Risk Assessment

A Presentation and Discussion for the NDSU Institutional Biosafety Committee Meeting 8-11-14

Jodie Haring

What is Risk Assessment?

- CDC's Biosafety in Microbiological and Biomedical Laboratories (BMBL) definition: The process that enables the appropriate selection of microbiological practices, safety equipment, and facility safeguards that can prevent laboratory-associated infections (LAI)
- Description in the NIH Recombinant or Synthetic Nucleic Acids Guidelines:
  - Subjective process which requires a comprehensive approach
  - Investigator makes initial risk assessment based on agent Risk Group (RG) assignment
  - Protocol requirements are considered
  - RG assignment and protocol requirements are considered together in order to set the appropriate containment level

Why is Risk Assessment important?

- It identifies the hazards of working with an infectious agent to decrease the risk of an exposure, which might lead to an infection (or release) and the consequences of that infection (or release)
- The process identifies the practices and procedures required to work safely with infectious agents to therefore decrease the risk of exposure
  - determining the Biosafety Level (BSL)
- Successful control of the hazards associated with infectious agents protect not just the people directly involved, but also the other occupants of the building/space, the public, and the environment
- The process is critical: underestimation of risk puts people and the environment at more risk of exposure to infection/release, but over estimation can add burden and may lead to circumvention of recommended safeguards

Who is involved in the Risk Assessment Process?

- The PI is tasked with providing the initial risk assessment
- IBC members
- IACUC members
- BSO and other Safety Professionals
- Animal Veterinarians
- Whoever has expertise in a hazard associated with the study

Components of Risk Assessment:

- **Agent Hazards**
- Procedure Hazards
- Capability of laboratory staff to control hazards
  - Training
  - Technical proficiency
  - Overall good habits of all members of the laboratory
  - Operational integrity of containment equipment
  - Facility safeguards

Agent Hazards

- Its capability to infect and cause disease in a susceptible host
- Its virulence as measured by the severity of disease
- The availability of preventive measures and effective treatments for the disease

Risk Group Classification – they correlate, but do not equate to BSL

Table 1: Classification of Infectious Microorganisms by Risk Group

Risk Group Classification	NIH Guidelines for Research involving Recombinant DNA Molecules 2002[2]	World Health Organization Laboratory Biosafety Manual 3rd Edition 2004[1]
Risk Group 1	Agents not associated with disease in healthy adult humans.	(No or low individual and community risk) A microorganism unlikely to cause human or animal disease.
Risk Group 2	Agents associated with human disease that is rarely serious and for which preventive or therapeutic interventions are *often* available.	(Moderate individual risk; low community risk) A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.
Risk Group 3	Agents associated with serious or lethal human disease for which preventive or therapeutic interventions may be available (high individual risk but low community risk).	(High individual risk; low community risk) A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.
Risk Group 4	Agents likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available (high individual risk and high community risk).	(High individual and community risk) A pathogen that usually causes serious human or animal disease and can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.[3]

Risk Groups for Veterinary Pathogens

Risk Group	Definition	Biosafety Level recommendation for Animals Large / Small	
1	Unlikely to spread; may cause mild disease; low risk; no official control program	1 or 2	1
2	Limited spread; produces moderate disease; moderate risk; possible control programs	2 or 3	2
3	Can spread readily; causes serious disease; high risk; control programs in place; treatment and prevention available	3 or 3-Ag	3
4	Can spread rapidly; causes severe disease; maximum risk- exotic; strict control programs in place; treatment and prevention not effective	3-Ag	3-Ag

Credit: Emerging Diseases of Animals: Chapter 2- Biosafety Classification of Livestock and Poultry Animal Pathogens, J. Scott Rusk

Agent Hazards to Consider

- probable routes of transmission
  - direct skin, eye or mucosal membrane exposure to an agent
  - parenteral inoculation by a syringe needle or other contaminated sharp, or by bites from infected animals and arthropod vectors
  - ingestion of liquid suspension of an infectious agent, or by contaminated hand to mouth exposure
  - inhalation of infectious aerosols
- infective dose
- stability in the environment (biological decay)
- host range
- endemic nature
- reports of LAIs are a clear indicator of hazard, though the absence of a report does not indicate minimal risk

Genetically Modified Agent Hazards

- May have to consider the risk assessment for the wild-type organism as the baseline, therefore the initial protocol risk assessment may be incomplete
- Genetic alterations have the capacity to alter virulence
  - Change tropism (example: viral receptor modification)
  - Alter susceptibility to available treatments (example: antibiotic resistance, susceptibility to apoptosis)
  - Merge characteristics of two organisms (example: gain of function experiments in flu research)

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Procedure Hazards

- The source of up to 50% of all LAIs can be attributed to:
  - parenteral inoculations with syringe needles or other contaminated sharps
  - spills and splashes onto skin and mucous membranes
  - ingestion through mouth pipetting
  - animal bites and scratches
  - inhalation exposures to infectious aerosols
- However, in the other 50% of reports, not enough information is available to determine the source/incident that resulted in the LAI

Procedure Hazard: Aerosols

- Aerosols are a serious laboratory procedure hazard
- They are ubiquitous in laboratory procedures such as:
  - Pipetting
  - Blending
  - Non aerosol-tight centrifuges cups
  - Sonicators
  - Vortexors
- They are usually undetected and are extremely pervasive, placing the laboratory worker carrying out the procedure and other persons in the laboratory at risk of infection
- There is general agreement among biosafety professionals, laboratory directors and principal investigators who have investigated LAIs that an aerosol is the probable source of many LAIs, particularly in cases involving workers whose only known risk factor was that they worked with an agent, or in an area where that work was done

Procedure Hazards

- Splash Hazards
- Working with animals (bites, scratches, exposure to zoonotics, another source of aerosols)
- Sharps (needles, dissecting tools, razor blades, and good sharps practices)
- Agent concentration and volumes worked with in the procedure
- Complexity of the proposed procedures
  - How many manipulations?
  - Is transportation of the agent required?
  - Injections vs just culturing?
  - Are there genetic manipulations/alterations involved?
  - Are other hazards involved (chemicals, radiation, etc.)? These can divide focus, possibly be a source for error.

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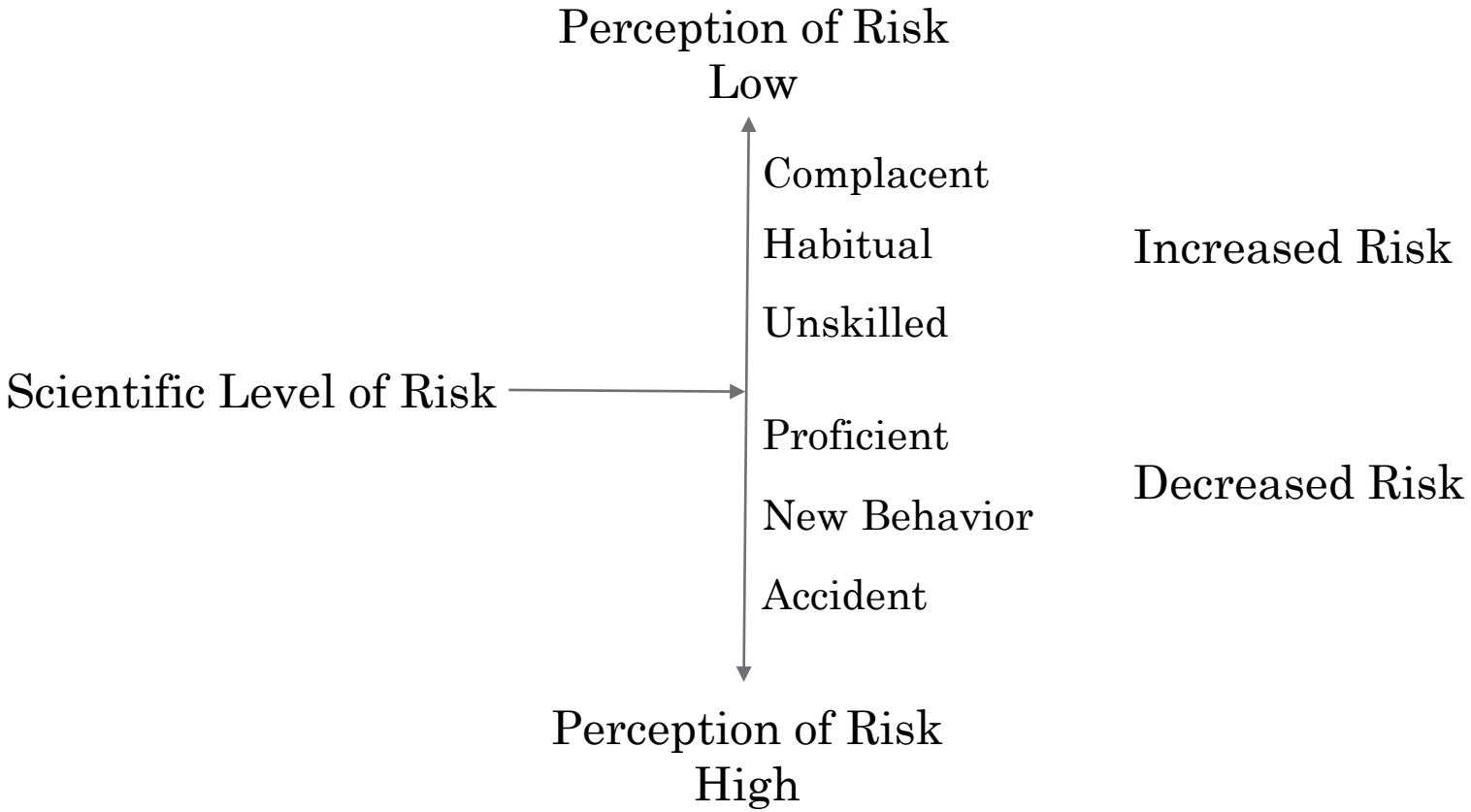
Evaluation of Laboratory Personnel



"It's often not what you don't know that gets you in trouble. It's what you don't do about what you know that gets you into trouble." Dr. Bob Ellis

Slide Credit: Sean Kaufman

Risk Assessment: A Plan

1. Identify Agent Hazards and do an initial Risk Assessment.
2. Identify the protocol-specific, laboratory procedure hazards.
3. Make a determination of the appropriate Biosafety Level at which the work can be conducted safely.
4. Evaluate the proficiencies of the staff, and the integrity of the safety equipment.
5. Review completed Risk Assessment.

What is the best Biosafety Movie?

What is the best Biosafety Movie?

- JAWS!
  - Rule #1: There is always a shark.
  - Rule #2: There is more than one shark in the ocean.
  - Rule #3: Not all sharks pose the same risk, so categorize your sharks.
  - Rule #4: More people are stung by jellyfish than are attacked by sharks.
  - Rule #5: You're going to need a bigger boat sometimes.

Credit: Jim Welch, the Elizabeth R. Griffin Foundation

BSL-1 vs. BSL-2

BSL-1

- for work with well defined and characterized strains of viable microorganisms not known to consistently cause disease in healthy adult humans
- basic level of containment that relies on standard microbiological practices
- no special primary or secondary barriers recommended, other than a sink for hand washing
- basic PPE requirements (gloves, lab coats and eye protection recommended as needed)

BSL-2

- for work with a broad spectrum of indigenous moderate-risk agents that are present in the community and associated with human disease of varying severity
- with good microbiological techniques, these agents can be used safely in activities conducted on the open bench, when potential for producing splashes or aerosols is low
- primary hazards to personnel are accidental percutaneous or mucous membrane exposures, or ingestion of infectious materials; procedures with aerosol or high splash potential must be conducted in primary containment equipment, such as a BSC
- PPE requirements: gloves, lab coats, gloves; splash shields, face protection, gowns, and additional PPE based on risk assessment
- waste decontamination facilities, must be available to reduce potential environmental contamination.

BL-P

- Physical and biological containment conditions for recombinant or synthetic nucleic acid molecule containing plants, plant-associated microorganisms, and small animals
- Describe greenhouse conduct of experiments
- Based on the recognition that the organisms used pose no threat to humans, or higher animals
- These containment levels are designed to minimize the possibility of an unanticipated deleterious effect on organisms and/or ecosystems outside the facility where the experiments are being conducted

BL1-P vs. BL2-P

BL1-P

- Access is limited or restricted (discretion of greenhouse manager)
- Records of experiments are kept
- Experimental organisms must be made biologically inactive before disposal
- Control undesired pests; properly house experimental pests

BL2-P

- Access is limited or restricted to those involved with the experiments
- Records of experiments and inventory must be kept
- Inadvertent releases or spills must be reported
- Experimental organisms must be made biologically inactive before disposal
- Periodic decontamination of flooring is required (if gravel); run-off water doesn't necessarily need to be decontaminated
- Must control undesired pests; properly house experimental pests
- Must have appropriate signage
- Careful transfer of experimental microorganisms
- Must have a greenhouse manual that outlines practices, contingencies, and plans if a release does happen
- Must have an autoclave in the greenhouse
- Design features are also outlined for screening, ventilation, etc.

Helpful chart for determining BL-P Category from A Practical Guide to Containment

Criteria	Tg Plant	Tg Exotic Microbe	Tg Non-Exotic Microbe
Not noxious weed/cannot outcross with one	BL1-P		
Not easily disseminated			BL1-P
No detriment to environment		BL2-P or BL1-P+	BL1-P
Noxious weed/can interbreed	BL2-P or BL1-P+		
Contains complete genome of non-Exotic Infectious Agent	BL2-P or BL1-P+		
Contains genome of EIA*	BL3-P or BL2-P+		
Treated with EIA	BL3-P or BL2-P+		
Detriment to environment			BL2-P or BL-1P+
EIA with detriment to environment	BL3-P or BL2-P+		
May reconstitute genome of infectious agent in planta	BL3-P or BL2-P+		
Contains vertebrate toxin	BL3-P	BL3-P	BL3-P
PMP and PMI (drugs, chemicals)	BL3-P		
Select agent plant pathogen	BL-3P		

*EIA= Exotic infectious Agent

Credit: Dan Adair and Ruth Irwin

What does the “+” mean in BL2-P+?

- Biological Control methods
- Definition: the use of biological means to block plant sexual and vegetative reproduction and to prevent the spread and persistence of genetic material in the environment
- Adds another layer of containment that may result in the overall biosafety level being lowered
- Examples:
  - Gene expression limitation to non-reproductive parts of plants
  - Producing Tg plants with sterile seeds
  - Covering or preventing pollen dissemination from Tg plants
  - Using experimental plants/pests when plants are not growing in the natural environment
  - Use experimental hosts/pests in the absence of natural vectors
  - Make experimental pests disabled so as to minimize their survival in the environment
  - Make arthropods non-flying/sterile
  - Chemically treat run-off water to prevent escape of organisms

References

- Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules, U.S. Department of Health and Human Services, National Institutes of Health. 59 FR 34496
- Biosafety in Microbiological and Biomedical Laboratories, 5th Ed., U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention
- 2014 Biosafety and Biosecurity Training Course Material, Dr. Bob Ellis – Organizer
- A Practical Guide to Containment: Plant Biosafety in Research Greenhouses (2008); Dan Adair and Ruth Irwin