

How to Conduct a Biological Risk Assessment

Adapted from the [“Guidelines for Safe Work Practices in Human and Animal Medical Diagnostic Laboratories: Recommendations of a CDC-convened, Biosafety Blue Ribbon Panel”](#)

Risk Assessment

A risk assessment should always be conducted prior to initiating any work in a laboratory. For work that needs to be registered with and approved by the Institutional Biosafety Committee (IBC), a risk assessment is a key part of the registration process. The Principal Investigator (PI)/Laboratory Director is responsible for identifying potential hazards, assessing risks associated with those hazards, and establishing precautions and standard procedures to minimize employee exposure to those risks. These should be documented in a laboratory-specific Biosafety manual and made available to all staff working in the laboratory. The risk assessment conducted by the PI will be reviewed by the IBC who may require changes prior to the approval of the work.

Qualitative biological risk assessment is a subjective process that involves professional judgments. Because of uncertainties or insufficient scientific data, risk assessments sometimes are based on incomplete knowledge or information. Inherent limitations of and assumptions made in the process also exist, and the perception of acceptable risk differs for everyone. The risk is never zero, and potential for human error always exists.

Identifying potential hazards in the laboratory is the first step in performing a risk assessment. A comprehensive approach for identifying hazards in the laboratory will include information from a variety of sources. No one standard approach or correct method exists for conducting a risk assessment; However, several strategies are available, such as using a risk prioritization matrix, conducting a job hazard analysis; or listing potential scenarios of problems during a procedure, task, or activity. The process involves the following five steps:

1. Identify the hazards associated with an infectious or biohazardous agent or material, including human pathogens, recombinant viral vectors, and acute biological toxins.
2. Identify the activities that might cause exposure to the agent or material.
3. Consider the training, competencies and experience of laboratory personnel.

4. Evaluate and prioritize risks (evaluate the likelihood that an exposure would cause a laboratory-acquired infection [LAI] and the severity of consequences if such an infection occurs).
5. Develop, implement, and evaluate controls to minimize the risk for exposure and establish plans for how to deal with an exposure, should it occur.

Step 1. Identify the hazards associated with an infectious or biohazardous agent or material.

- The potential for infection, as determined by the most common routes of transmission (i.e., ingestion by contamination from surfaces/fomites to hands and mouth; percutaneous inoculation from cuts, needle sticks, nonintact skin, or bites; direct contact with mucous membranes; and inhalation of aerosols) (Table 1);
- The volume and concentration of organisms handled
- Intrinsic factors (if agent is known):
 - Pathogenicity, virulence, and strain infectivity/communicability;
 - Mode of transmission (mode of laboratory transmission may differ from natural transmission);
 - Infectious dose (the number of microorganisms required to initiate infection can vary greatly with the specific organism, patient, and route of exposure) or LD50 for toxic materials;
 - Genetic modifications that alter the risk, such as expression of oncogenes or siRNAs to knockdown tumor suppressors;
 - The risk of the formation of replication competent viruses when using recombinant viral vectors;
 - Form (stage) of the agent (e.g., presence or absence of cell wall, spore versus vegetation, conidia versus hyphae for mycotic agents);
 - Invasiveness of agent (ability to produce certain enzymes);
 - Origin of the material being handled. For example human tissues or cell lines make harbor pathogens (Table 2);
 - Availability of vaccines and/or prophylactic interventions; and
 - Resistance to antibiotics.

Step 2. Identify activities that might cause exposure to the agent or material.

- The facility (e.g., BSL-2, BSL-3, open floor plan [more risk] versus separate areas or rooms for specific activities [less risk], sufficient space versus crowded space, workflow, equipment present);
- The equipment (e.g., uncertified Biological Safety Cabinets [BSCs], cracked centrifuge tubes, improperly maintained autoclaves, overfilled sharps containers, Bunsen burners);
- Potential for generating aerosols and droplets.

Aerosols can be generated from most routine laboratory procedures but often are undetectable. The following procedures have been associated with generation of infectious aerosols.

- Manipulating needles, syringes and sharps
 - Subculturing positive blood culture bottles, making smears
 - Expelling air from tubes or bottles
 - Withdrawing needles from stoppers
 - Separating needles from syringes
 - Aspirating and transferring body fluids
 - Harvesting tissues
- Manipulating inoculation needles, loops, and pipettes
 - Flaming loops
 - Cooling loops in culture media
 - Subculturing and streaking culture media
 - Expelling last drop from a pipette (including Eppendorff pipettes)
- Manipulating specimens and cultures
 - Centrifugation
 - Setting up cultures, inoculating media
 - Mixing, blending, grinding, shaking, sonicating, and vortexing specimens or cultures
 - Pouring, splitting, or decanting liquid specimens
 - Removing caps or swabs from culture containers, opening lyophilized cultures, opening cryotubes
 - Spilling infectious material
 - Filtering specimens under vacuum

- Preparing smears, performing heat fixing, staining slides
 - Performing serology, rapid antigen tests, wet preps, and slide agglutinations
 - Throwing contaminated items into biohazardous waste
 - Cleaning up spills
- Use of animals;
 - Use of sharps;
 - Production of large volumes or concentrations of potential pathogens or agents;
 - Improperly used or maintained equipment;

Examples of possible hazards are decreased dexterity or reaction time for workers wearing gloves, reduced ability to breathe when wearing N95 respirators, or improperly fitting personal protective equipment (PPE).

- Working alone in the laboratory.

No inherent biologic danger exists to a person working alone in the laboratory; however, the supervisor is responsible for knowing if and when a person is assigned to work alone. Because assigning a person to work alone is a facility-specific decision, a risk assessment should be conducted that accounts for all safety considerations, including type of work, physical safety, laboratory security, emergency response, potential exposure or injury, and other laboratory-specific issues.

Step 3. Consider the competencies and experience of laboratory personnel.

- Age (younger or inexperienced employees might be at higher risk);
- Genetic predisposition and nutritional deficiencies, immune/medical status (e.g., underlying illness, receipt of immunosuppressive drugs, chronic respiratory conditions, pregnancy, nonintact skin, allergies, receipt of medication known to reduce dexterity or reaction time);
- Education, training, experience, competence;
- Stress, fatigue, mental status, excessive workload;
- Perception, attitude, adherence to safety precautions; and

- The most common routes of exposure or entry into the body (i.e., skin, mucous membranes, lungs, and mouth) (Table 1).

Step 4. Evaluate and prioritize risks.

Risks are evaluated according to the likelihood of occurrence and severity of consequences.

- Likelihood of occurrence:
 - Almost certain: expected to occur
 - Likely: could happen sometime
 - Moderate: could happen but not likely
 - Unlikely: could happen but rare
 - Rare: could happen, but probably never will

- Severity of consequences:

Consequences may depend on duration and frequency of exposure and on availability of vaccine and appropriate treatment. Following are examples of consequences for individual workers:

- Colonization leading to a carrier state
- Asymptomatic infection
- Toxicity, oncogenicity, allergenicity
- Infection, acute or chronic
- Illness, medical treatment
- Disease and sequelae
- Death

Step 5. Develop, implement, and evaluate controls to minimize the risk for exposure.

- Engineering controls:

If possible, first isolate and contain the hazard at its source.

- Primary containment: BSC, sharps containers, centrifuge safety cups, splash guards, safer sharps (e.g., autoretracting needle/syringe combinations, disposable scalpels), and pipette aids

- Secondary containment: building design features (e.g., directional airflow or negative air pressure, hand washing sinks, closed doors, double door entry)
- Administrative and work practice controls
 - Strict adherence to standard and special microbiological practices
 - Adherence to signs and standard operating procedures
 - Frequently washing hands
 - Wearing PPE only in the work area
 - Minimizing aerosols
 - Prohibiting eating, drinking, smoking, chewing gum
 - Limiting use of needles and sharps, and banning recapping of needles
 - Minimizing splatter (e.g., by using lab "diapers" on bench surfaces, covering tubes with gauze when opening)
 - Monitoring appropriate use of housekeeping, decontamination, and disposal procedures
 - Implementing "clean" to "dirty" work flow
 - Following recommendations for medical surveillance and occupational health, immunizations, incident reporting, first aid, post-exposure prophylaxis
 - Training
 - Implementing emergency response procedures
- PPE (as a last resort in providing a barrier to the hazard)
 - Gloves for handling all potentially contaminated materials, containers, equipment, or surfaces
 - Face protection (face shields, splash goggles worn with masks, masks with built-in eye shield) if BSCs or splash guards are not available. Face protection, however, does not adequately replace a BSC. At BSL-2 and above, a BSC or similar containment device is required for procedures with splash or aerosol potential.
 - Laboratory coats and gowns to prevent exposure of street clothing, and gloves or bandages to protect nonintact skin
 - Additional respiratory protection if warranted by risk assessment

- Job safety analysis

One way to initiate a risk assessment is to conduct a job safety analysis for procedures, tasks, or activities performed at each workstation or specific laboratory by listing the steps involved in a specific protocol and the hazards associated with them and then determining the necessary controls, on the basis of the agent/organism. Precautions

beyond the standard and special practices for BSL-2 may be indicated in the following circumstances:

- Organisms transmitted by inhalation
 - Work with vectors expressing oncogenes or toxins
 - Work with large volumes or highly concentrated cultures
 - Compromised immune status of staff
 - Training of new or inexperienced staff
 - Technologist preference
- Monitoring effectiveness of controls

Risk assessment is an ongoing process that requires at least an annual review because of changes in new and emerging pathogens and in technologies and personnel.

- Review reports of incidents, exposures, illnesses, and near-misses.
- Identify causes and problems; make changes, provide follow-up training.
- Conduct routine laboratory inspections.
- Repeat risk assessment routinely.

TABLE 1. Laboratory activities associated with exposure to infectious agents

Routes of exposure/transmission	Activities/practices
Ingestion/oral	<ul style="list-style-type: none">• Pipetting by mouth• Splashing infectious material• Placing contaminated material or fingers in mouth• Eating, drinking, using lipstick or lip balm
Percutaneous inoculation/nonintact skin	<ul style="list-style-type: none">• Manipulating needles and syringes• Handling broken glass and other sharp objects• Using scalpels to cut tissue for specimen processing• Waste disposal (containers with improperly disposed sharps)
Direct contact with mucous membranes	<ul style="list-style-type: none">• Splashing or spilling infectious material into eye, mouth, nose• Splashing or spilling infectious material onto intact and nonintact skin• Working on contaminated surfaces• Handling contaminated equipment (i.e., instrument maintenance)• Inappropriate use of loops, inoculating needles, or swabs containing specimens or culture material• Bites and scratches from animals and insects• Waste disposal• Manipulation of contact lenses
Inhalation of aerosols	<ul style="list-style-type: none">• Manipulating needles, syringes, and sharps• Manipulating inoculation needles, loops, and pipettes• Manipulating specimens and cultures• Spill cleanup
Source: Sewell DL. Laboratory-associated infections and biosafety. Clin Microbiol Rev 1995;8:389–405 (18).	

TABLE 2. Selected adventitious agents associated with cell cultures, organs and tissues that could be used to generate cell cultures, and cell culture reagents

Infectious agent	Source
Adenovirus	Human kidney, pancreas, some adenovirus transformed cell lines, rhesus monkey kidney cells
Bovine viruses: Bovine rhinotracheitis virus Bovine diarrhea virus Parainfluenza type 3 Bovine enterovirus Bovine herpesvirus Bovine syncytial virus	Bovine serum, fetal bovine serum (substantially lower risk today due to ultrafiltration of bovine serum)
Cytomegalovirus	Kidney, human foreskin, monkey kidney cells
Epstein-Barr virus (EBV)	Some lymphoid cell lines and EBV-transformed cell lines, human kidney
Hepatitis B virus	Human blood, liver
Herpes simplex virus	Human kidney
Herpesvirus group	Monkey kidney cells
Human or simian immunodeficiency virus	Blood cells, serum, plasma, solid organs from infected humans or monkeys
Human papilloma virus (HPV)	HeLa cell lines
HTLV-1	Human kidney, liver
Lymphocytic choriomeningitis virus	Multiple cell lines, mouse tissue
Mycoplasmas	Many cell cultures
Myxovirus (SV5)	Monkey kidney cells
Porcine parvovirus	Fetal porcine kidney cells, trypsin preparations
Rabies virus	Human cornea, kidney, liver, iliac vessel conduit
Simian adenoviruses	Rhesus, cynomologous, and African green monkey kidney cells
Simian foamy virus	Rhesus, cynomologous, and African green monkey kidney cells
Simian virus 40 (SV40)	Rhesus monkey kidney cells
Simian viruses 1–49	Rhesus monkey kidney cells
Swine torque teno virus	Trypsin, swine-origin biological components
Squirrel monkey retrovirus	Multiple cell lines, commercial interferon preparations
West Nile virus	Human blood, heart, kidney, liver, lung, pancreas