SAND2011-8526P

Introduction to Biorisk Management
Algiers, Algeria

International Biological Threat Reduction
Sandia National Laboratories

SAND No. xxxx-xxxx
Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company,
for the United States Department of Energy's National Nuclear Security Administration
under contract DE-AC04-94AL85000.

PAGE BLANK

Table of Contents: Introduction to Biorisk Management

Agenda
Schedule 2
Learning Objectives: Introduction to Biorisk Management 3

Glossary
Glossary 4

Session 1 – Introduction to Laboratory Biorisk Management
Course Introduction and Overview 8
Key Components of Biorisk Management 19

Session 2 - Risk Assessment
Risk Assessment Presentation and Exercises 23
WIV Scenario 36
BioRAM 43

Session 3 - Mitigation
Risk Mitigation Presentation and Exercises 47

Session 4 - Performance
Performance presentation and Exercises 61
Performance Scenario 64
Introduction to CEN Standard Presentation 71

Course Summary
Summary 81

References
List of References xx
CEN Workshop Agreement 15793:2008 86

Course Schedule

8:30	**Welcome Message** **Course Introduction**
8:45	**Session 1 - Introduction to Biorisk Management**
9:50	**Break**
10:00	**Session 2 - Principles of Biorisk Assessment**
12:30	**Lunch Break**
1:00	**Session 2 – Principles of Risk Assessment – Continued**
2:30	**Break**
2:40	**Session 3 – Introduction to Biorisk Mitigation**
3:50	**Break**
4:00	**Session 4 – Biorisk Management Performance**
4:50	**Course wrap and summary**
5:00	**Course end**

Learning Objectives: Introduction to Biorisk Management

This lesson will expose students to the basic principles of laboratory biorisk management. By the end of the lesson, participants should be able to:

- Understand the need for laboratory biorisk management
- Understand and define the concepts of hazard, threat, and risk
- Be familiar with the AMP (Assessment, Mitigation, Performance) model for laboratory biorisk management
- Recognize basic aspects of the risk assessment process
- Be familiar with the major categories of biorisk mitigation measures
- Understand the concept of biorisk management system performance

These objectives form the foundation of the lesson materials and are reinforced through guided discussion sessions and interactive exercises.

Acronyms:

ABSL - Animal Biosafety Level
BSC - Biosafety Cabinet
BSL - Biosafety Level
HEPA - High Efficiency Particulate Air
HPAI - Highly Pathogenic Avian Influenza
IACUC - Institutional Animal Care and Use Committee
IBC - Institutional Biosafety Committee
IBTR - International Biological Threat Reduction
MDR - Multi-drug resistant
PCR - Polymerase Chain Reaction
PPE - Personal Protective Equipment
RT-PCR - Reverse transcriptase polymerase chain reaction
SNL - Sandia National Laboratories
UN - United Nations
WHO - World Health Organization

Glossary:

Aerosol - A substance consisting of very fine particles of a liquid or solid suspended in a gas.

Animal Biosafety Level - Combinations of laboratory practices and techniques, safety equipment, and laboratory facilities appropriate for the operations performed and are based on the potential hazards imposed by the agents used and for the laboratory function and activity in an area where animals are present.

Autoclave - An apparatus in which steam under pressure effects sterilization.

Biohazard - A biological agent, such as an infectious microorganism, that constitutes a threat to humans or to the environment.

Biosafety Cabinet - A device enclosed (except for necessary exhaust purposes) on three sides and top and bottom, designed to draw air inward by means of mechanical ventilation, operated with insertion of only the hands and arms of the user, and in which virulent pathogens are used. Biosafety Cabinets are classified as: Class I, Class II and Class III, each providing different levels of protection.

Biosafety Level - A combination of work practices, primary containment devices and construction technology to reduce the risk of exposure resulting in laboratory acquired infection or release of a microbe to the environment.

Biosafety Level 1 – Represents a basic level of containment that relies on standard microbiological practices with no special primary or secondary barriers recommended, other than a sink for hand washing.

Agents that can be worked with at BSL1: Microorganisms not known to cause disease in healthy adult humans

Biosafety Level 2 – Similar to Biosafety Level 1 and is suitable for work involving agents of moderate potential hazard to personnel and the environment. It differs from BSL-1 in that (1) laboratory personnel have specific training in handling pathogenic agents and are directed by competent scientists; (2) access to the laboratory is limited when work is being conducted; (3) extreme precautions are taken with contaminated sharp items; and (4) certain procedures in which infectious aerosols or splashes may be created are conducted in biological safety cabinets or other physical containment equipment.

Agents that can be worked with at BSL2: Indigenous, moderate-risk agents associated with human disease of varying severity

Biosafety Level 3 – All procedures in this laboratory involving the manipulation of infectious materials are conducted within biological safety cabinets or other physical containment devices, or by personnel wearing appropriate personal protective clothing and equipment. The laboratory has special engineering and design features.

Agents that can be worked with at BSL3: Indigenous or exotic agents where the potential for infection by aerosol exists and disease may have serious-to-lethal consequences

Biosafety Level 4 – The facility is either in a separate building or in a controlled area within a building, which is completely isolated from all other areas of the building. A specific facility operations manual is prepared or adopted.

Within work areas of the facility, all activities are confined to Class III biological safety cabinets, or Class II biological safety cabinets used with one-piece positive pressure personnel suits ventilated by a life support system. The Biosafety Level 4 laboratory has special engineering and design features to prevent microorganisms from being disseminated into the environment.

Agents that can be worked with at BSL4: Dangerous and exotic agents that pose a high risk of life threatening disease

Blood-borne Pathogen - Micro-organisms that are present in human/ primate blood, tissues or fluids that can cause disease in humans. These pathogens include (but are not limited to) hepatitis B virus (HBV) and human immunodeficiency virus (HIV).

Carrier - A person, animal, or plant that serves as a host for a pathogen and can transmit it to others, but is immune to it.

Centrifuge - Equipment that separates substances of different densities in a sample by rotation at very high speed, forcing the substance to be displaced outward, sometimes through a series of filters or gratings. Substances with greater density are displaced from the center more than ones that are less dense.

Containment - The control of biohazards through practices & procedures, primary barriers, and secondary barriers.

Decontamination – Removing disease-causing organisms from contaminated articles or surfaces.

Disinfection - Selective elimination of certain undesirable microorganisms in order to prevent their transmission.

Doffing - To remove or take off.

Donning - To put on or dress in.

Endemic - Relating to a disease consistently present in a population in a particular locality.

Enzootic - Relating to a disease consistently present in a population of animals in a particular locality.

Epidemic – Disease occurring in larger numbers than usual or in excess of normal expectancy.

Epizootic - A disease affecting many animals at the same time, and spreading from animal to animal in a particular locality.

Fomite - An inanimate object or substance that is capable of transmitting infectious organisms from one individual to another.

Germicide - Any antimicrobial chemical agent used to kill disease-causing organisms.

Homogenize - To form by blending unlike elements; to make uniform or similar, as in composition or function.

Host - The animal or plant on which or in which another organism lives.

Incident - abnormal or unplanned event or conditions that adversely affect or potentially affect safety or security.

Infection - Invasion by and multiplication of pathogenic microorganisms in body tissues, which may produce subsequent tissue injury and progress to overt disease through a variety of cellular or toxic mechanisms.

Laboratory biosafety - A set of preventive measures designed to reduce the risk of accidental exposure to or release of a biological hazard

Laboratory biosecurity - A set of preventive measures designed to reduce the risk of intentional removal (theft) of a valuable biological material

Latent infection - An infectious agent or disease that remains in an inactive or hidden phase; dormant.

Lyophilizer - Equipment used for freeze-drying.

Mucous membrane - Any of the membranes lining the passages of the body, such as the respiratory and digestive tracts, that open to the outside. Cells in the mucous membranes secrete mucus, which lubricates the membranes and protects against infection.

Pathogen - An agent that causes infection or disease, such as a bacterium or protozoan, or a virus.

Polymerase Chain Reaction - A technique for amplifying DNA sequences in vitro by separating the DNA into two strands and incubating it with oligonucleotide primers and DNA polymerase.

Reservoir - An organism or a population that directly or indirectly transmits a pathogen while being virtually immune to its effects.

Risk - The function of the likelihood and consequences of an adverse event; biorisks involve biological agents or their products.

Risk assessment - A systematic, structured process for analysis and determination of risks

Risk Group - Infectious agents are categorized in risk groups based on their relative risk. Risk group classifications are primarily used in the research environment as part of a comprehensive biosafety risk assessment.

Risk Group 1 - No or low individual and community risk, A microorganism unlikely to cause human or animal disease.

Risk Group 2 - Moderate individual risk, low community risk. Pathogen causes human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment. May cause serious infection but effective treatments and preventive measures are available. Risk of spread is limited.

Risk Group 3 - High individual risk, low community risk. Pathogen usually causes serious human or animal disease but does not ordinarily spread to others. Effective treatment and preventive measures are available.

Risk Group 4 - High individual and community risk. A pathogen causes serious human or animal disease; readily transmitted from one individual to another. Effective treatment and preventive measures are usually not available.

Rotor - The device used to hold tubes during centrifugation.

Reverse transcriptase polymerase chain reaction - PCR process by which copies of DNA are generated from RNA.

Valuable Biological Material – A biological agent that has use either in research or for malicious purposes, commonly both

Vector -

a. An insect or other organism that transmits a pathogenic fungus, virus, bacterium, etc.

b. Any agent that acts as a carrier or transporter, as a virus or plasmid that conveys a genetically engineered DNA segment into a host cell.

Vortexer - A device used to mix, by means of a rapid whirling or circular motion.

Zoonotic Diseases - A disease of animals, such as rabies or psittacosis, which can be transmitted to humans.

PAGE BLANK

Scenario
Wooly Infectious Virus (WIV)

Summary of Experiment
A veteran researcher is working to create a new animal model for WIV studies. Using nude mice, he plans on injecting the mice with high titer cultures of WIV using 1ml needles. A recently hired technician will hold the animals for the researcher during inoculation. They plan on using a biosafety cabinet, nitrile gloves, goggles, and lab coats. The researcher recently has been distracted with personal issues and appears stressed. All details of this research are kept in the researcher's log book, which he keeps to himself.

Agent Criteria

Infectious Dose: Unknown, but thought to be around 500 – 10,000 viral particles for percutaneous route and much higher for contact with non-intact skin or mucosal membranes.

Stability:

SUSCEPTIBILITY TO DISINFECTANTS: Susceptible to many disinfectants - 1% sodium hypochlorite, 2% glutaraldehyde, formaldehyde, ethanol

PHYSICAL INACTIVATION: Effectiveness of 56·C - 60·C heat in destroying WIV in serum not certain, however, heating small volumes of serum for 30 min at 56·C before serologic testing reduces residual infectivity to below detectable levels

SURVIVAL OUTSIDE HOST: Drying in environment causes rapid (within several hours) 90-99% reduction in WIV concentration

Incubation Period: Epidemiologic evidence suggests that duration from exposure to onset of symptoms has a minimum range from 6 months to more than 7 years.

Mortality Rate: 100% of untreated patients will die from various complications related to compromise of the immune system within 10 years. Patients can be treated and survive with WIV as a chronic infection. However, the treatment can be expensive and there is evidence that some strains of WIV will mutate and develop resistance to the treatments.

Morbidity:

Duration of Illness: Initial infection produces flu-like symptoms. An WIV positive patient can be asymptomatic for many years before developing the disease. Untreated patients may survive 6-10 years post-infection, with illness worsening towards the end of this period.
Severity of Illness: High.
Duration of Infection: Lifetime
Long term effects after infection: Active disease can be triggered at any time after the establishment of a latent infection, though the probability of developing active

disease is higher 1-2 years after infection, in immune compromised patients, small children, young adults, and the very old.

Allergen (yes/no): No

Carcinogenic/mutagenic (yes/no): Potentially

Abortogenic (yes/no): No

Toxin Production (yes/no): No

Immune Suppression (yes/no): Yes

Ability to Mutate in Host or Environment (yes/no): Yes

Infection Mitigation Measures:

For human pathogens

Immunization: No. (Various experimental vaccines have been developed)
Prophylaxis: Anti-WIV drugs
Post Infection Treatment: Anti-WIV drugs
Existence of Diagnostic tests: Yes.

Routes of Infection:

Inhalation: No

Ingestion: No

Percutaneous: Yes

Contact: Possible (fluid contact with damaged skin or mucosal membranes)

Vector-Borne: No

Sexual Transmission: Yes

Vertical Transmission: Yes

Communicability: WIV is a virus that only infects humans. Studies indicate that it replicates only in a certain subset of human T-lymphocytes. Infections occur primarily through contact with infected body fluids, sexual transmission, during child birth, blood transfusions, and sharing intravenous needles. Efforts are underway to engineer animal models that will be able to be infected with the virus.

Human to Human: Yes

Human to Animal: No Evidence

Animal to Animal: No Evidence

Animal to Human: No Evidence (although some theories on the emergence of WIV involve animal to human transmission through fluid contact)

Multiple Species: No

Where is it present: Worldwide.

Perception of malicious use: LOW
Culture: Virus isolation and culture is possible in a relatively simple diagnostic laboratory using fresh peripheral blood cells from healthy donors or suitable culture lines such as T-lymphomas. This procedure is typically not used in diagnosis as it is tedious and lengthy in comparison with other diagnostic techniques. It is mainly used in characterizing viruses.

Performance Scenario

An employee of a waste transport and disposal company was diagnosed with Tuberculosis. After his diagnosis, he recalled an incident in which waste leaked from biohazard waste bags he carried from the local "TB Reference Laboratory," but did not report it at the time. During the same period, he visited relatives and went to public places in a country where TB was prevalent. One of his relatives in that country had just started TB treatments during his visit. The laboratory did not know about his infection until it was notified of this person's pending lawsuit, which claimed that the facility had not sufficiently treated the waste. Laboratory tests on samples from his lungs did not clearly point to a laboratory-based exposure. The waste transport and disposal company does not maintain an employee health monitoring program.

Upon review of lab and autoclave records, it was identified that on one day out of five the autoclave temperature, pressure, and time recordings were not available. Some staff seemed to think that this may have been because the autoclave printer ran out of paper on that day. The reference lab does not perform regular validation of its autoclaves.

Six months prior to this incident, in an internal occupational health and safety audit, it was recognized that autoclave printout records were kept in a drawer that was also used to store laboratory supplies. The internal audit was reviewed, and the laboratory manager determined that these records should be stored in a more appropriate and secure location. Another issue identified during the audit was that employees were not aware of autoclave maintenance procedures. The assistant laboratory manager was ordered to secure the records in a specific location and train lab personnel in autoclave procedures. However, he subsequently went on extended leave of absence, and no other effort was made to correct these problems.

The lawsuit resulted in a $5 million fine for the laboratory because the laboratory could not prove that the waste was treated appropriately as stipulated in its contract with the waste transport and disposal company.

Cataract University Scenario

Amil works in a Biosafety Level 2 research lab at Cataract University studying anthrax vaccines. He recently visited the emergency room with a serious skin infection on his neck. Doctors determined this infection was caused by *Bacillus anthracis* and started treating him with antibiotics. He is expected to make a full recovery.

Amil was surprised to learn of this diagnosis because he only works in the lab with the Sterne strain of *Bacillus anthracis,* a non-lethal strain used to vaccinate animals. Although the high containment lab in the adjacent building works with the fully virulent Ames strain, Amil never enters there.

Upon learning of the infection through the news, the lab director asked for a study to be done to determine what went wrong and whether or not Amil contracted the agent in the lab. Amil reported that he had been working with Barbara two weeks prior to grow up cultures of the non-lethal, live vaccine strain. Barbara was working in the Biological Safety Cabinet (BSC) to prevent contamination. After transferring a small amount of broth culture to a micro-centrifuge tube, Barbara sealed the tube and wiped it down with alcohol before transferring the tube to Amil, who placed the tubes in a labeled container and walked them down the hallway to put them in a common use refrigerator. Amil was not wearing gloves during the process as he explained "I was not directly handling the agent and Barbara was wiping them down with alcohol so I did not think there was anything to worry about." Neither researcher was aware of the fact that alcohol would have little effect on Bacillus spores.

The lab director suggested that the cultures in the lab be tested to determine whether or not the strains were indeed the vaccine version or the fully virulent strain. However, the samples turned up missing after a search of the common refrigerator where they had been stored. No one is sure what happened to them. The custodian cleaned out the refrigerator the week before and may have inadvertently tossed them in the trash but he does not remember. Fortunately, Barbara saved some of the stock solution and upon testing was surprised to find that it was the fully virulent Ames strain of *B. anthracis* and matched the strain that was cultured from Amil's lesion. Barbara had ordered the vaccine strain from Acme Labs several months ago.

When questioned about the possibility of sending the wrong strain to Cataract University, a manager at Acme lab reported that it is very unlikely because they only shipped the virulent strains to labs that are registered with Acme and Cataract was not registered. However, the manager did concede that their shipping supervisor happened to be on vacation when the shipment was sent to Cataract so some of the records were not kept during that period.