BIOSAFETY RISK ASSESSMENT GUIDELINES v.11.13.13

The primary goal of a Biosafety risk assessment is to identify and mitigate risk. A second equally important facet of the process is documentation of compliance to the standards of good science as set by regulatory bodies.

Risk analysis involves not only identifying the hazards but evaluating the hazards in terms of probability of occurrence and determining the impact should the hazard not be addressed. The ultimate objective is to implement appropriate measures to reduce the risk, as appropriate. When applied to biological agents (human, animal, zoonotic or plant pathogens) the risk may be increased or reduced, depending on the nature of the experimental work, containment available and a variety of factors as outlined below.

The benefits of undertaking a biosafety risk assessment are:

- Safeguarding the health and safety of lab personnel.
- Preventing the accidental release or contamination of research samples; and
- Demonstration of due diligence and compliance.

Other benefits include:

- Identification of training and supervision needs;
- Evaluation of procedural changes;
- Justification for space and equipment needs;
- Evaluating security controls; and
- Evaluation of emergency planning, including spill response.

Frequency of Risk Assessment:

The preferred timing of a risk assessment coincides with:

- Planning the research project,
- A significant change in the project (new employees, a new infectious, or potentially infectious agent, new procedures or technique, new equipment, a relocation of activities, or during/after renovations), or
- Upon BAF renewal (more frequent depending upon nature of risk).

Qualifications for a Risk Assessor:

The principal investigator and their employees are in the best position to evaluate the potential or existing risk associated with their research and laboratory practices. The qualifications required by these individuals and others mandated to under take a risk assessment are:

- An understanding of the relationship between personnel, operational procedures, agent specific risk, work flow, and facility design;

- Knowledge of the hazards associated with the material (pathogenicity, infectious dose, mode of transmission, environmental stability etc.);
- Knowledge of the procedures and techniques which present risk ; and
- Knowledge of containment requirements, national standards and guidelines.

Activities and tools to assist in a risk assessment are:

- Reviewing published materials (MSDS, scientific journals, published safety manuals, manufacturer's bulletins, newsletters, equipment manuals),
- Reviewing laboratory records (injury or incident, equipment maintenance, training, environmental monitoring),
- Inspecting laboratories (daily monitoring by employees, periodic walk through, formal inspections),
- Observing laboratory operations (new procedures, new employees, new equipments, work-flow),
- Consulting biosafety professionals (biosafety officers, infection control specialists, experts in specific fields (technical/procedural, virologists, bacteriologist etc.), and
- Reviewing reports of laboratory associated infections (LAI).

Factors Affecting Risk:

The main areas that need to be considered when undertaking a risk assessment are:

1. Agent characteristics
2. Personnel factors
3. Experimental factors
4. Environmental factors
5. Equipment

1) Agent Characteristics

Not all agents pose the same degree of risk, and depending upon the nature of the risk engineering or procedural changes can greatly reduce the risk. The analysis may become more challenging in the cases of emerging pathogens, genetically modified organisms, or when vectors are involved. There are 11 risk factors that need to be considered, and these address the agent's characteristics and potential impacts under certain environmental conditions, or when modifications are introduced. These are summarized below, while the "Risk Assessment Associated with Agent Characteristics" outlines in greater detail the influencing factors.

Pathogenicity /virulence	*Infectious Dose*	*Mode of transmission*
Transmissibility	*Environmental Stability*	*Host Range*
Endemicity	*Economic Considerations*	*Vectors*
Recombinants	*Availability of Prophylactic and therapeutic treatments*	

2) Personnel

Although engineering, procedural and administrative controls can help mitigate risk; the degree of understanding, diligence and compliance by the individual can undermine these primary controls. The health status of an individual can greatly influence the outcome of a personal exposure. In order to identify and minimize the risk of human error or exposure a number of factors should be considered.

- Level of training and experience (in general, and specific to the procedure or agent),
- Competency level and demonstration of diligence,
- Health status,
- Use of personal protective equipment,
- Allergies (determines vaccination restrictions), and
- Availability of prophylaxis and first aid.

3) Experimental Factors

Numerous experimental procedures can introduce the potential for risk. Often each procedure is viewed as only one step in the process, and not reviewed independently for the potential of risk. These include:

- Aerosol generating activities (pipetting, vortexing, centrifuging…),
- Potential for self-inoculation (recapping needles, disposal of sharps...),
- Concentration of samples.
- Nature of sample (clinical, pure culture, previously manipulated),
- Volume of pathogen,
- Animal use (species, potential viral shredding, bites, scratches),
- Cell line characteristics,
- Toxin production,
- Vector use,
- Contingency plan (exposure, spill, accidental release, equipment failure),

- Techniques (cryogenics, cell sorting …), and
- Decontamination procedures.

4) Environmental

The environment can be considered the work area, laboratory, and facility. Should a release of the agent occur which impacts the larger general environment; an additional risk assessment will be required. Factors to be considered are modes of transmission, environmental stability and spread of contaminated material. From a laboratory perspective issues to be considered are:

- Level of containment (required, available)
- Factors affecting containment (air flow, pressurization, certification)
- Impact of external activities (construction, traffic flow, new routes of egress)
- Biosecurity (access and inventory control)
- Lab facility conditions (clean, non-porous benches...)
- Availability and status of emergency support (first aid, eye wash, spill kits …)
- Housekeeping and trades personnel (trained, procedures)
- Access by public (students, visitors, trades personnel)

5) Equipment

The last factor to consider is how equipment may actually increase the risk of an exposure of spill. Factors to consider area:

- Equipment maintenance (frequency and status),
- Periodic decontamination (incubators, centrifuge etc.),
- Training and correct operation of equipment (compliance to manufactures recommendations),
- Equipment specific hazards (centrifuges, homogenizer, autoclaves),
- Standard operating procedures,
- Ventilation considerations, and
- Location within lab or adjoining labs.

The Final Step (Implementation and Documentation):

All activities summarized above identify and require risk analysis. To attain the goal of a risk assessment, one must identify and implement changes which reduce the hazard. When the ideal solution is not feasible (due to financial, operation or logistical constraints), and the risk can be reduced to an acceptable level by other means the secondary recommended approach can be implemented.

It is important to document your findings for a variety of reasons:

1. To document the steps taken to identify and reduce risk,
2. To provide a point of reference for future assessments; this will greatly reduce future time requirements,
3. Justifies restricting assessments to just those elements which have changed, and
4. To provide records which demonstrate diligence and compliance.

Biosafety Risk Assessment

For more information on Risk Assessment see Supplemental Resource F at the end of this document.

Principal Investigator: _____

Approved by: (signature of Principal Investigator) _____

Date of Risk Assessment: _____

Risk Assessment undertaken by: _____

Action required completed on: _____

Signature above indicates that the Risk assessment has been reviewed by the PI and all needed changes have been incorporated into the Biosafety Manual

SECTION A: AGENT CHARACTERIZATION

Research Activity (BAF#)	**Title & Brief Description of Research Activity** (attach second page if required)	**Biohazardous Materials in use**	**Overall Risk Group** Based on Factor Analysis (see supplemental resources F for more information)

Part B: Personnel Factors

Research Personnel ***B - Beginning,** **I - Intermediate,** **A – Advanced**	**Name:**	**Name:**	**Name:**	**Name:**	**Name:**	**Name:**
Biosafety training Date completed						
SOP training Date completed						
Health Assessment (immunosuppressed)	☐Completed	☐Completed	☐Completed	☐Completed	☐Completed	☐Completed
Experience with the Agent (B, I, A)*						
MSDS read (y/n)						
Experience with the procedures (B, I, A)*						
Use of PPE training Date completed						
Job hazard analysis undertaken (y/n)						
Allergies (animal, environmental)	☐Assessment Completed	☐Assessment Completed	☐Assessment Completed	☐Assessment Completed	☐Assessment Completed	☐Assessment Completed

Part C: Experimental Factors	Examples	Comments	Action Required (Y/N) (specify action)
Aerosol generating potential	☐centrifuging, ☐vortexing, ☐homogenizing, ☐flaming loops ☐shaking, ☐other		Y, done in aerosol resistant containers
Potential for self-inoculation (needle stick, lesion)	☐recapping, ☐incorrect disposal of sharps ☐ other		
Sample origin and concentration	Origin: ☐clinical, ☐pure culture, ☐ previously manipulated, ☐characterized, concentration		
Volume of pathogen used	☐ >10L large scale, max. volume		
Animal use (types, potential viral shedding, bites and scratches)			
Replication competency	☐low, ☐medium, ☐high		
Recombinants	Inserted gene is an ☐oncogene, ☐alters cell cycle, ☐integrates with host DNA,		
Cell line characteristics	☐established, ☐new ☐attenuated ☐non-replicating (documented)		
Toxin production (y/n, MSDS))			
Modification of pathogen (y/n, result / implication)			
Vector use (y/n, describe)			
Inventory Records	☐centralized, catalogued by ☐agent, ☐user, ☐location, ☐searchable		
Contingency plan (exposure, accidental releases / spills)	☐written, ☐included in biosafety manual, ☐posted in work area		
Techniques – cryogenics, cytometry			
Disinfectant used as directed	☐appropriate for agent, ☐concentration ☐ contact time		

Part D: Environmental Factors		Comments	Action Required (Y/N) (specify action)
Level of containment available	☐as per regulations, ☐status not compromised due to age or use		

Degree of monitoring of containment factors	☐air flow /☐ pressurization, ☐biological safety cabinet, ☐certification		
Impact of external activities	☐construction altering pressure differentials, ☐new routes of egress created, ☐increase traffic by the public		
Biosecurity (access and inventory control)	☐appropriate level of security in place		
Availability and status of emergency support	☐eye wash, ☐first aid, ☐ spill kits		
Housekeeping and Trades Personnel	☐trained, ☐procedures		
Access by public	☐students, ☐visitors, ☐trades personnel		

Part E: Equipment Factors		**Comments**	**Action Required (Y/N) (specify action)**
Equipment Maintenance (frequency, status)	☐centrifuge, ☐pumps, ☐aspirators, ☐autoclaves ☐cell cytometers		
Manual	☐available and ☐ used		
Reservoirs empty &disinfected	☐aspirators, ☐tubing clean		
Standard Operating Procedures	☐Biosafety Manual read and available to all in work area		
Location of use	☐consideration of room ventilation, ☐ow traffic area ☐minimal transport		
Ventilation Consideration	☐Potential disruption of biological safety cabinets.		

Overall Biological Risk Group - Based on Risk Factor Analysis

When assessing a biological agent specific risk, consider the following: pathogenicity, transmission, endemicity, the impact (health and economic) and the availability for prophylactic or therapeutic treatments.

The tables below summarize in general terms, factors to be considered and provide a rating scale which helps in determining the potential risk. A risk level one represents a minimal risk category, where as a risk level four indicates a very high potential risk to health or the economy. By considering each factor and assigning a risk level to each; one can quickly determine the overall risk level for an agent. This information can then be entered into the WSU risk management grid to help determine when engineering and procedural controls should be implemented to reduce risk.

Table 1: Risk Summary Table

Risk Factor	Risk Group	Risk Factor	Risk Group	Risk Factor	Risk Group
Pathogenicity /virulence		Infectious Dose		Mode of transmission	
Transmissibility		Environmental Stability		Host Range	
Endemicity		Economic Considerations		Vectors	
Recombinants		Availability of Prophylactic and therapeutic treatments		**Overall Risk Group**	

Table 2: Risk Factor Assessment Table

Risk Factor	Risk Level 1	Risk Level 2	Risk Level 3	Risk Level 4
Pathogenicity / Virulence	Unlikely to cause disease, low individual and community risk	Mild or moderate disease, moderate individual risk, low community risk, any pathogen that can cause disease but under normal circumstances, is unlikely to be a serious hazard to a healthy laboratory worker, the community, livestock or the environment	Serious livestock, poultry or wildlife disease; high individual risk, low community risk: any pathogen that usually causes serious disease or can result in serious economic consequences or does not ordinarily spread by causal contact form one individual to another	Severe livestock, poultry or wildlife disease / high individual risk, high community risk, also causes human disease, any pathogen that usually produces very serious and often fatal disease, often untreatable and may be readily transmitted form one individual to another, or from animal to human or vice-versa, directly or indirectly, or by casual contact.
Infectious Dose	Not applicable (not known to cause disease in healthy adults)	Variable or high (1,000-5,000 organisms or greater)	Medium (10 –1,000 organisms)	High (1-10 organisms)
Mode of Transmission / Route of Infection	Not applicable (not known to cause disease in normal healthy adult plants or animals)	Primary exposure hazards are through ingestion, inoculation and mucous membrane route (not generally through the airborne route)	May be transmitted through airborne route; direct contact; vectors	Readily transmitted, potential for aerosol transmission
Risk Factor	**Risk Level 1**	**Risk Level 2**	**Risk Level 3**	**Risk Level 4**
Ability to Spread / Transmission / Communicability	Not applicable (not known to cause disease in normal	Geographical risk of spread if released form the laboratory is limited,	Geographical risk of spread if released from the laboratory	Geographical risk of spread if released from the laboratory is

	healthy adult plants or animals)	very limited or no transmission is relatively limited	is moderate, direct animal to animal or human to human transmission occurs relatively easily – transmission between different animal species may readily occur	widespread
Environmental Stability	Not applicable	Short term survival (days); can survive under ideal conditions	Resistant (days to months)	Highly resistant (months to years) e.g. spores
Host Range	Not applicable (not known to cause disease)	Infects a limited number of species	Infects multiple species	Infects many species of animals/plants
Endemicity	Enzootic	Generally enzootic (some low-risk exotics,zoonotics or reportable diseases)	Exotic, zoonotic or enzootic but subject to official control	Exotic
Economic aspects of introduction and/or release into the environment of the public	No economic and /or clinical significance	Limited economic and/or clinical significance	Severe economic and/or clinical significance	Extremely severe economic and/or clinical significance
Risk Factor	**Risk Level 1**	**Risk Level 2**	**Risk Level 3**	**Risk Level 4**
Availability of prophylactic and therapeutic treatments	Not applicable (not known to cause disease)	Effective treatment and preventive measures are available	Prophylactic and /or treatments may or may not be readily available (or of limited benefit)	Prophylactic and/or treatments are not usually available

Disease Transmission Vectors	Not applicable (not known to cause disease)	Do not depend on vectors or intermediate hosts for transmission May depend on vectors or intermediate host for transmission	May depend on vectors or intermediate host for transmission	May depend on vectors or intermediate host for transmission
Risk Factor	**Risk Level 1**	**Risk Level 2**	**Risk Level 3**	**Risk Level 4**

Recombinants	The recombinant is a risk group 1 organism; modifications have not changed the risk	The recombinant is a risk group 2 organism; modifications have not changed the risk - DNA from risk group 2 or 3 organism is transferred into risk group 1 organism: but not the whole genome. - DNA from risk group 4 organism is transferred into risk group 1 organism (only after demonstration of a totally and irreversible defective fraction of the organism genome is present in the recombinant. - The recombinant is a risk group 3 or 4 organism; however, the modification has resulted in proven attenuation.	The recombinant is a risk group 3 organism and modifications have not changed the risk - The recombinant is based on a risk group 2 organism, however, the modifications have increased the risk group to a 3.	The recombinant is a risk group 4 organism; modifications have not changed the risk - DNA from risk group 4 organisms is transferred into a risk group 1 organism in the without being able to demonstrate a lack of virulence or pathogenicity.

Recombinants Continued**:** Consider the effect of the modification on all previous 10 risk factors; plus the NIH Guidelines provide standard risk group assessment based on the modifications. A comprehensive look at the effect of the modification is required.

Consideration to be made include:

Does the inserted material increase virulence or decrease the effectiveness of any anti-infective agents?
Does the inserted gene encode a known toxin or a relatively uncharacterized toxin?
Does the modification have the potential to alter the host range or cell tropism of the virus?
Does the modification have the potential to increase the replication capacity of the virus?
Does the inserted gene encode a known oncogene?
Does the inserted gene have the potential for altering the cell cycle?
Does the viral DNA integrate into the host genome?
What is the probability of generating replication –competent viruses?
If the modification has resulted in a form of attenuation, how extensively has this strain been utilized without incident and/or has the attenuation been proven in animal models?
Does the modification have an effect of increasing or decreasing the efficacy of available treatment or prophylaxis?

Rating of Risk Consequence and Probability

Each hazard / risk observed was rated according to possible consequence (Table 1) and probability (Table 2) according to the criteria listed in these Tables as follows:

Rating of Risk Consequences

Class	*Rating*	*Consequences*
4	**Catastrophic**	**People:** fatalities, evacuation outside site area **Environment:** irreversible, long-term damage outside site area **Business:** total loss: > $2 million Interruption: > 2 months image: severely damaged, > 1 week, national
io	**Critical**	**People:** serious injuries, effects outside site area **Environment:** reversible, short-term damage outside site area **Business:** total loss: > $100,000 - $2 million Interruption: > 2 – 8 weeks image: damaged, > 1 week, regional
2	**Marginal**	**People:** minor injuries, annoyance outside site area **Environment:** only site area effected **Business:** total loss: > $5,000 - $100,000 Interruption: > 1 – 2 weeks Image: < 1 week, local
1	**Negligible**	**People:** no effects **Environment:** only building effected **Business:** total loss: < $ 10,000 Interruption: > 1 week Image: no effects

Table 2 - Rating of Probability

Class	*Rating*	*Probability*	*Definition*
A	**Frequent**	**More than once a year**	**Likely to occur repeatedly in life cycle system**
B	**Moderate**	**Once per year**	**Likely to occur several times in life cycle system**
C	**Occasional**	**Once in 5 years**	**Likely to occur sometime in life cycle system**
D	**Rare**	**Once in 25 years (e.g. once in the life cycle of the system)**	**Not likely to occur in system life cycle, but possible**
E	**Unlikely**	**Once in 100 years**	**Will occur once in a lifetime of a site**

F	**Very Unlikely**	**Once in 1,000 years**	**Almost impossible to occur**

Risk Profile

Based on the previous general and specific observations, a risk profile is developed for this area, laboratory, or facility as follows. The hazards / risks in the gray zone are considered acceptable risks (although risk reduction is always a research goal); the hazards / risks in the white zone are not considered acceptable and need to be abated and improved. The numbers in the table refer to the Risk / Hazard Observations in the previous sections.

Risk Profile/Probability

Consequences / ***Probability***	Negligible 1	Marginal 2	Critical 3	Catastrophic 4
Frequent A				
Moderate B				
Occasional C				
Rare D				
Unlikely E				
Very Unlikely F				

Biosafety Risk Assessment Resources

PubMed	CABI Compendium	ProMed Mail	ABSA Risk Group
OIE Disease Cards	OIE Animal Diseases	Merck Vet Manual	BMBL
Foreign Animal Disease	Animal Health Australia	CDC Disease Information	Diseases Database

Acha PN, Szyfres B (Eds.). 2003. *Zoonoses and Communicable Diseases Common to Man and Animals*. 3rd Edition. Scientific and Technical Publication No. 580. Pan American Health Organization (WHO), Washington, D.C.

Beran GW, Steele JH, Benenson AS, Tsai TF, Fenner F, Torten M (Eds.). 1994. Handbook of Zoonoses. 2nd Edition. CRC Press, Washington, D.C.

Brown C and C. Bolin (Eds.). 2000. *Emerging Diseases of Animals*. ASM Press, Washington D.C.

Fleming, D. and D. Hunt (Eds). 2000. *Biological Safety: Principles and Practices*. 3rd edition. American Society for Microbiology, Washington, D.C.

Kahn C.M. (Ed). 2005. *Merck Veterinary Manual*. 9th edition. Merck & Co. Inc., Whitehouse Station, N.J.

Knudsen R.C. 1999. *Risk Assessment for Biological Agents in the Laboratory*. Journal of the American Biological Association. 3: 99-104.

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

Murphy FA, Gibbs APJ, Horzinek MC, Studdert MJ (Eds). 1999. *Field's Virology*. 3rd Edition. Lippincott Williams & Wilkins, Philadelphia, P.A.

Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH. 1999. *Manual of Clinical Microbiology*. 7th Edition. ASM Press Washington D.C.

Quinn PJ, Carter ME, Markey BK, Carter GR (Eds.). 2002. *Clinical Veterinary Microbiology*. Mosby International Limited, New York, N.Y.

Radostits, OM, Gay CC, Blood DC, Hinchcliff KW (Eds.). 2000. *Veterinary Medicine: A Textbook of the Diseases of Cattle, Sheep, Pigs, Goats and Horses*. 9th edition. W.B. Saunders Company Ltd., New York, NY.