DRAFT
Biosafety RAM Outline
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Biosafety Risk Assessment Methodology

Drafted by biosafety, infectious disease, and risk experts
Modeled by Sandia National Laboratories

In this model, risk is defined as a function of the likelihood of infection by the agent, the likelihood of exposure through an infectious route and the consequences of disease assuming infection.

$$R = \mathcal{F}(L_i, L_e, C_d)$$

Likelihood of infection (L_i) is defined by the biological factors of the agent that influences the ability to cause infection. These include factors of transmissibility, agent stability, and also include infection mitigation measures, e.g. vaccine availability and effectiveness.

Likelihood of exposure (L_e) is defined by exposure hazards that exist in and around the specific activity with that agent. These factors are defined by a route of exposure, e.g. percutaneous hazards. In place biosafety practices are included as exposure reduction measures.

Consequence of disease (C_d) is defined by the factors used to define disease in a specific host as based upon a normalized population. These factors include, for example, morbidity, mortality, and disease mitigation measures like effective and available anti-microbials.

Scalars are used to influence the consequence and likelihood based upon unique characteristics of the environment or people in and around the bioscience laboratory or facility.

Likelihood of Infection

These criteria define the biological properties that influence an agent's likelihood of infection post exposure to a human. Infection is defined as the ability to enter an organ/cell, replicate or spread within the host, or integrate into or become part of the genetic material.

a. Transmissibility

These criteria define the ability of this agent to move from anything, including inanimate objects, into the host (routes of infection). These will be scored based on the agent's ability to be transmitted in a laboratory setting. Therefore, for some agents, there will be routes identified in this section that are not considered typical routes of infection.

i. Inhalation

These criteria define the agents ability to cause infection via droplets that have entered the upper or lower respiratory tract.

1. Route of infection
2. Infectious dose for this route

ii. Ingestion

These criteria define the agent's ability to cause infection via contact with the GI tract

1. Route of infection
2. Infectious dose for this route

iii. Contact

These criteria define the agent's ability to cause infection through the mucosal membranes.

1. Route of infection
2. Infectious dose for this route

iv. Percutaneous

This criteria defines the agents ability to cause infection through compromised skin

1. Route of infection
2. Infectious dose for this route

v. Vector-borne

This criterion defines the agent's ability to cause infection by an animate carrier; this criterion was added to help capture agents that have an increased likelihood of infection if transmitted by a vector than from a percutaneous exposure.

1. Route of infection
2. Infectious dose for this route

b. Stability outside the host

This criterion defines the agent's stability outside the host. This criterion will be scored highest for those agents which have a high degree of stability outside of a host and will be calculated by mapping the agent to a standard disinfection table definitions.

c. Infection Mitigation Measures / Existence of prophylaxis

This criterion measures the availability and effectiveness of medical treatment that can be given to the host prior to the onset of symptoms of infection (either post exposure or prior to initiating work).

Likelihood of Exposure

These criteria define the laboratory procedures that exist for an individual who performs direct manipulation of an agent, and those biosafety practices that help to mitigate the likelihood of exposure. The criteria below include the biosafety risks associated with working with animals, these criteria will not exist if no animal work is being conducted.

Different criteria are used to define the laboratory hazards for the other biosafety risks, e.g. the risks to the human community, the animal community, the risk of secondary infection, etc.

Laboratory and person specific factors, e.g. host immune status, are included as scalars which should be applied to adjust the risk after calculating the starting point risk (this model does not include the 'human' factor specifically).

Laboratory Hazards that influence likelihood of exposure

a. Inhalation

   i. Aerosol generating procedures
      Aerosols are generated as a byproduct of the procedure, e.g. pipetting, sonicating, etc. This criterion determines if procedures in the laboratory can produce aerosols.
   ii. Potential for an accidental aerosol release
      E.g. agent exists and therefore always has a potential for an accidental aerosol release e.g. spill or system with mechanical failure. The quantity and quality of the material is captured in additional criteria
   iii. Aerosolization experiments
      This criterion determines if aerosols are intentionally generated in the laboratory.
   iv. Equipment maintenance or repair
      This criterion determines if the process of equipment maintenance could produce aerosols. This criterion is included to capture the person(s) who maintain equipment which may have viable agents (e.g. the person maintaining duct work prior to the HEPA filter or the person fixing the seals on a non-decontaminated centrifuge. This may be the researcher or an external contractor or any others who have that role at the facility.)
   v. Animals
      This criterion determines if the presence of animals in the laboratory could generate aerosols.

b. Percutaneous
   Transmission of a pathogen through compromised skin
   i. Animals
      a. Quantity of animals in laboratory
      b. Potential level of aggression
      c. Size of animals in laboratory
   ii. Sharps (e.g. needles, scalpels) in the laboratory
      This criterion determines if there sharps in the laboratory.
   iii. Sharps (e.g. breakable material (e.g. glass), sharp edges) in the laboratory
      This criterion determines if there sharps in the laboratory.
   iv. Animals and sharps (sharps are handled while working with animals not animals with sharps)
   vi. Equipment maintenance or repair

This criterion determines if the process of equipment maintenance could produce aerosols. This criterion is included to capture the person(s) who maintain equipment which may have viable agents (e.g. the person maintaining duct work prior to the HEPA filter or the person fixing the seals on a non-decontaminated centrifuge. This may be the researcher or an external contractor or any others who have that role at the facility.)

c. Contact

Transmission of a pathogen through contact with unbroken skin or mucosal membrane

i. Spill / Splash (higher kinetic energy)

This criterion determines if there is a potential for droplets to become airborne

ii. Contaminated surfaces

This criterion determines if there are surfaces in the laboratory that can be contaminated.

iii. Animals

This criterion determines if there are animals in the laboratory.

iv. Contaminated Waste

This criterion determines if there is waste in the lab that a presents a contact hazard.

vii. Equipment maintenance or repair

This criterion determines if the process of equipment maintenance could produce aerosols. This criterion is included to capture the person(s) who maintain equipment which may have viable agents (e.g. the person maintaining duct work prior to the HEPA filter or the person fixing the seals on a non-decontaminated centrifuge. This may be the researcher or an external contractor or any others who have that role at the facility.)

d. Ingestion

These criteria determine the potential transmission of a pathogen through contact with the gastrointestinal tract after exposure to the agent cause by an individual eating or drinking.

i. Splash

This criterion determines if there are infectious liquids in the laboratory that constitute a splash hazard.

ii. Material in lab with potential to be ingested (mouth pipetting, eating, drinking, smoking, hand touching one's mouth, etc..)

viii. Equipment maintenance or repair

This criterion determines if the process of equipment maintenance could produce aerosols. This criterion is included to capture the person(s) who maintain equipment which may have viable agents (e.g. the person maintaining duct work prior to the HEPA filter or the person fixing the seals on a non-decontaminated centrifuge. This may be the researcher or an external contractor or any others who have that role at the facility.)

e. Quality and Quantity of Infectious Material

a. Quality
b. Quantity

Biosafety Practices which mitigate the likelihood of exposure

a. Management oversight
   Management at the facility who review the mitigation measures and procedures on a regular basis – these criteria will be scored based upon principles of biosafety, minimum best practices, and standards. (Definitions still to be drafted)
   a. Material Management
   b. Equipment Maintenance
      Set procedures for preventative equipment maintenance that reduce/eliminate accidents or equipment failure, and that meet defined best practices. Calibration of equipment, validation, certification, (judge overall maintenance of all biosafety related equipment)
   c. Medical Surveillance
   d. Incident response plan
   e. Training, resources, and procedures
      i. PPE procedures
      ii. Good lab practices (proper agent handling) – BMBL normal practices and procedures
      iii. Entry and exit
      iv. Waste and decontamination

b. Inhalation
   a. <u>Physical/ Engineering Controls</u>
      The protection of personnel from exposure to infectious agents through mechanical and architectural devices
      i. Primary containment
      ii. Primary containment of animals
   b. <u>PPE</u>
      The protection of personnel from exposure to infectious agents with barriers that protect the respiratory route
      i. Respiratory protection
   c. <u>Procedural / Administrative</u>
      The protection of personnel and the environment from exposure to infectious agents with documented and implemented regulations, procedures, and SOPs.
      i. Proper agent handling techniques that reduce/eliminate aerosols

c. Percutaneous
   Transmission of a pathogen through compromised skin
   a. <u>Physical / Engineering Controls</u>
      The protection of personnel from exposure to infectious agents with mechanical and architectural devices
      i. Using non-sharps instead of sharps
      ii. Safe animal handling systems (e.g. restraining devices)
      iii. Mechanical safe sharp handling systems (e.g. recapping systems, scalpel replacement systems)
   b. <u>PPE</u>
      The protection of personnel from exposure to infectious agents with barriers that protect the skin
      i. Gloves

ii. Gowns

c. Procedural/Administrative

These criteria measure the protection of personnel and the environment from exposure to infectious agents with documents and implemented regulations, procedures and SOPs.

i. Proper sharp handling technique
ii. Proper animal handling technique

d. Contact

Transmission of a pathogen through contact with unbroken skin or mucosal membrane

a. Physical/ Engineering Controls

The protection of personnel from exposure to infectious agents with mechanical and architectural devices

i. Mechanical systems which prevent direct contact (tongs, tweezers, etc)
ii. Absorbent material to contain spills
iii. Safe animal handling systems (e.g. restraining devices)

b. PPE

The protection of personnel from exposure to infectious agents with barriers that protect against skin and mucous membranes

i. Gloves
ii. Laboratory clothing
iii. Protective eyewear
iv. 'Surgical Mask' or Face shield
v. Solid shoes
vi. Head covering

c. Procedural/Administrative

The protection of personnel from exposure to infectious agents with documented and implemented regulations, procedures, and SOPs

i. Emergency spill response
ii. Proper broken skin handling procedure
iii. Proper animal handling technique

e. Ingestion

Transmission of a pathogen through contact with the gastrointestinal tract after exposure to the agent cause by an individual eating or drinking.

a. Physical Control Measures

The protection of personnel and the environment from exposure to infectious agents with mechanical devices

i. Mechanical systems which prevent direct contact/ingestion (tongs, tweezers, mechanical pipettes, animal handling techniques)

b. PPE

The protection of personnel from exposure to infectious agents with barriers that protect against skin, mucous membrane, and respiratory routes of infection

i. 'Surgical Mask' or Face shield
ii. Gloves

c. Procedures/Administration

The protection of personnel and the environment from exposure to infectious agents with documented and implemented regulations, procedures, and SOPs

i. Good hand hygiene procedures
ii. Good laboratory practices (No eating drinking/mouth pipetting)
iii. Good laboratory cleaning practices

Laboratory Hazards that influence likelihood of exposure to a community

a. Inhalation
   i. Aerosol generating procedures
b. Percutaneous
   i. Animals
   ii. Sharps (e.g. needles, scalpels) in the laboratory
   iii. Sharps (e.g. breakable material (e.g. glass), sharp edges) in the laboratory
c. Contact
   i. Animals
d. Ingestion
   i. Liquids in the laboratory
      This criterion determines if there are infectious liquids in the laboratory that could be released into the community water system
e. Quality and Quantity of Infectious Material
   a. Quality
   b. Quantity

Biosafety Practices which mitigate the likelihood of exposure

f. Management oversight
   a. Facility Environment Impact Measures
      Assurance that the facility has been designed to account for environment issues like floods, tornados, etc…
   b. Material Management
      i. Shipping and receiving system
      ii. Quality Control on material
      iii. Quality Control on animals
   c. Exit Procedures
   d. Pest Control
   e. Equipment Maintenance
   f. Incident response plan
   g. Waste and decontamination

a. Inhalation
   a. Secondary containment
b. Percutaneous
   a. Sharps waste and decontamination
c. Contact
   a. Emergency spill response
d. Ingestion
   a. Waste and decontamination

Consequence of disease

Consequence is defined by the extent of disease and those factors which may be used to mitigate the consequence for a specific host population and normalized to that population.

a. Agent Characteristics
    a. Carcinogenic/mutagenic
    This criterion measures the causation of a carcinogenic or mutagenic reaction in the host by the pathogen or one of its by-products.
    b. Toxin/enzyme production
    This criterion measures the toxin or enzyme production of the pathogen, and its negative impact to a healthy human host.
    c. Does this agent impact the host's immune response?
    d. Ability to alter once in a host or in the natural environment to become infectious through new routes, new hosts, or a greater level of consequences
b. Morbidity
    Morbidity is the severity of illness that the pathogen creates in the host. Severity is measured by these sub-criteria.
    a. Duration of illness
    b. Severity of illness
    c. Duration of infection (chronicity)
    d. Sequelae
c. Mortality

Consequence Mitigation Measures

These are criteria that can reduce the impact of an infection to the primary host. These criteria measure the existence of effective (judged relatively) diagnosis, treatment, and vaccines. Additional criteria will assess their availability in the community and laboratory environment.

a. Existence of diagnostic tests
b. Existence of post exposure treatments (including immuno-globulin, vaccines and anti-microbials)
c. Existence of preventative measures (vaccines)

Scalars

Scalars can adjust the consequence and likelihood based on unique characteristics of the human and animal environment in and around the bioscience facility. This includes the unique characteristics of people who work in the laboratory.

Laboratory Scalars

Scalars that change the risk because of specific issues associated with a laboratory.

a. Host immune status
b. Prior exposure to agent
c. Vaccines available at laboratory for this agent
a. Prophylaxis available at laboratory for this agent

Community Scalars

a. Economic impact of outbreak of this agent to the community
b. Endemicity of this agent in the community
c. Active eradication programs of this agent in the community
d. Social impact of outbreak of this agent in the community
e. Population density of the community
f. Diagnostic tests for this agent available in community
g. Post-exposure treatments available in community of this agent
h. Vaccines available in the region for this agent

Biosafety Risk Assessment Criteria:

Secondary infection Criteria

Secondary Infection Scalars

Scalars alter the risk based upon the impact of a secondary transmission. The secondary infection risk is based upon the combine primary exposure risks with the scalars used to highlight agent specific impacts.

a. Communicability

Host to host transmission

a. Human to human
b. Animal to Human
c. Human to Animal
d. Animal to Animal

b. Natural routes of infection

These will be defined as they were for laboratory routes of infection, but the scores will reflect the natural routes of infection and included routes which are not seen in a laboratory.

i. Inhalation
ii. Ingestion
iii. Contact
iv. Percutaneous
v. Vector-borne
vi. Vertical
vii. Sexual

c. Survivability in the environment

Secondary Infection mitigation measures

These are criteria which can reduce the impact of an infection to the primary host. These criteria measure the existence of effective (judged relatively) diagnosis, treatment and vaccines. Additional criteria will assess the availability of these within the community and laboratory environment. These criteria will be calculated only once for each agent but the data propagated as needed.