboratory work with pathogens will always involve some level of safety and security risk**
  - Need to recognize that we cannot protect against every conceivable adverse event
  - Need to distinguish between “acceptable” and “unacceptable” risks
- **Resources for risk mitigation are not infinite**
  - Resources should be used as efficiently as possible
- **Risk assessment determines and prioritizes the risks that exist at a laboratory**
  - Ensure that protection and the cost is proportional to the risk (implement graded levels of protection)



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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"

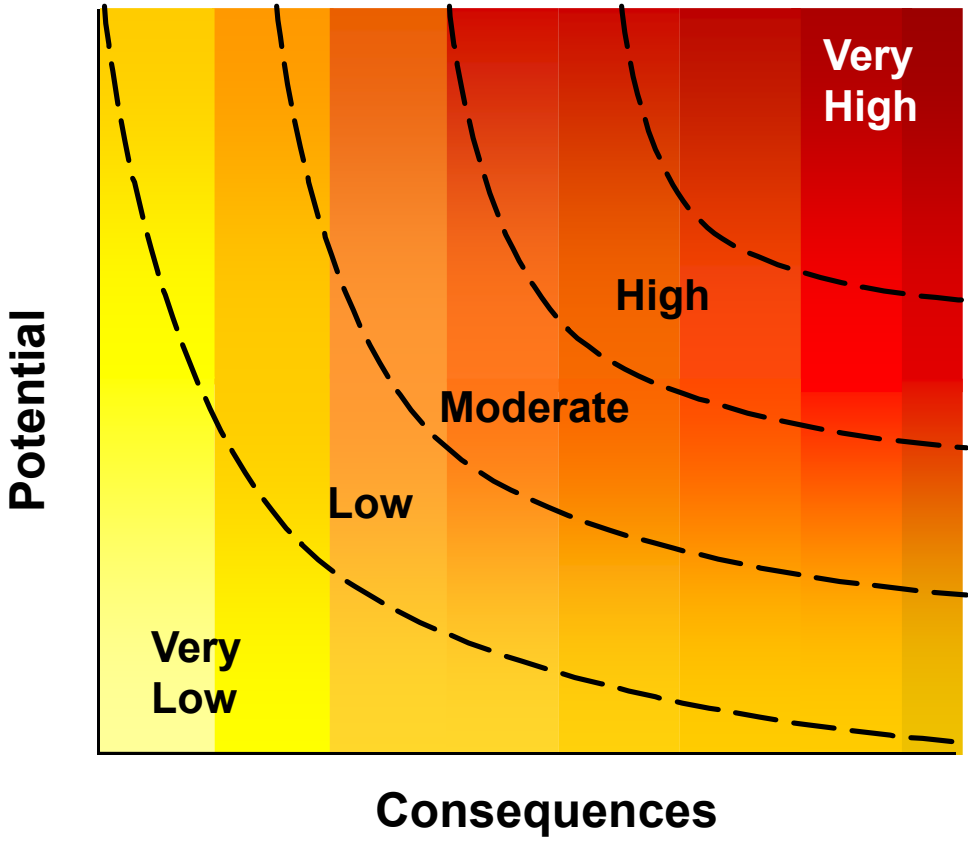
Biosecurity Risk Assessment

1. **Characterize assets (pathogens and toxins) and threats**
   a. Evaluate pathogens and toxins at facility (asset assessment)
   b. Evaluate adversaries who might attempt to steal those pathogens or toxins (threat assessment)

2. **Evaluate scenarios**
   a. Create scenarios consisting of “specific adversaries” attempting to steal and misuse a specific biological agent
   b. Determine how the various scenarios could be perpetrated (vulnerability assessment)

3. **Characterize the risk**
   a. Evaluate threat potential and consequences of each scenario
   b. Determine acceptable and unacceptable risks; develop risk statement

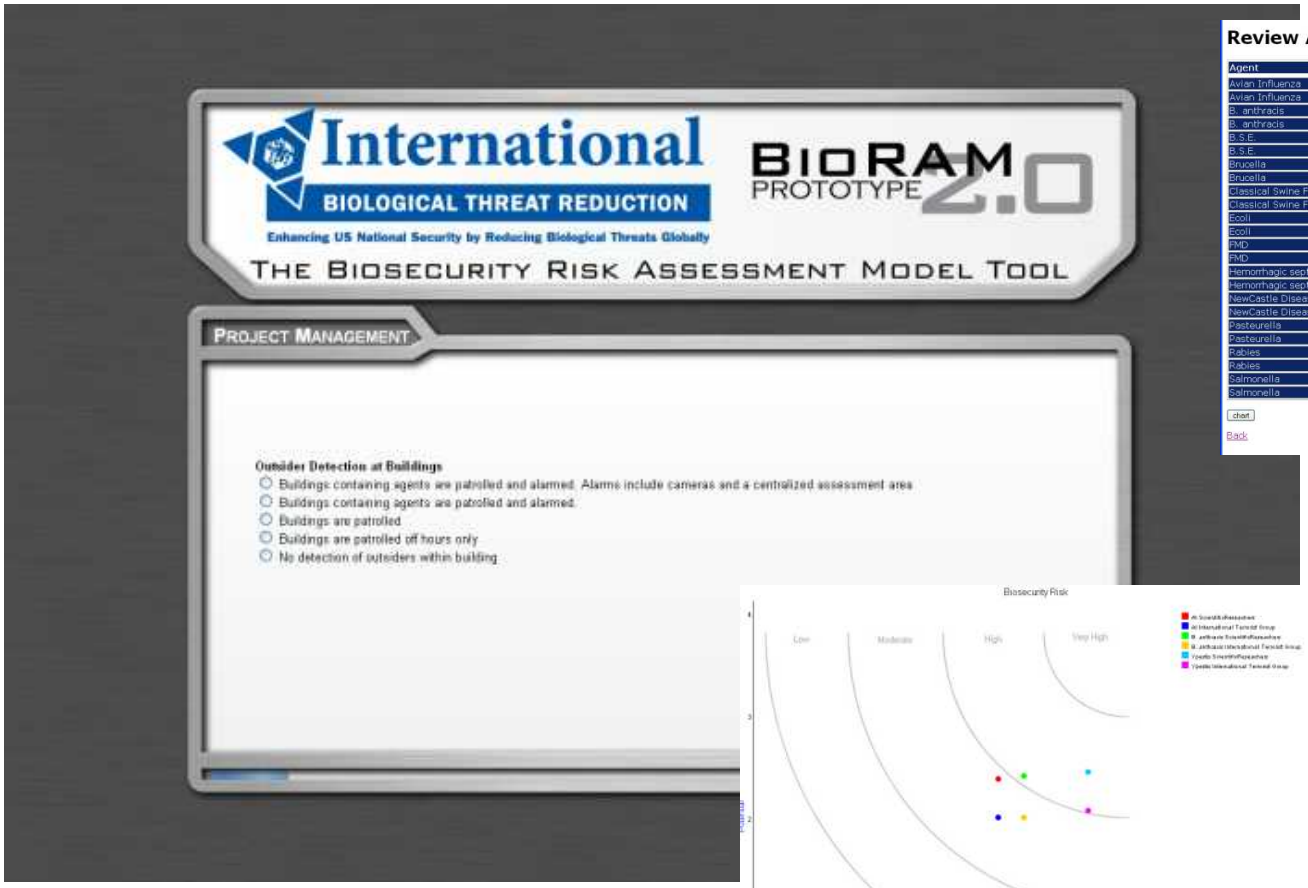
Characterizing Scenarios by Risk



- Protect against unacceptable risk scenarios

- Develop incident response plans for acceptable risk scenarios

SNL/IBTR BioRAM Software Tool



Review Assessment for BAI Post Upgrade

Agent	Adversary	Consequences	Threat Potential
Avian Influenza	ScientificResearchers	1.61	2.77
Avian Influenza	International Terrorist Group	1.61	2.39
B. anthracis	ScientificResearchers	2.74	2.75
B. anthracis	International Terrorist Group	2.74	2.33
B.S.E.	ScientificResearchers	1.49	2.66
B.S.E.	International Terrorist Group	1.49	2.23
Brucella	ScientificResearchers	1.62	2.84
Brucella	International Terrorist Group	1.62	2.41
Classical Swine Fever	ScientificResearchers	2.16	2.86
Classical Swine Fever	International Terrorist Group	2.16	2.48
Ecoli	ScientificResearchers	0.73	2.73
Ecoli	International Terrorist Group	0.73	2.3
FMD	ScientificResearchers	2.3	3.04
FMD	International Terrorist Group	2.3	2.63
Hemorrhagic septicemia	ScientificResearchers	1.89	2.81
Hemorrhagic septicemia	International Terrorist Group	1.89	2.38
NewCastle Disease Virus	ScientificResearchers	2.84	2.76
NewCastle Disease Virus	International Terrorist Group	2.84	2.34
Pasteurella	ScientificResearchers	1.1	2.73
Pasteurella	International Terrorist Group	1.1	2.31
Rabies	ScientificResearchers	2.16	2.64
Rabies	International Terrorist Group	2.16	2.21
Salmonella	ScientificResearchers	1.34	2.78
Salmonella	International Terrorist Group	1.34	2.35

chart

Back

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2nd Biorisk Management Workshop

- **Held at the Canadian Science Centre for Human and Animal Health**
  - Organized by the National Microbiology Laboratory's Office of Biorisk Management (part of the Public Health Agency of Canada)
  - Winnipeg, Manitoba, February 2007
- **Participants charged with discussing and, if possible, developing a common approach to biological risk assessment for the laboratory**
  - Discussed individual parts of the risk assessment process (three days)
  - Developed a draft conceptual model of a unified risk assessment process (two days)
- **From the workshop report: "The current lack of a clearly quantifiable processes makes biological risk assessment a predominantly qualitative approach and, as such, potentially highly subjective, variable, and inconsistent."**
  - Next steps include "the establishment of a comprehensive toolkit for biological risk assessment"
- **Following the workshop, IBTR sought and received three years of internal Sandia R&D funding to develop a quantitative biosafety risk assessment methodology and software tool**
  - Biosafety RAM

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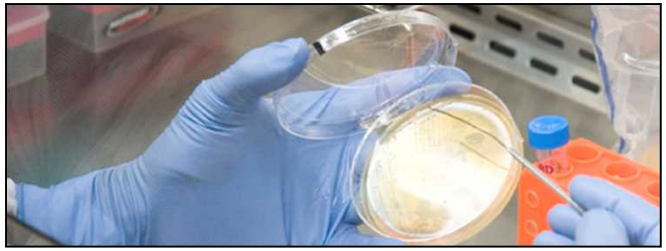
Sandia's Laboratory Directed Research & Development

- **The LDRD Program aims to**
  - Maintain the scientific and technical vitality of Sandia and the US Government
  - Enhance Sandia's ability to address future national and international security needs

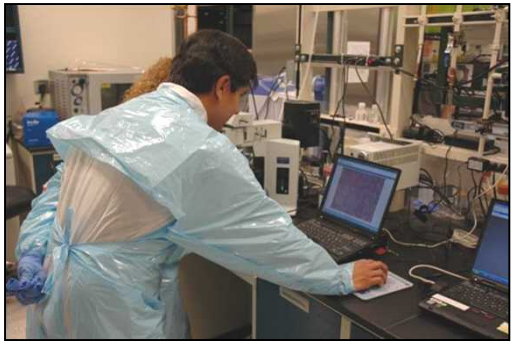


- **Sandia and the US Department of Energy expect the LDRD Program to**
  - Foster creative and leading-edge R&D
  - Serve as a proving ground for new research
  - Support high-risk, potentially high-value R&D

Biosafety RAM Project Objectives

- **To produce a methodology that helps standardize biological safety risk assessments**
  - Repeatable
  - Quantifiable

- **To develop a systematic, standardized tool that includes**
  - Accepted criteria for assessing the risk
  - A “scoring system” for evaluating the situation against the criteria
  - Relative weights for the criteria
  - An equation that combines the criteria scores and the relative weights to produce a measure of risk



Project Goals and Milestones

Goal	Milestone	Completion Date
Outline Methodology	***Review method with SMEs***	***03/2008***
Establish criteria	Agent hazard criteria	05/2008
	Laboratory hazard criteria	05/2008
	Hazard mitigation criteria	05/2008
Determine relative importance among criteria	Determine relationship among the criteria	06/2008
	Weight the criteria	**08/2008**
Create prototype model	Create prototype model	11/2008
	Test model with SMEs	**12/2008**
	Present overall methodology/model for peer review	02/2009
Develop software tool	Develop alpha software tool to implement model	09/2009
	Validate software tool	**12/2009**
	Finalize software tool and implement revisions	04/2010
SAND report		**09/2010**

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Expected Project Results

- **Deliver a quantitative, repeatable biosafety risk assessment methodology and accompanying tool**
- **Promote the use of the tool throughout the international bioscience community**
  - Especially in the many new high containment laboratories around the globe
- **Improve understanding that there is no such thing as zero risk in biocontainment facilities**
  - Help to articulate the real risks at these facilities -- for users, managers, and the public
- **Strengthen the practice of biosafety and biosecurity globally, and improve the reliability of infectious disease research and diagnostics globally**
  - And thus, enhance biological threat reduction

Biosafety Risk Assessment Methodology LDRD Current Definitions and Model

Susan Caskey
International Biological Threat Reduction
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March 2008

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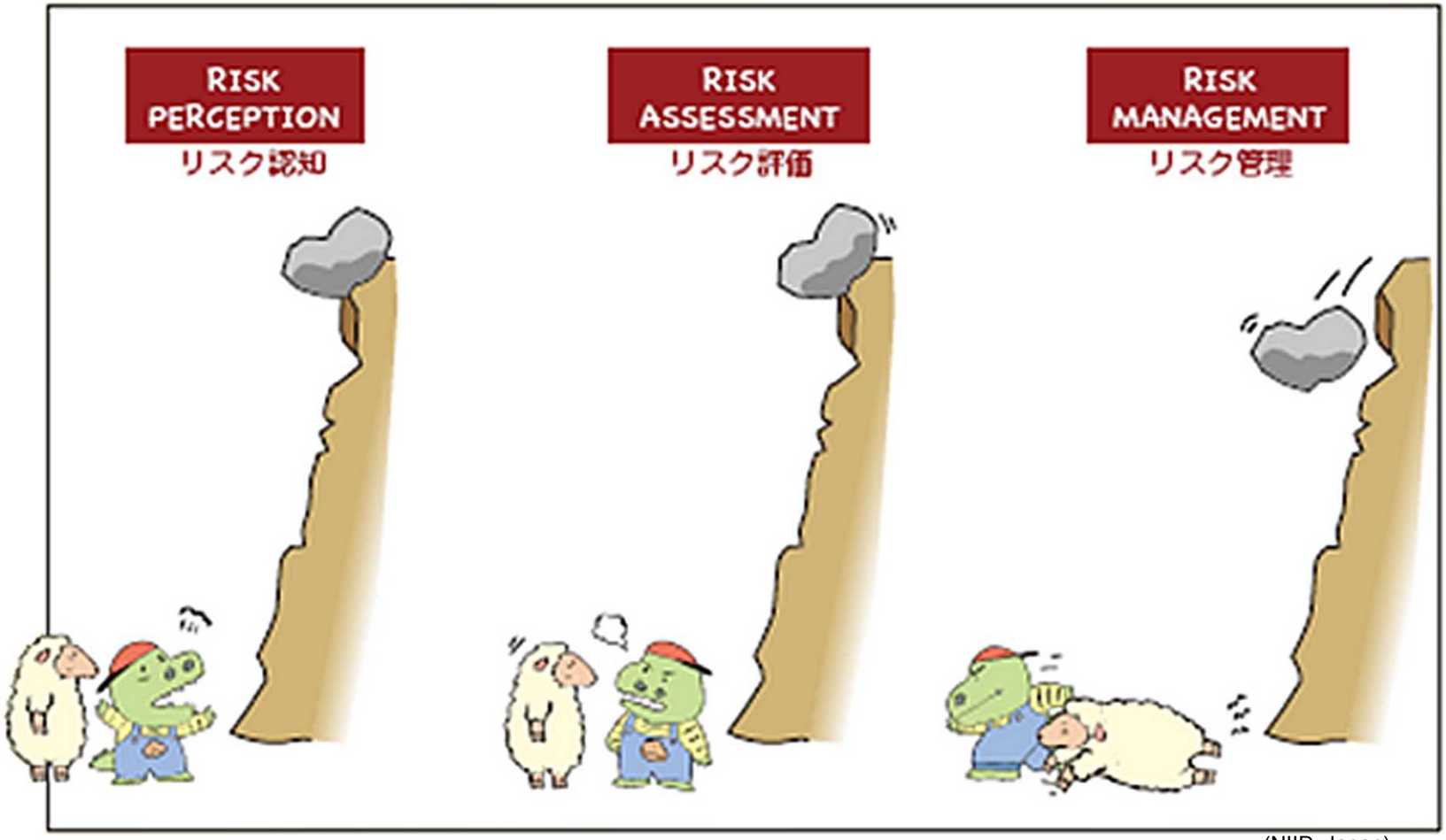
Risk Assessment



(NIID, Japan)

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Risk Assessment Model

- Identify criteria
- Rank criteria based on importance (weighting)
- Determine metric for evaluating criteria (scoring)
- Determine model for combining criteria along with their importance to arrive at a final assessment of risk

Hazard vs. Risk

- **Hazard: The way in which an object or a situation may cause harm**
  - **A hazard exists where an object (or substance) or situation has an inherent ability to cause an adverse effect**

- **Risk: The chance that harm will actually occur**
  - **The risk can be high or negligible**

- **Risk is a function of likelihood AND consequences**

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Biosafety Risk

- **Likelihood of infection of a given biological agent**
  - Potential of exposure of a given biological agent
    - **To the individual working in the laboratory**
    - **To the community via secondary infection**
    - **To the community via release of agent**
  - Potential of exposure to cause infection
    - **Exposure via infectious route**
    - **Exposure greater than infectious dose**

- **Consequences of infection of a given biological agent**
  - To individuals working in the laboratory
  - To the human community outside the laboratory
  - To the animal community outside the laboratory (domestic, agricultural and wildlife)

Biosafety Risk

R_i – Risk

L_i – Likelihood for infection

C_a – Consequences of infection

L_a – Biological properties of an agent

L_h – Laboratory Hazards

$$R_i = L_i (L_a \cdot L_h) * C_a$$

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Biological Properties - L_a, C_a

- **Properties that categorize an agent's**
  - Potential for infection
  - Consequence of exposure
  - Consequence of infection
  - Potential for secondary infection

- **Bacteria, viruses, rickettsia, fungi, parasites, and prions**
  - Toxins are excluded accept as byproducts of bacteria

- **Current criteria classifications**
  - Pathogenicity
  - Routes of Infection
  - Transmissibility
  - Host Range

Laboratory Hazards - L_h

- **Potential for exposure to a given agent**
  - Potential of an individual working in the laboratory
  - Potential of exposure to the community
- **Current exposure classifications**
  - Aerosol exposure
  - Contact exposure
  - Oral exposure
- **Perfect controls would reduce the laboratory hazard to zero**
  - There is no perfect system
- **Laboratory hazards include the vulnerabilities or gaps in biosafety controls**

Biosafety Gap Assessment - L_h

- **Biosafety risk mitigation measures**

- **Deviation from standard best practices**
  - Engineering controls
  - Procedural controls
  - Program oversight
- **Standard best practices?**

Critical Topics
to be discussed through out the week

These discussions will help to
Scope the path forward for the
biosafety risk assessment methodology

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Critical Issues

- **Modeling risk with a tight/focused scope provides more fine grained results then modeling risk with a general scope**
- **Scoping biosafety risk for this model will allow better determination of criteria and better defined weights**

- **Community vs. Individual Risk**
  - Individual Risk
  - Community risk via secondary infection
  - Community risk via release of agent
  - Health risk
  - Organizational risk
- **Humans vs. Animals**
  - Human Community
  - Animal Community
  - Comparison of consequences
    - **E.g. FMD as compared to Anthrax**

Weeks's Objectives

- **Critical discussions to scope risk assessment**
- **Discussion and weighting of agent properties**
- **Categorization of laboratory hazard criteria**
- **Discussion and categorization of risk mitigation measures**
  - Discussion of biosafety standards

Critical Issue Discussion 1

- **Goal:**
  - To identify key differences between individual and community risk
  - To determine if individual and community can be assessed using the same criteria and weights or if they should be assessed independently
  - To determine if the risk to the organization should be included in addition to the risk of infection

Agent Hazard Criteria

Discussion and Weighting of Agent Hazard Criteria

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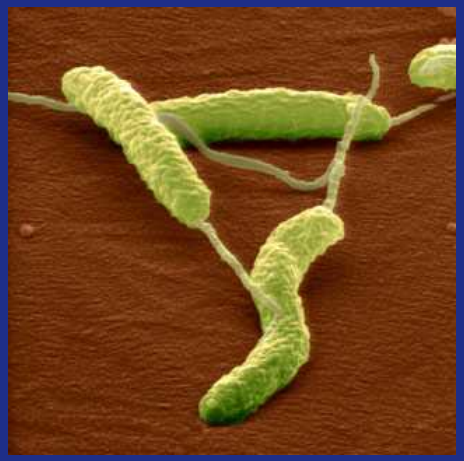
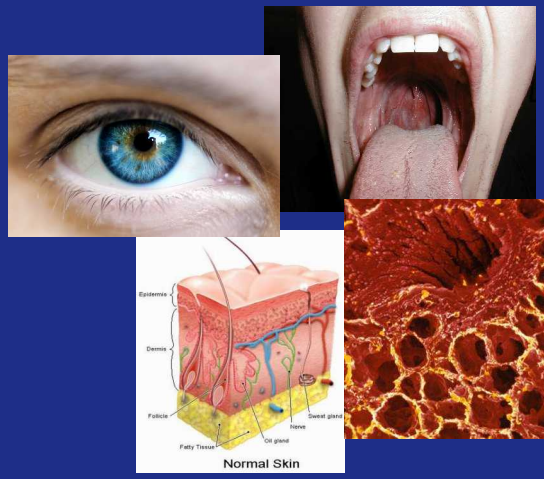
Overview of Agent Hazard Criteria



Pathogenicity



Routes of Infection

Transmissibility

Host Range

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Objectives

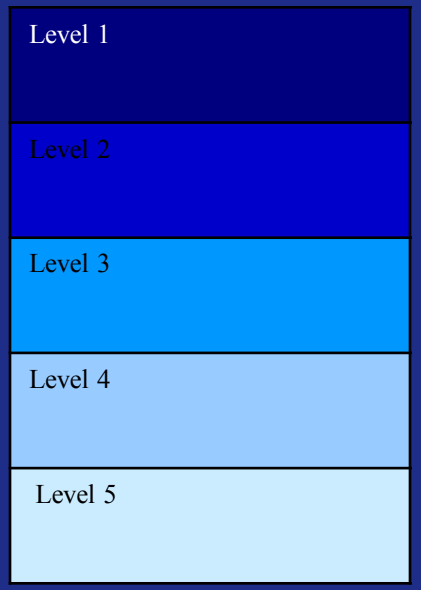
- **Discussion**
  - Review whether criteria are complete and correct
- **Weighting Exercise**
  - Weight the relative importance of the criteria to the overall risk

What is a Weighting Exercise?

- **A hierarchical listing of criteria will be discussed in small groups**
  - Goal: to review criteria definitions
  - Goal: to review criteria groupings, including placement as likelihood or consequence or both
- **Goal: each group member will review the criteria and provide a relative listing of its importance in the grouping**
  - Using a numeric scale rank each criteria
    - **1 is the most important**
    - **NA for criteria with no importance**

How the Criteria are Organized

- **Include criteria for both potential and consequences**
- **Includes a definition and a question for each criteria**
- **Some questions will not apply to all agents**
- **The criteria chart is color coded**
  - Dark colors correspond to high level criteria and light colors are lower level criteria



Pathogenicity

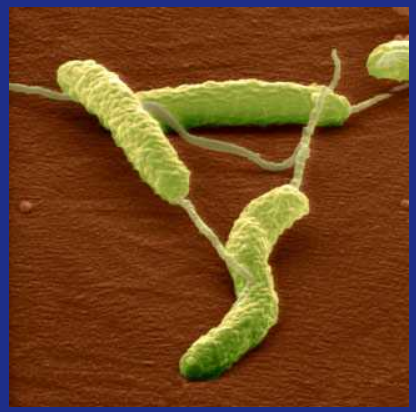
Pathogenicity

Virulence

- Ability to defeat and evade hosts systems
- Stability
  - Survival outside host
  - Chemical Inactivation
  - Physical Inactivation
- Infectious Dose
- Incubation Period
- Latency
- Colonization
- Agent State (Bacteria only)
- Incidence of disease
- Morbidity
- Mortality
- Duration of illness
- Allergen
- Toxin production
  - Effects
  - Half-life
  - Lethal Dose

Treatment

- Drug Resistance
- Immunization
- Prophylaxis
- Post-infection treatment



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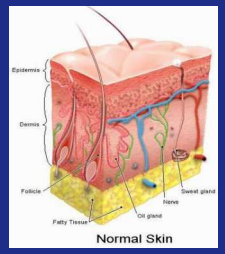
Routes of Infection

Routes of Infection

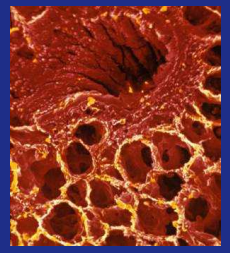


Natural

- Airborne
- Contact
- Oral
- Vector

Laboratory

- Airborne
- Contact
- Oral
- Vector



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Transmissibility

Transmissibility

Human to Human

Animal to Human

Animal to Animal

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Host Range

Host Range

Human Pathogen

Zoonotic Pathogen

Animal Pathogen

Reservoirs

Vectors

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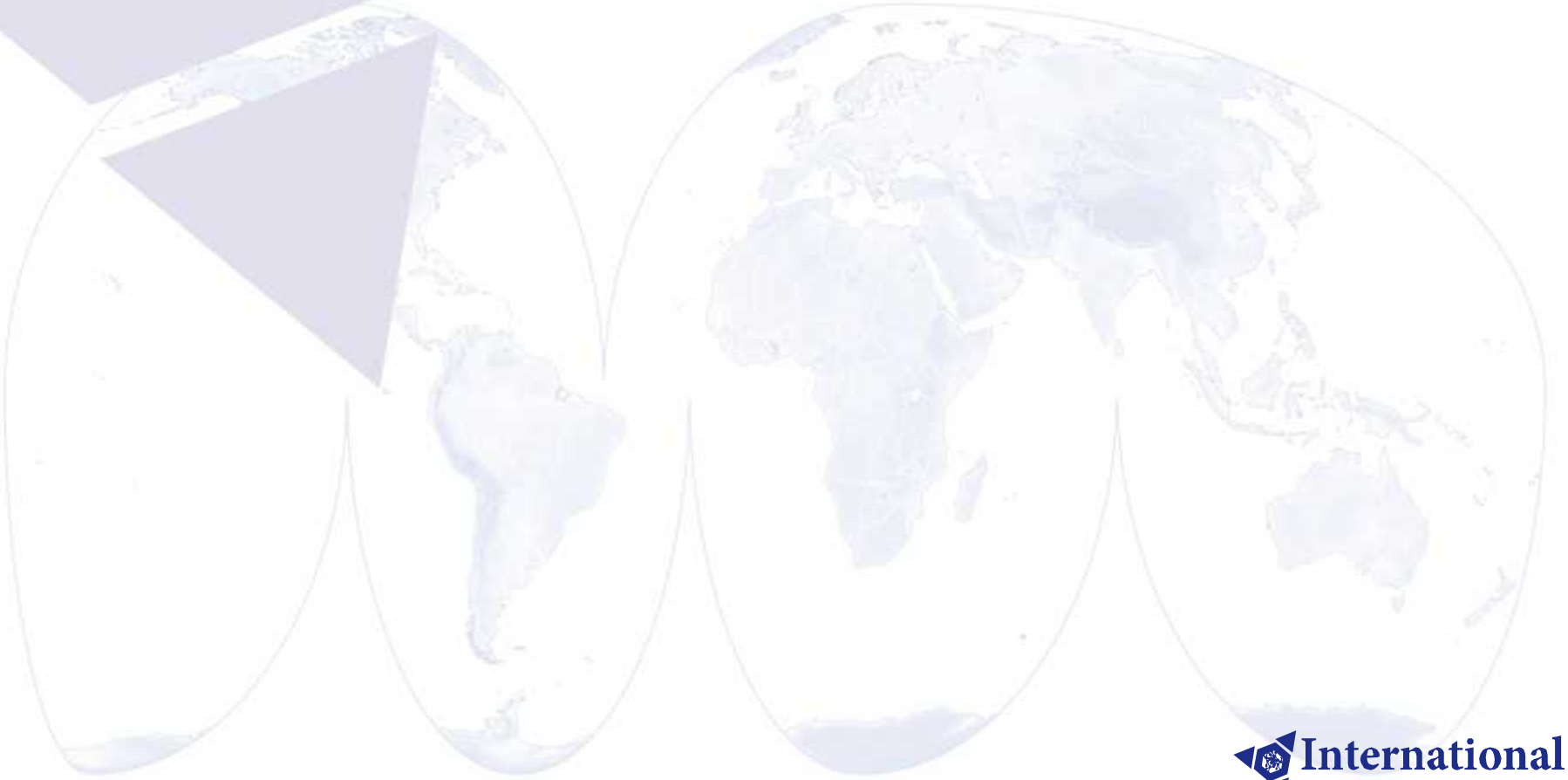
Critical Topics



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Critical Issue Discussion 2

- **Goal:**
  - To identify key differences between the animal communities
    - Agricultural
    - Domestic
    - Wildlife
  - To determine if risk can be assessed using the same criteria and weights for each animal community
  - To determine which animal communities should be assessed

Critical Issue Discussion 3

- **Goal:**
  - To identify the key differences in risk between human and animal diseases
  - To determine if risk can be calculated for humans and animals using the same criteria and weights
  - To determine how risk should be calculated for zoonotic diseases

Laboratory Hazard Criteria

Discussion and Development of Laboratory Hazard Criteria: Criteria which increase potential exposure to individual or community to an agent

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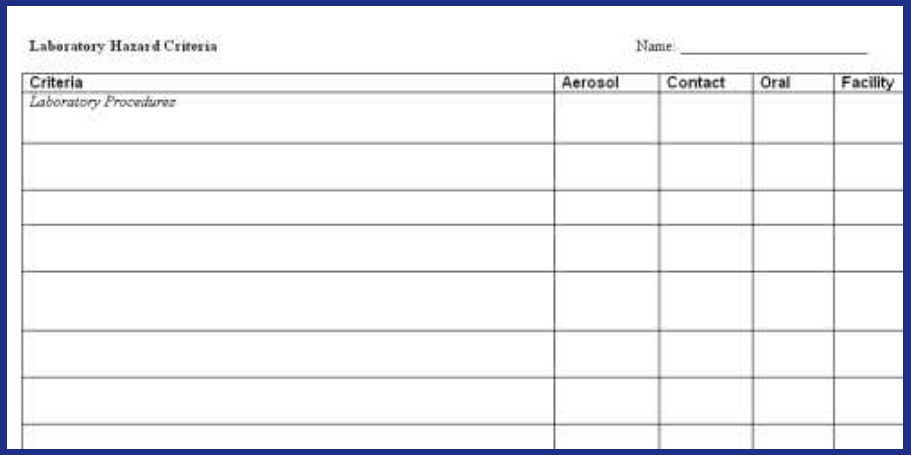
Overview of Laboratory Hazard Criteria

- **Individual laboratory worker**
  - Potential for aerosol exposure
  - Potential for contact exposure
  - Potential for oral exposure
  - Facility factors
- **Community**
  - Potential for aerosol exposure
  - Potential for contact exposure
  - Potential for oral exposure
  - Facility factors



Laboratory Hazard Criteria

Name: _____

Criteria	Aerosol	Contact	Oral	Facility
Laboratory Procedures				

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Risk Mitigation

Discussion and Criteria Development

Factors which reduce the risk

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Risk Mitigation Criteria

- **Biosafety controls are those controls that, if used correctly, reduce the laboratory hazards**
- **To calculate the effectiveness of biosafety controls, a risk assessment needs to measure the deviation from a standard**
- **Currently, there are no formal biosafety control standards**

- **This methodology will define a standard for the assessment process**
  - Engineered controls
  - Procedural controls
  - Program oversight

Biosafety Standard Discussion

- **Goal:**
  - To discuss the biosafety guidelines and principles currently used
  - To determine the best path forward for developing of standards for this risk assessment
    - **WHO's LBM**
    - **NIH/CDC's BMBL**
    - **PHAC LBG**
    - **Others**

Risk Mitigation Criteria

- **Goal:**
  - To work in a small group and discuss the biosafety controls that are most important for conducting a risk assessment
  - To develop a list of biosafety criteria which should be addressed in the risk assessment standard

  - Each group will have a biosafety control focus
    - **Group 1: Engineering controls**
    - **Group 2: Procedural controls**
    - **Group 3: Program oversight**

Critical Topics

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Critical Issue Discussion 4

- **Goal:**
  - To determine the scope of the risk assessment methodology
  - To determine the scope of the risk assessment tool

Critical Issue Discussion 5

- **Goal:**
  - To review the central definition of risk for this methodology
    - **To define: likelihood of infection of a given biological agent**
    - **To define: consequences of infection of a given biological agent**