



The Rational Investigation into Safety and Containment as Applied to the Laboratory Environment

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Abstract

This presentation defines the various components of a risk assessment and explains the role of the risk assessment in the risk management process. The rationale component, the investigative component, the safety component, and the containment component are discussed. Components are based on an industrial hygiene approach (anticipation, recognition, evaluation, control) to evaluate hazards in the workplace. An effective, risk assessment process is an essential tool to maintain the management of risk. This presentation creates a management tool for the assumption of risk for PIs, safety professionals, process managers, and personnel with oversight in pharmaceutical, healthcare, and other industrial processes.

Introduction

What is risk? In short, risk can be defined as the degree of probability of an unwanted event (a hazard) given a defined set of circumstances (University of Western Sydney, 2004). The assessment of risk is the formal and systematic analysis to identify and quantify probabilities and consequences for personnel, environment, production, etc., given unwanted events (Bureau Veritas). The information obtained through risk assessments is then evaluated to determine if the assessed risk needs to be reduced to protect public health and the environment. The Biosafety Professional must decide the means to reduce

that risk if such action is required. This decision-making process defines Risk Management (U.S. Army Corps of Engineers, 2004).

From a health and safety point of view, risk assessment is composed of hazard identification, dose-response assessment, exposure assessment, and risk characterization (Nelson, 1997) while risk management consists of developing regulatory options and evaluating public health and technical considerations. It also considers the economic, social, and political consequences of these regulatory options (Nelson, 1997).

The following describes a management tool to be used when performing risk assessments. This tool will assist in the identification and anticipation of potential hazards; aid in the recognition of safety and containment deficiencies; quantify and rank hazards based on severity; and explore actions that can be implemented to reduce the hazard to an acceptable level. Questions regarding when and how risk assessments should be performed, what benefit risk assessments provide, and the risk assessment role in the risk management process will be reviewed.

Discussion

An effective risk management program should consist of the following six components, which are discussed in more detail below:

1. Hazard identification and evaluation

2. Hazard ranking according to risk
3. Management decision making
4. Establishing preventive and corrective measures
5. Monitoring
6. Evaluating program effectiveness (Krieger, 1997)

1. Hazard Identification and Evaluation

The first component in a successful risk management program is to identify and evaluate all workplace hazards by understanding all procedures and processes, safety and containment, and agents and chemicals used (Knudsen, 2000) (Table 1: Agent Risk Factors). Biological agent information as well as safety and containment recommendations can be obtained through published materials. These include:

- The CDC/NIH publication *Biosafety in Microbiological and Biomedical Laboratories (BMBL)*, 4th edition, www.cdc.gov/od/ohs/biosfty/bmbl/bmbl-1.htm
- *NIH Guidelines for Research Involving Recombinant*

DNA Molecules, www4.od.nih.gov/oba/rac/guidelines/guidelines.html

- *Biological Safety: Principles and Practices*, 3rd edition, edited by D. O. Fleming and D. L. Hunt. ASM Press, Washington, DC, 2000.
- Health Canada's web sites for Material Safety Data Sheets (MSDS) of biological agents, www.hc-sc.gc.ca/pphb-dgsp/msds-ftss/
- Health Canada's *Laboratory Biosafety Guidelines*, www.hc-sc.gc.ca/pphb-dgsp/publicat/lbg-ldmbl-96/index.html
- Accident reports from medical journals

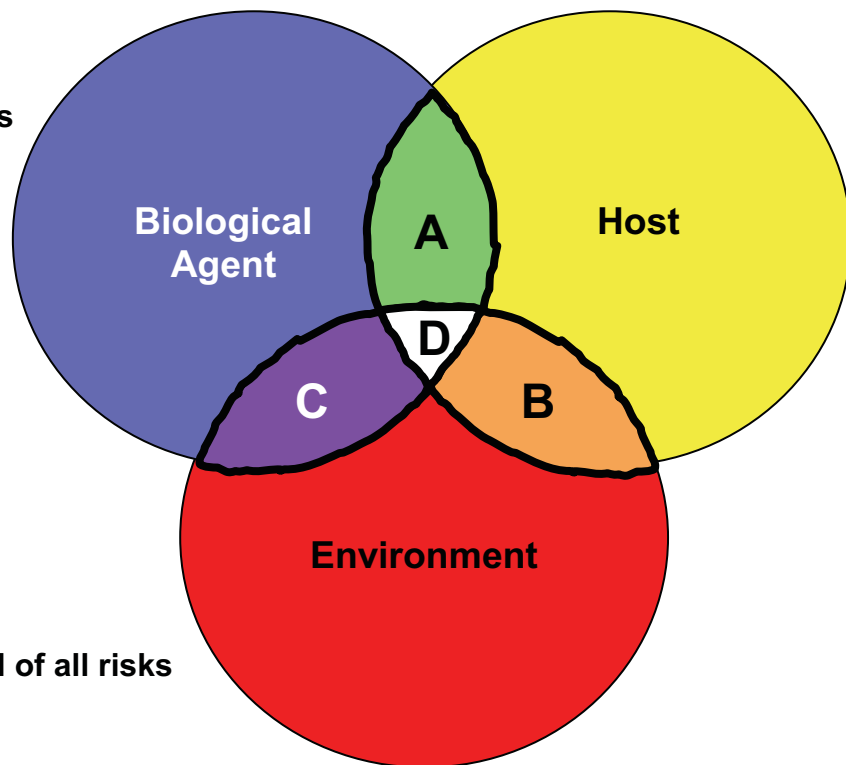
In performing a risk assessment, each step in the handling of a biological agent is scrutinized by the biosafety professional/risk manager as both an independent event and as a part of the entire process. The process should examine the interactions between the biological agent, the host, and the environment (Johnson, 2001). The Venn diagram (Figure 1) illustrates these interactions (Johnson,

Figure 1

Risk Assessment Factors

Risk Assessment Factors

- A. Mode of Transmission
- B. Perception of Risk
- C. Facility Design



Summation and Control of all risks

$$\sum [\text{Bio Agent (A+C)} + \text{Host (A+B)} + \text{Environment (B+C)}] = \text{D}$$

D = Risk Management

Table 1

Agent Risk Factors	Description
1. Agent ID, Characterization	If determined and well characterized, then published biosafety levels and disease information should be employed. If determined but not well characterized, examine data on similar microbial agents within the same family. Examine clinical literature for presumptive transmissibility as well as signs and symptoms of disease. If undetermined, examine field outbreak data if available. Assume high risk to laboratory worker.
2. Pathogenicity	The ability to cause disease; varies with subtype, strain and antimicrobial resistance.
3. Virulence	The degree of pathogenicity; depends on the agent's ability to infect, the severity of the disease, transmissibility, etc.
4. Infectious Dose	If available from studies on humans, examine all routes of infection. If unavailable, use animal models as a guide. Note: animal model data may or may not be relevant to humans.
5. Severity of Disease	The greater the severity, the greater the risk to laboratory workers and often means the greater the biological safety level (BSL). The BSL also looks at transmissibility of the agent.
6. Regulatory Requirements	CDC Import permit—if the agent is a human pathogen and comes from a foreign country. USDA permit—if the agent is a livestock or poultry pathogen imported or transferred domestically. CDC and/or USDA Registration- for the possession use or transfer of select agents or toxins. OSHA- Special practices and procedures for working with bloodborne pathogens in the laboratory. NIH rDNA- for funded NIH work
7. Host Range	Humans, animals, insects.
8. Laboratory Sample	Clinical, diagnostic or environmental samples pose a less risk before they are concentrated. Concentrated agents pose a higher risk to laboratory workers.
9. Laboratory Animals	The risk is in the ability of the animal to transmit the agent (bite, scratch, urine, feces, contaminated bedding or water).
10. Insect Vectors	Strict entity insect control program and special containment processes.
11. Transmission Potential	Can the agent be transmitted from the sample to the worker (aerosol, ingestion, mucous membrane exposure or parenteral inoculation)?
12. Susceptible Route	Dependent on the infecting agent. If not documented, then assume the agent can be transmitted by multiple routes.
13. Susceptible Host	Susceptibility of an agent depends upon age of host, current health, immune status of host, etc.
14. Prophylaxis	The most effective way of reducing susceptibility to an agent is through vaccination. Note: Immunity after vaccination declines over time necessitating a surveillance program to include revaccinations.
15. Treatment	The availability of effective treatment after an exposure minimizes the risk to the worker.
16. Skill Level	The greater the knowledge and experience of a worker in working with an agent along with the biological safety training and safe work practices employed significantly influences the level of risk.

Knudsen, R. C. (2000). *Risk Assessment for Working with Infectious Agents in the Biological Laboratory*. In J. Y. Richmond (Ed.), pp. 1-10. Anthology of Biosafety III: Application of Principles. Mundelein, IL: American Biological Safety Association.

Table 2
Facility Considerations

Facility Risk Factors	Description
1. Is the work with potentially infectious material? Is the mode of transmission via aerosol? Is the mode of transmission via direct contact?	<p>Aerosolization transmission: Provide appropriate containment (sealed centrifuge cups and rotors, use non breakable materials for work with the agent as well as transporting the agent).</p> <p>Biological Safety Cabinets: Properly functioning BSCs Class II or Class III, BSC annual certification</p> <p>Security/Facility requirements: Restricted access to area and/or agent, double door entry, sink present inside each laboratory room, eyewash area readily available, sealed penetrations, log of entry and exit, electronic locking mechanism to area, biometric readers, motion sensors, video surveillance, lockable cabinets and/or equipment.</p> <p>Special ventilation requirements: Directional airflow, visual monitoring devices to indicate directional air, HEPA filtration of room Exhaust, single-pass air, audible alarm system to warn of HVAC failure, Supply tied into Exhaust to prevent positive pressure of room if exhaust system failure, Emergency power back-up, Redundant exhausts. Waste decontamination and sterilization process available.</p> <p>Direct contact transmission: Provide hands-free sinks.</p>
2. Is work with infected animals expected?	<p>Special ventilation requirements: HEPA filtration of exhaust air at minimum, directional air, visual device to indicate directional air, Supply tied into Exhaust to prevent positive pressure of room if exhaust system failure, Emergency power back-up, Redundant exhausts.</p> <p>Facility design: Separated from unrestricted personnel traffic, Double door entry (self-closing, self-locking), doors to animal rooms open inward, sink present inside each infected animal room and may require hands-free operation, sealed penetrations, may require shower facilities, cage washing area (may require mechanical means), waste decontamination and sterilization processes in place.</p> <p>Security requirements: Restricted access to area and/or agent, log of entry and exit, electronic locking mechanism to area, biometric readers, motion sensors, video surveillance, lockable cabinets and/or equipment.</p> <p>Biological Safety Cabinets: Proper functioning BSCs Class II or Class III, BSC annual certification.</p>
3. What are the anticipated guidelines/regulations?	<p>CDC/NIH Biosafety in Microbiological and Biomedical Laboratories, OSHA General Laboratory Standard 29 CFR 1910.1450, OSHA Bloodborne Pathogens 29 CFR 1910.1030, DHHS Possession, Use and Transfer of Select Agents and Toxins; Interim Final Rule 42 CFR Part 73, DOD The Biological Defense Safety Program Title 32 Parts 626 & 627 World Health Organization Local and State Regulations.</p>
4. Is there risk to support staff, other lab personnel or public?	<p>Laboratory location is separated from areas that are open to unrestricted traffic flow. Transportation routes for biological agents should not be in public access corridors. The transportation of agents in a durable leak-proof container that has been appropriate decontaminated prior to it leaving the laboratory. Single-pass HEPA filtered exhaust air for the laboratory. Restrict access to areas containing the agent (lab and storage rooms) and to equipment used to contain the agent (freezers, incubators and lab room exhaust systems).</p>
5. Are the appropriate sterilization and decontamination equipment present inside the lab area?	<p>Yes; Are routine maintenance schedules performed on such equipment (autoclaves)? There should be scheduled efficacy testing of the autoclaves (spore testing and heat and pressure tests). Decontamination solutions should be made up on a regular basis. Spill procedures should be developed and posted.</p> <p>No; The waste must be transported in a durable leak-proof container that has been appropriately decontaminated prior to it leaving the laboratory. The waste should not be transported through public corridors. If waste is stored in another location, that location should have controlled access and special consideration to install single-pass exhaust (and HEPA depending on the agents used). The storage area should have spill procedures posted.</p>

Hunt, D. L. (1997). *Design Issues at the Management/Facility*. In J. Y. Richmond (Ed.), pp. 25-43. Anthology of Biosafety I. Perspectives on Laboratory Design. Mundelein, IL: American Biological Safety Association.

2001). These interactions can be viewed as individual risk assessments. For example, the interaction between the biological agent and the environment relies heavily on facility design. The facility design is based on the characterization of the biological agent (Knudsen, 2000) (Table 1), and the environmental and regulatory requirements (Hunt, 1997) (Table 2). In both tables, each risk factor is determined from its own risk assessment. The culmination of risk assessments and their interactions create the central triangle in the Venn diagram. The ability to administer effective controls over the interaction of the biological agent, the host, and the environment is considered risk management.

2. Hazard Ranking According to Risk

Once the risk assessments have been performed, the hazards should then be ranked based upon the severity, probability, and exposure potential beginning with the worst case (Krieger, 1997). The numerical hazard ranking system described below can be used to rate the significance of various identified risks:

A. Consequence

Consequence should be based on severity of the identified hazard and assigned numerical values as follows:

1. Negligible (no injury or illness)
2. Marginal (minor injury or illness)
3. Critical (severe injury or illness)
4. Catastrophic (loss of life)

B. Probability

Probability should consider the chance that things will go wrong when the task is performed and assigned the following numerical value:

1. Low chance of negative occurrence
2. Moderate chance of negative occurrence
3. High chance of negative occurrence

C. Exposure

When evaluating exposure, one should consider both the frequency of performing a task and the number of individuals performing the task. The fol-

lowing numerical values can be assigned for potential exposure:

1. Few people performing the task a few times per day
2. Few people performing the task frequently
3. Many people performing the task frequently

To derive a composite hazard ranking, add up the three components for each evaluated task. The overall score will be between 3 and 10. The greater the overall score, the greater the risk will be to the worker and the environment. This hazard ranking allows the biosafety professional to prioritize corrective measures based on potential severity given current work conditions.

3. Management Decision Making

The numerical values obtained from the hazard ranking allow management to determine which tasks pose the greatest potential hazard (i.e., the greater the hazard ranking number, the greater potential risk).

The decision-making component of the risk management process describes corrective actions or control measures for each task. Such actions may involve additional training of personnel, better methods and procedures to characterize biological agents (Table 1) (Knudsen, 2000), equipment repair or replacement, environmental controls, and laboratory redesign (Table 2) (Hunt, 1997).

4. Establishing Preventive and Corrective Measures

After the control measures have been determined, those measures then need to be implemented. The best way to control a hazard is at the hazard source (i.e., substitution of a nonvirulent strain of an organism in place of a virulent strain). Another way to control a hazard is along its path (e.g., use of sealed centrifuge cups to prevent aerosolization of the hazard). The final way to control a hazard is at the receiver. A primary example would be to require researchers to use personal protective equipment when working with hazardous agents. The three types of control measures are:

1. *Administrative controls*: training and education, security requirements, maintenance, purchasing and housekeeping
2. *Engineering controls*: HVAC monitoring controls and warnings, laboratory design, Security and BSC selection
3. *Personal Protective Equipment (PPE)*: respirators, gloves, lab coats, aprons, etc.

The implementing of controls should be in the order listed above. Notice that PPE should be used for controlling hazards only as a last resort. This is because nothing has been done to eliminate the hazard. If the PPE should fail, the worker is exposed directly to the hazard and the PPE may restrict the worker's ability to perform certain tasks.

5. Monitoring

Monitoring of risk and/or potential hazards is an often overlooked phase of the risk management process. Monitoring consists of the continual evaluation of activities to identify new hazards and assess the effectiveness of existing controls.

6. Evaluating Program Effectiveness

A risk management program is only as effective as its implementation. The biosafety professional or risk manager needs to institute a mechanism to evaluate the effectiveness of the program. The evaluation should address the benefits of the program and the impact of those benefits. These benefits may include:

1. Maximizing the effective use of available resources
2. Pointing out training needs and areas of supervision
3. Developing an effective procedural evaluation tool
4. Assisting in preventing exposure situations
5. Ensuring compliance with governmental regulations
6. Providing justification for space and/or equipment
7. Evaluating costs associated with operations
8. Aiding in the evaluation of security, contain-

ment, emergency response, and training (Tipple et al., 1998)

These benefits strengthen the risk management triangle. However, those benefits should be reviewed at least annually or whenever any laboratory changes occur. Examples of changes that may affect the impact of the benefit include:

1. Moving to a new location or facility renovation
2. Hiring a new employee
3. Beginning work with new infectious agents or chemicals
4. Obtaining a new piece of laboratory equipment (e.g., BSC)
5. Instituting a new SOP (Tipple et al., 1998)

In these instances, a risk assessment of each derivation would be needed in order to determine if the same level of benefit is maintained.

Conclusion

The ability of a laboratory to operate safely depends upon how well each hazard is defined, characterized, and controlled. The mechanism of obtaining answers to these questions is through risk assessments. Risk assessments allow the biosafety professional to quantify and rank both real and potential hazards given a defined task. The sum of all risks defines the hazard level. Risk management examines those risks, weighs the benefit to cost, and develops corrective measures to maximize risk reduction. The Risk Management triangle (Figure 1) is that focal point which combines the three main factors associated with laboratory risk (Biological Agent, Host, Environment) and creates controls that uniformly reduce hazards while maximizing benefits.

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