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laboratories in human and animal medicine. In 2008, CDC convened a Blue Ribbon Panel of laboratory representatives from a variety of agencies, laboratory organizations, and facilities to review laboratory biosafety in diagnostic laboratories. The members of this panel recommended that biosafety guidelines be developed to address the unique operational needs of the diagnostic laboratory community and that they be science based and made available broadly. These guidelines promote a culture of safety and include recommendations that supplement BMBL-5 by addressing the unique needs of the diagnostic laboratory. They are not requirements but recommendations that represent current science and sound judgment that can foster a safe working environment for all laboratorians. Throughout these guidelines, quality laboratory science is reinforced by a common-sense approach to biosafety in day-to-day activities. Because many of the same diagnostic techniques are used in human and animal diagnostic laboratories, the text is presented with this in mind. All functions of the human and animal diagnostic laboratory — microbiology, chemistry, hematology, and pathology with autopsy and necropsy guidance — are addressed. A specific section for veterinary diagnostic laboratories addresses the veterinary issues not shared by other human laboratory departments. Recommendations for all laboratories include use of Class IIA2 biological safety cabinets that are inspected annually; frequent hand washing; use of appropriate disinfectants, including 1:10 dilutions of household bleach; dependence on risk assessments for many activities; development of written safety protocols that address the risks of chemicals in the laboratory; the need for negative airflow into the laboratory; areas of the laboratory in which use of gloves is optional or is recommended; and the national need for a central site for surveillance and nonpunitive reporting of laboratory incidents/exposures, injuries, and infections. This report offers guidance and recommends biosafety practices specifically for human and animal clinical diagnostic laboratories and is intended to supplement the 5th edition of Biosafety in Microbiological and Biomedical Laboratories (BMBL-5), developed by CDC

and the National Institutes of Health (1). This document was written not to replace existing biosafety guidelines, but to 1) improve the safety of activities in clinical diagnostic laboratories, 2) encourage laboratory workers to think about safety issues they might not previously have considered or addressed, and 3) encourage laboratorians to create and foster a culture of safety in their laboratories. Should any of the guidelines provided herein conflict with federal, state, or local laws or regulatory requirements, the laboratorian should defer to the federal, state, or local requirements. This culture of safety is also supported by the Clinical and Laboratory Standards Institute (2). Work in a diagnostic laboratory entails safety considerations beyond the biological component; therefore, these guidelines also address a few of the more important day-to-day safety issues that affect laboratorians in settings where biological safety is a major focus. According to the U.S. Bureau of Labor Statistics, in 2008, approximately 328,000 medical laboratory technicians and technologists worked in human diagnostic laboratories in the United States. An estimated 500,000 persons in all professions work in human and animal diagnostic laboratories. Any of these workers who have chronic medical conditions or receive immunosuppressive therapy would be at increased risk for a laboratory-acquired infection (LAI) after a laboratory exposure. Precise risk for infection after exposure is unknown because determining the source or the mode of transmission often is difficult. No national surveillance system is available. LAIs and exposures have been reported since early in the 20th century, but only in the 1970s were sufficient data available to attempt quantitative assessments of risk. Recent MMWR reports (3–11) have indicated that bacteria account for >40% of infections, with >37 species reported as etiologic agents in LAIs; however, other microbes are often implicated. Hepatitis B has been the most frequent laboratory-acquired viral infection, with a rate of 3.5–4.6 cases per 1000 workers, which is two to four times that of the general population. Any laboratorian who collects or handles tubes of blood is vulnerable (12). Early surveys of LAIs found that laboratory

personnel were three to nine times more likely than the general population to become infected with Mycobacterium tuberculosis (13,14). In a 1986 survey of approximately 4000 workers in 54 public health and 165 hospital laboratories in the United States, 3.5/1000 employee infections occurred in hospital laboratories, and 1.4/1000 employee infections occurred in public health laboratories (15). In a 1994–1995 survey of 25,000 laboratory workers from 397 clinical laboratories in the United Kingdom, the overall rate of LAI was 18/100,000 employees (16). In a 2005 CDC study of bacterial meningitis in U.S. laboratorians, Neisseria meningitidis accounted for a substantial number of LAIs. The attack rate of this organism in the general population was 13/100,000 persons. The attack rate in the general population aged 30–59 years (the estimated age range of the average laboratorian) was 0.3 per 100,000. The attack rate for microbiologists (aged 30–59 years) was 20/100,000 (17). LAIs have also included fungal and parasitic infections. The most common agents of laboratory-acquired fungal infections are the dimorphic fungi Blastomyces, Histoplasma, and Coccidioides (18,19); most reported infections were caused by inhalation of conidia. Reported parasite-associated LAIs were caused primarily by Leishmania, Plasmodium, Toxoplasma, Chagas disease organism, and other trypanosomes (20). Of the 52 cases of laboratory-acquired malaria, 56% were vector borne (from mosquitoes used in research, not clinical laboratories). Most infected health-care workers acquired infection from needle sticks during preparation of blood smears or while drawing blood. In clinical chemistry laboratories, data from 17 New York hospitals listed needle puncture (103 cases), acid or alkali spills (46), glass cuts (44), splash in eye (19), and bruises and cuts (45) as the most frequent exposures (21). Needle puncture, glass cuts, splash in eye, and bruises and cuts have the highest potential for infection from microbes. In the hematology laboratory, the major causes of injuries are likely to be exposure to blood and body fluids; needle sticks, aerosols from centrifuge or removal of tube stoppers, tube breakage; or contaminated gloves (22). In non-microbiology sections of the diagnostic laboratory, the primary mistake may be

assuming that a given specimen contains no infectious agents and then working with little attention to risk for infection. This scenario can be particularly problematic in laboratories developing new technologies, such as molecular and biochemical technologies, and in point-of-care diagnostics performed by staff unaccustomed to testing that requires biosafety considerations and use of barrier techniques such as personal protective equipment. The risks and causes of LAIs have been documented. However, there is a dearth of evidence-based research and publications focused on biosafety; particularly missing are studies documenting safe practices in the day-to-day operations of diagnostic laboratories. In 2008, CDC convened a Blue Ribbon Panel of laboratory representatives from a variety of agencies, laboratory organizations, and facilities to review laboratory biosafety in diagnostic laboratories. Members of the panel were either selected by the invited national laboratory organization they represented or were invited by CDC because of their roles in biosafety at the national level. The organizations participating in the panel represented the majority of laboratory technologists in the United States. In addition, some members of the panel were representatives of the biosafety community. The Blue Ribbon Panel recommended that biosafety guidelines be developed to address the unique operational needs of the diagnostic laboratory community and that they be science based and made available broadly. Panel members reviewed the guidelines that were developed and synthesized by the writing team. Official endorsements by the organizations they represented were not required, although each representative was required to submit written approval of the recommendations. Edits and comments from each participant were carefully considered and incorporated where appropriate. The guidelines provided herein are synthesized and supported from systematic reviews of peer-reviewed publications of evidence-based data from which recommendations could be made, justifying common-sense approaches that should be articulated, and where safe procedures have been described and proven. Because of the lack of evidence-based research in much of

the current literature on biosafety practices, no attempt was made to weight the evidence and resulting recommendations (i.e., strong or weak). In the absence of supporting evidence-based research and documentation, some recommendations are based on expert opinion by international experts in the field of microbiology and must be appropriately applied until evidence-based research can substantiate their validity. The authors reviewed and approved their own sections and also evaluated how their topics accurately reflected and supported the goals of the entire document. Each section of recommendations was reviewed both within CDC and by the relevant national organizations whose members would embrace these guidelines. These included the College of American Pathologists, Greater New York Hospital Association Regional Laboratory Task Force, American Society for Microbiology, American Clinical Laboratory Association, Association of Public Health Laboratories, American Society for Clinical Laboratory Science, American Society for Clinical Pathology, American Biological Safety Association, American Association of Veterinary Laboratory Diagnosticians, and individual physicians and subject matter experts. Future research in biosafety practices in the laboratory will contribute to further recommendations and will substantiate others as well as provide opportunities to revise this document. Persons working in clinical diagnostic laboratories are exposed to many risks (1). Whether the patients are humans or animals and whether laboratorians work in microbiology or elsewhere in the laboratory, the human and animal diagnostic laboratory is a challenging environment. The more that laboratorians become aware of and adhere to recommended, science-based safety precautions, the lower the risk. The goal of a safety program is to lower the risk to as close as possible to zero, although zero risk is as yet unattainable as long as patient specimens and live organisms are manipulated. Protection of laboratorians, coworkers, patients, families, and the environment is the greatest safety concern. Laboratory exposures occur more often than is generally suspected. Other laboratory incidents such as minor scrapes or cuts, insignificant spills, or unrecognized

aerosols occur even more frequently and might not cause an exposure that results in an LAI. In this report, "laboratory exposures" refer to events that put employees at risk for an LAI and events that result in actual acquisition of LAIs. Except for reporting requirements imposed by CDC's Select Agent Program, which deals with handling of specific, potentially hazardous biological agents and toxins, no national surveillance system is in place to which medical laboratory exposures and subsequent work-related infections are reported. Increased attention has been focused on laboratory biosafety and biosecurity since 2001 but has been largely limited to precautions required for agents of bioterrorism. Other laboratory exposures and LAIs continue to occur, almost always because of a breakdown of established safety protocols. Because of the lack of an official surveillance mechanism for reporting LAIs and because of the fear of punitive action by an oversight agency if injuries are reported, the data needed to determine the extent and cause of LAIs are unavailable. In addition, there is a dearth of science-based insights on prevention of LAIs. The Blue Ribbon Panel recognizes the need for a voluntary, nonpunitive surveillance and reporting system with the potential for anonymity to be implemented in the United States. Such a system would allow for reporting and evaluation of all LAIs and would potentially lead to training and interventions to facilitate a negligible incidence rate. The five most predominant routes of LAIs are The first four routes are relatively easy to detect, but they account for <20% of all reported LAIs (23,24). No distinguishable exposure events were identified in approximately 80% of LAIs reported before 1978 (24–26). In many cases, the only association was that the infected person worked with a microbiological agent or was in the vicinity of a person handling a microbiological agent. The inability to identify a specific event was also reported in a more recent study (27), which found that the probable sources of LAIs were apparent in only 50% of cases. These data suggest that unsuspected infectious aerosols can play a large role in LAIs (1,23,24,28). The concept of a "culture of safety," as described in this report, encourages all human and animal

diagnostic laboratories to promote an organizational culture of systematic assessment of all work processes and procedures to identify associated risks and implement plans to mitigate those risks. In addition to the often unknown biohazard risk associated with handling diagnostic specimens, each section of the diagnostic laboratory has procedures and processes for handling known infectious agents that convey excessive risk for exposure and possible infection and/or occupational injury. These risks typically are associated with design flaws or lack of or inadequacy of safety procedures and training (1,2). In addition, the day-to-day operations of a human or animal diagnostic laboratory differ markedly from those of an academic or research laboratory and require different biosafety guidelines; these differences prompted the focus of this report on medical laboratory communities, their occupational risks, potential for exposure, and opportunities to mitigate those risks. Successful establishment of a culture of safety requires that laboratory safety become an integral and apparent priority to the organization, embraced first and foremost by top management and with the concomitant infrastructure support required to foster safe behaviors among its employees (29–31). As required by the Clinical Laboratory Improvement Amendments, the College of American Pathologists, and other accrediting agencies, a laboratory director needs to assume the responsibility for Laboratory design is fundamental to the safety of laboratory workers, hospital staff, and patients. The Clinical and Laboratory Standards Institute document, Laboratory Design; Approved Guideline (32), discusses laboratory design in detail. Because remediating poorly designed laboratory workspace is difficult, or even impossible, design warrants careful planning and consideration of safety issues. The following are suggestions to consider in the design or renovation of the diagnostic laboratory. Although there is no national standard requirement for an amount of space per person working in the laboratory, 300–350 sq. ft/person within a laboratory department is a reasonable figure to provide a safe work area. Ideally, allow a minimum 5-foot space between the worker (at a laboratory chair) and any object

behind the worker to provide reasonable maneuverability. The laboratory director is ultimately responsible for identifying potential hazards, assessing risks associated with those hazards, and establishing precautions and standard procedures to minimize employee exposure to those risks. Because the identity of an infectious agent is initially unknown in the clinical laboratory, the general recommendation is that the biosafety level (BSL)-2 standard and special practices in Biosafety in Microbiological and Biomedical Laboratories, 5th edition (1) be followed for all work in the clinical laboratory, and the Occupational Safety and Health Administration's (OSHA's) Standard Precautions (gloves, gowns, and protective eyewear) (33) and BSL-2 practices (2) be employed during handling of all blood and body fluids. Other comprehensive resources are available (34,35). Risk assessment, as outlined here and in Section 12, may determine that decreasing or increasing the BSL practices or facilities is warranted (Figure 1). Qualitative biological risk assessment is a subjective process that involves professional judgments. Because of uncertainties or insufficient scientific data, risk assessments often 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. Many categories of microbiological hazards are encountered from the time a specimen is collected until it is disposed of permanently. A comprehensive approach for identifying hazards in the laboratory will include information from a variety of sources. Methods to ascertain hazard information can include benchmarking, walkabouts, interviews, detailed inspections, incident reviews, workflow and process analysis, and facility design. 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: Identify the hazards associated with an infectious agent or material. Identify the activities that might cause exposure to the agent or material. Consider the competencies and experience of laboratory personnel. 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). Develop, implement, and evaluate controls to minimize the risk for exposure. Standardization of the risk assessment process at an institution can greatly improve the clarity and quality of this process. Training staff in risk assessment is critical to achieving these objectives. 2.1.1. Step 1. Identify the hazards associated with an infectious agent or material. 2.1.2. Step 2. Identify activities that might cause exposure to the agent or material. 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 Flaming loops Cooling loops in culture media Subculturing and streaking culture media Expelling last drop from a pipette (including Eppendorff pipettes) 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 isolates for automated identification/susceptibility testing Preparing smears, performing heat fixing, staining slides Performing catalase test Performing serology, rapid antigen tests, wet preps, and slide agglutinations Throwing contaminated items into biohazardous waste Cleaning up spills 2.1.3. Step 3. Consider the competencies and experience of laboratory personnel. 2.1.4. Step 4. Evaluate and prioritize risks. Risks are evaluated according to the likelihood of occurrence and severity of consequences (Table 2). 2.1.5. Step 5. Develop, implement, and evaluate controls to minimize the risk for exposure. 2.2.1. Containment "Containment" describes safe methods for managing

infectious materials in the laboratory to reduce or eliminate exposure of laboratory workers, other persons, and the environment. BSLs provide appropriate levels of containment needed for the operations performed, the documented or suspected routes of transmission of the infectious agent, and the laboratory function or activities. The four BSLs, designated 1–4, are based on combinations of laboratory practice and techniques, safety equipment (primary barriers), and laboratory facilities (secondary barriers). Each BSL builds on the previous level to provide additional containment. Laboratory directors are responsible for determining which BSL is appropriate for work in their specific laboratories. Material Safety Data Sheets (MSDS) for chemicals are available from the manufacturer, supplier, or an official Internet site. The Division of Occupational Health and Safety, National Institutes of Health, has promulgated guidelines for handling genetically manipulated organisms and has additional instructions for accessing MSDS (http://dohs.ors.od.nih.gov/material_safety_data_main.htm). Many safety procedures, guidelines, and principles apply to all sections of the diagnostic laboratory. The recommendations presented in this section represent a broad view of safety throughout the laboratory. More detailed recommendations can be found in

Biosafety in Microbiological and Biomedical Laboratories (BMBL-5) and in the

World Health Organization's

Laboratory Biosafety Manual (1,36). Hospitals, clinical laboratories, state and local health departments, CDC, and the American Society for Microbiology have established and/or published guidelines to follow when suspected agents of bioterrorism have been or could be released in the community. However, routine clinical laboratory testing may provide the first evidence of an unexpected bioterrorism event. Routine clinical specimens also may harbor unusual or exotic infectious agents that are dangerous to amplify in culture. These agents are often difficult to identify, and the routine bench technologist might continue work on the culture by passage, repeated staining, nucleic

acid testing, neutralization, and other methods. This continued workup places the technologist and others in the laboratory at risk for infection. Ideally, these specimens are not to be processed or tested in the routine laboratory, and they can be removed from the testing stream if the suspected agent is known. Relationships with the state public health laboratory, and subsequently with the Laboratory Response Network, are critical in this effort. Once the testing process has begun, the bench technologist must have clear and concise instructions about when to seek assistance from the laboratory supervisor and/or director. 3.1.1. Leaking containers 3.1.2. Visible contamination of the outside of containers 3.1.3. Loose caps 3.1.4. Operational procedures 3.1.5. Manual removal of sealed caps; specimen aliquotting and pipetting 3.1.6. Pneumatic tube systems If engineering controls are in place to prevent splashes or sprays, the requirement for PPE can be modified on the basis of a risk assessment and evidence of the effectiveness of the engineering control to prevent exposure from splashes or sprays. Examples of engineering controls include use of a BSC, having sealed safety cups or heads in centrifuges, and negative air flow into the laboratory. 3.2.1. Work at the open bench CDC continues to recommend that sniffing culture plates should be prohibited. Isolates of small gram-negative or gram-variable rods (e.g., gram-negative coccobacilli) should be manipulated within a BSC. 3.2.2. Personal protective equipment Engineering controls (2.1.5. Step 5) should always be the first line of defense to minimize exposures. PPE includes a variety of items, such as gloves, laboratory coats, gowns, shoe covers, boots, respirators, face shields, safety glasses, and goggles, that are designed to protect the laboratory worker from exposure to physical, biological, and chemical hazards. Distributing PPE to each employee as needed helps to ensure access to appropriate PPE. PPE is often used in combination with BSCs and other devices that contain the agents or materials being handled. In some situations where working in a BSC is impractical, PPE, including splash shields, may form the primary barrier between personnel and hazardous materials (1). (See Section 3.1). The Occupational Safety and

Health Administration (OSHA) defines PPE as "appropriate" if it does not permit blood or other potentially infectious materials to pass through or reach the employee's street clothes, undergarments, skin, eyes, mouth, or other mucous membranes under normal conditions of use (33). When PPE is necessary What PPE is necessary How to properly put on, take off, adjust, and wear PPE Limitations of PPE Proper care, maintenance, useful life, and disposal of PPE 3.4.1. Good work practices 3.4.2. Bleach solutions (sodium hypochlorite) (38) A clinical laboratory must establish a waste management plan. 3.5.1. Decontamination of medical waste before transport and disposal 3.5.2. Management of discarded cultures and stocks 3.5.3. Discarding a select agent 3.5.4. Autoclave safety 3.6.1. General information Under certain circumstances, dry ice can be an explosion hazard. Dry ice is solidified carbon dioxide (CO) and it is extremely cold (-109° F [-79° C]). Unlike water-ice, dry ice sublimates (changes directly from solid to gas) as it warms, releasing CO gas. CO vapor is considerably heavier than air; in confined, poorly ventilated spaces, it can displace air, causing asphyxiation. 3.6.2. Disposal of dry ice Compressed CO cylinders are often used to provide gases for CO incubators; the risks associated with these incubators are minimal as long as the room is well ventilated. 3.8.1. Hazards 3.8.2. Minimizing hazards Many of these potential hazards can be minimized by adoption of safe handling practices. Cryogenic liquids are liquefied gases that have a normal boiling point below -238°F (-150°C). Liquid nitrogen is used in the microbiology laboratory to freeze and preserve cells and virus stocks. The electron microscopy laboratory, frozen section suites, and grossing stations for surgical pathology frequently use liquid nitrogen; some laboratories also use liquid helium. The principal hazards associated with handling cryogenic fluids include cold contact burns and freezing, asphyxiation, explosion, and material embrittlement. 3.9.1. Cold contact burns and freezing 3.9.2. Asphyxiation hazards 3.9.3. Explosion hazards 3.9.4. Cryotube explosions 3.9.5. Embrittlement 3.9.6. Infectious disease hazards Slips, trips, and falls can cause a laboratory worker to drop or spill vessels containing infectious agents or

dangerous chemicals. They can also lead to skin punctures and abrasions that make laboratory workers more vulnerable to LAIs. Good housekeeping is the most fundamental means for reducing slips, trips, and falls. Without good housekeeping, any other preventive measures (e.g., installation of sophisticated flooring, specialty footwear, or training on techniques of walking and safe falling) will never be fully effective. 3.10.1. Slips 3.10.2. Trips Wear thermally resistant gloves and a laboratory coat when handling items stored at ultralow temperatures. Specimens stored at ultralow temperatures are extremely cold [-70°C to -85°C]), and paradoxically, direct contact with the skin can cause severe burns. Vacuum-assisted filtration devices and side-arm suction flasks are used routinely in the general laboratory, whereas the electron microscopy laboratory uses vacuum-assisted evaporators, freeze-driers, freeze-fracture, and sputter coater units. Vacuum-assisted devices present implosion hazards and risk aerosol generation. 3.13.1. Implosion safety 3.13.2. Aerosol generation 3.13.3. Aerosol protection measures 3.13.4. Disposal of liquid wastes from vacuum-assisted aspiration traps 3.14.1. Punctures and cuts Skin punctures and cuts can directly introduce an infectious agent into the body and can provide a route whereby a secondary agent can enter. Wear appropriate gloves for this procedure (based on risk assessment and protection needed). Cover the broken container and spilled infectious substance with a cloth or with paper towels.

For the routine BSL-2 laboratory, pour a disinfectant or a fresh 1:10 household bleach solution over the covered area and leave for a minimum of 20 minutes. It would take 23 minutes to clear the air of airborne

M. tuberculosis from a spill at 99% removal efficiency if the room had 12 room air changes per hour, and 35 minutes for this removal with 99.9% efficiency (46). Given the variability of the number of room air changes per hour in diagnostic laboratories, the wait time has to be carefully evaluated. The cloth or paper towels and the broken material should be cleared away into biohazard sharps receptacles. Fragments of glass

are to be handled with forceps, not gloved hands. (Using wadded up tape with forceps facilitates this procedure). Small HEPA vacuum cleaners are also available for removal of fine glass particulates. 3.14.2. Ingestion and contact with infectious agents 3.14.3. Spills and splashes onto skin and mucous membranes 3.14.4. Aerosols and droplets Any procedure that imparts energy to a microbial suspension can produce infectious aerosols (1,23). Procedures and equipment frequently associated with aerosol production include pipetting, mixing with a pipette or a vortex mixer, and use of blenders, centrifugation, and ultrasonic devices (sonicators) (1,23,47). These procedures and equipment generate respirable particles that remain airborne for protracted periods. When inhaled, these tiny particles can be retained in the lungs. These procedures and equipment also generate larger droplets that can contain larger quantities of infectious agents. The larger droplets settle out of the air rapidly, contaminating, work surfaces as well as the gloved hands and possibly the mucous membranes of persons performing the procedure. Respirable particles are relatively small and do not vary widely in size distribution. In contrast, hand and surface contamination is substantial and varies widely (1,48). The potential risk from exposure to larger-size droplets requires as much attention in a risk assessment as the risk from respirable particles. In the microbiology laboratory, all the technical work areas of the department are considered dirty. The same concepts of demarcation and separation of molecular testing areas that are described in this section can be used to establish clean and dirty areas in other parts of the diagnostic laboratory. 3.16.1. Clean areas 3.16.2. Offices Offices (e.g., of supervisors and laboratory director) that open into the clinical laboratory represent hybrid areas within the laboratory. These offices are not typically designed or maintained in a manner that allows for easy or efficient disinfection. 3.16.3. Dirty areas Whether automated or manual, procedures with the potential for producing specimen aerosols and droplets (e.g., stopper removal, vortexing, opening or piercing evacuated tubes, using automatic sample dispensers) require PPE and engineering

controls designed to prevent exposure to infectious agents. 3.17.1. Water baths and water (humidification) pans in CO incubators 3.17.2. Centrifuges and cytocentrifuges 3.17.3. Automated analyzers 3.17.4. Vacuum-assisted aspiration devices (See Section 3.13.) 3.17.5. ELISA plate washers in microbiology 3.17.6. Identification, blood culture, and PCR instruments Bacterial identification and antimicrobial susceptibility instruments, blood culture instruments, PCR instruments, and other laboratory instruments and devices are to be cleaned or disinfected according to the manufacturer's directions or recommendations. The routine and emergency cleaning procedure for each instrument must be a part of the safety component of the procedure manual.

Tuberculosis (TB) resulting from exposure to infectious aerosols remains a major risk for laboratorians. There is no safe level of exposure since exposure to as few as 1–10 organisms can cause disease. An estimated 8%–30% of laboratorians may experience tuberculin conversions (52). To reduce exposures to

Mycobacterium tuberculosis, a hierarchy of controls must be employed, including safe work practices, use of containment equipment, and specially designed laboratory facilities (1). Tuberculosis laboratories need to be separate and isolated from the main microbiology laboratory. Develop all policies and practices related to safety using a risk assessment process that is documented in the laboratory's biosafety manual. In most clinical laboratories specimens are first received in the main microbiology laboratory (biosafety level [BSL]-2), where they are logged in and processed for other bacteriologic testing. The specimens submitted for TB analysis are moved to the TB laboratory for further processing specific for TB. 4.1.1. Specimen receiving in the main microbiology laboratory 4.1.2. Specimen receiving in other laboratory sections 4.1.3. Leaking containers 4.1.4. Visible contamination on the outside of container Prepare smears in a BSC because aerosols, droplets and splatters can be generated. Unstained smears may contain viable tubercle bacilli and are to be handled with caution. 4.2.1. Gram stain

Specimens submitted for routine cultures, especially sputum and other respiratory specimens, may contain tubercle bacilli and must be handled with care regardless of whether or not acid-fast bacillus (AFB) cultures were ordered. 4.2.2. Acid-fast stains — Kinyoun, Ziehl-Neelsen, auromine–rhodomine (fluorescent) Precautions and work practices are selected with regard to the potential quantity of tubercule bacilli encountered in the procedure being performed. Hence, specimens have a lower concentration than a culture, in which the number of organisms is amplified. Because aerosols are generated whenever energy is imparted into the specimen, all protocols in the TB laboratory are evaluated through the risk assessment process for the potential to generate aerosols. Common aerosol-generating procedures are pouring liquid cultures and supernatant fluids, using fixed-volume automatic pipetters, and mixing liquid cultures with a pipette. 4.4.1. Personal protective equipment 4.4.2. Respiratory protection 4.11.1. Rapid testing (direct molecular test kits) 4.11.2. Molecular testing The source of most laboratory-acquired infections and hazardous exposures that occur during autopsy/necropsy is unknown, and all autopsies and necropsies are to be considered risky (1,56). 5.1.1. Bloodborne pathogens Human-health–care workers involved in performance of autopsies are at high risk for occupationally acquired bloodborne pathogens because of both the injuries sustained and the population undergoing autopsy. Transmission risk is highest per exposure for hepatitis B virus, then hepatitis C virus and human immunodeficiency virus, respectively. These infections have been documented from autopsies as well as during embalming (1,2,56,60–62). 5.1.2. Other infections Specific data for other bloodborne pathogens, such as cytomegalovirus, are lacking, but infectious transmission is possible and risk may be higher especially for pregnant (serologically negative) or immunocompromised workers. Assess persons at higher risk for infection on a case-by-case basis and allow them to consent to participating in the autopsy only after being counseled (2,63). 5.1.3. Infectious aerosols Autopsies/necropsies of cadavers with suspected zoonotic agents

generate potentially infectious aerosols. Although

Mycobacterium tuberculosis is the prototypical pathogen most noted to be transmitted by aerosolization, persons who had meningococcemia, anthrax, rickettsiosis and legionellosis are other examples. Manipulation of infectious tissue can result in both airborne particles in a size (<5

μm) that floats on air currents for extended periods and can subsequently reach the pulmonary alveoli and small-droplet particles (>5

μm) that settle more quickly. Contamination may occur from fluid-aspirating hoses, from spraying the cadaver, and from oscillating saws. The aerosols created stay within the autopsy area and can result in subsequent contact with mouth and eyes, inhalation, or ingestion and can contaminate inanimate surfaces such as computers, telephones and camera equipment (56,57). 5.1.4. Organisms that require additional safety practices 5.1.5. Other biosafety exposures 5.1.6. Reporting to the mortician Report known bloodborne pathogens or other suspected aerosolization danger to the mortician and others potentially handling the body to limit subsequent transmissions that may occur during transport or embalming (69). 5.1.7. Necropsy remains of animals Dispose of animal cadavers with potential zoonotic infectious agents by appropriate decontamination (e.g., incineration, alkaline digestion or other methods), and do not return them to animal owners for private burial. 5.2.1. Inspect the body/carcass 5.2.2. Safety guidelines for the suite Formaldehyde (3.7%–4.0%) used for specimen preservation is the most common toxic chemical to which autopsy workers are exposed. The chemical is volatile and toxic and causes irritation to the eyes, mucous membranes, and skin and is associated with increased risk for all cancers. Occupational Safety and Health Administration (OSHA) regulations specify an exposure limit of 0.75 ppm as an 8-hour time-weighted average, and 2.0 ppm for short-term (15-minute) exposures (70). If formaldehyde can be detected by smell, it likely means exposure is occurring at a concentration beyond acceptable limits. Limit exposure to formaldehyde

in the following manner. 5.5.1. Safety equipment 5.5.2. PPE for autopsy/necropsy personnel 5.6.1. Human autopsy 5.6.2. Human autopsy/animal necropsy The following guidelines for disinfection and cleaning following an autopsy or necropsy apply to both types of procedures. Wash reusable, nonlaunderable items such as aprons with a detergent solution, decontaminate with bleach solution, rinse with water and allow to dry before next use. 5.7.1. Human tissue Either incinerate all pathological waste, since this is considered hazardous material and is regulated by the U.S. Department of Transportation (DOT), or transport pathological waste to on-site or off-site treatment facilities in clearly labeled, dedicated, leakproof containers or carts that meet DOT requirements. DOT sharps waste containers need to be puncture-proof in addition to meeting these requirements. State, local, and regional regulations may also apply and need to be addressed. 5.7.2. Animal tissue Dispose of all animal necropsy waste (tissues or postnecropsy cadaver) using an appropriate method as determined by the case-by-case risk analysis assessment (incineration, autoclaving and standard waste disposal, rendering, composting, cremation, private burial). 5.7.3. Other waste Shred autoclave red-bag waste if appropriate. State, local, and regional regulations may also apply and need to be addressed. (See Section 3.5, Waste Management.) Clean areas might include an administrative area and bathrooms with showers. Air from these areas should be exhausted differently than from the autopsy suite (56,76,77). All other areas are considered dirty, and appropriate PPE is required. 5.9.1. Specimen receiving and log-in 5.9.2. Work at the open bench 5.9.3. Clean versus dirty areas of the laboratory All of the surgical pathology specialty areas (cytology, histology, grossing or frozen section rooms) are considered dirty areas if fresh specimens or body fluids are received or processed in an open room (not in a BSC or separately vented area). 5.9.4. Tissue stains Multiple staining procedures are performed in histology and cytology. The most common are included here. Some of these stains are prepared with ethanol and some with methanol, which can have an impact on management options for their waste.

Provide material safety data sheets (MSDS) for each component in the laboratory. 5.9.5. Fixatives When updating or renovating autopsy and other areas of the anatomic pathology laboratory that process fresh tissue and body fluids, the following should be considered. Special precautions for autopsy and autopsy suite decontamination, brain-cutting, and histologic tissue preparation procedures are required when processing cases of possible CJD (1,56,65,67,86). 5.11.1. Autopsy Perform autopsies using BSL-2 precautions augmented by BSL-3 facility ventilation and respiratory precautions. Wear standard autopsy PPE. Limit the autopsy to brain removal. Restrict participants to only those who are necessary. Double-bag the brain and place it in a plastic container for freezing or fix it in 3.7%–4% formaldehyde after sectioning. Formaldehyde fixation occurs for 10–14 days before histologic sections are collected. 5.11.2. Histologic preparations Exposure to infectious parasites during diagnostic procedures may result from handling specimens, drawing blood, performing various types of concentration procedures, culturing organisms, and conducting animal inoculation studies. Relevant parasites and their possible routes of infection are listed in Table 7 and Box 1. Table 8 contains information on resistance to antiseptics and disinfectants. 6.1.1. Leaking containers 6.1.2. Loose caps 6.2.1. Trichrome stain 6.2.2. Hematoxylin stain 6.2.3. Iodine 6.2.4. Acid-fast stains (modified) 6.2.5. Giemsa stain 6.2.6. Wright stain 6.2.7. Formalin (HCHO) 6.2.8. Mercury-based fixatives 6.2.9. Zinc-based fixatives (containing formalin) 6.2.10. Copper-based fixatives (containing no formalin) 6.2.11. Xylene and alcohols 6.4.1. Biological safety cabinet versus fume hood 6.4.2. Personal protective equipment 6.4.3. Immunization 6.4.4. Disinfection General recommendations for the microbiology laboratory are sufficient for use in the diagnostic parasitology section; these would include guidelines for disinfection of countertops, telephones, computers, equipment, and hands-free telephones. General guidelines for the microbiology laboratory also apply for the parasitology section of the laboratory. No special recommendations are necessary. Safety requirements for the use of

instruments are the same as those used for a general microbiology laboratory and are primarily involved with specimen handling. Safety requirements for antibody and antigen testing are the same as those used for a general microbiology or immunology laboratory and are primarily involved with specimen handling. Although not a strict requirement, it is recommended that mycology laboratories that culture for filamentous fungi and manipulate those organisms be separate and isolated from the main microbiology laboratory with negative air pressure moving into the room from the main laboratory. Direct access to a Class II biological safety cabinet (BSC) is critical for this activity whether mycology work is conducted in a separate room or in an isolated section of the main laboratory. Most mycology diagnostic work can be conducted in the biosafety level (BSL)-2 laboratory. 7.1.1. Leaking containers Guidelines for the general microbiology laboratory apply also for the mycology laboratory. No special recommendations are necessary. 7.1.2. Visible contamination on outside of container Guidelines for the general microbiology laboratory apply also for the mycology laboratory. No special recommendations are necessary. 7.1.3. Loose caps Guidelines for the general microbiology laboratory apply also for the mycology laboratory. No special recommendations are necessary. 7.2.1. Gram stain The Gram stain is not the optimum stain for fungus, but if used particularly for yeast, the same guidelines that apply to bacteriology/clinical microbiology are followed for mycology. 7.2.2. Mycology stains 7.4.1. Biosafety cabinet 7.4.2. Personal protective equipment 7.4.3. Disinfection Recommendations for the general microbiology laboratory are sufficient for use in the mycology laboratory; these include guidelines for disinfection of countertops and items such as telephones, computers, equipment, and hands-free telephones. 7.4.4. Decontamination and disposal of laboratory waste Guidelines for the general microbiology laboratory apply also for the mycology laboratory. Instruments used for mycology studies are most commonly those for continuously monitored blood culture and for yeast identification. Follow the same guidelines that apply to

bacteriology/clinical microbiology. Follow the clinical microbiology safety guidelines for mycology with the additional advisory that mold isolates must be handled in a BSC during extraction of nucleic acids. 8.1.1. Biohazards associated with specimen receiving and log-in The clinical virology laboratory receives a wide variety of clinical specimens for virus detection. Because the infectious nature of this material is largely unknown, special care must be taken to prevent contamination of personnel, the environment, and other clinical specimens. 8.1.2. Leaking containers 8.1.3. Visible contamination on outside of container Specimens with a small amount of contamination (e.g., a dried blood spot) on the outside of the container are to be brought to the attention of the laboratory director. The director can examine the specimen and determine if it is suitable for testing and whether it constitutes a hazard to laboratory personnel. 8.1.4. Special precautions for suspicious specimens 8.2.1. Alcohols Ethanol, methanol, isopropyl alcohol, and alcohol blends are used in the virology laboratory to fix cells, for nucleic acid extraction and precipitation, and as a disinfectant. 8.2.2. Antibiotics Antibiotics in routine use include penicillin, streptomycin, gentamicin, ciprofloxacin, kanamycin, tetracycline, amphotericin B, and neomycin. These antibiotics can be found in culture media and viral transport media. Concentrated antibiotic mixtures are frequently used to increase the antibiotic concentrations in samples containing large numbers of bacteria or fungi. Concentrated antibiotic solutions can be purchased at 50 times (50×) and 100 times (100×) the working concentration. Although the risks associated with antibiotic preparation and use are relatively low in the virology laboratory, antibiotic preparation and handling has been associated with hypersensitivity reactions and contact dermatitus (115,116) and asthma (116–120) in hospital, pharmaceutical, and animal workers. 8.2.3. Bleach solutions (see 3.4.2) 8.2.4. Cycloheximide Cycloheximide is used as an antibiotic, protein synthesis inhibitor, and plant growth regulator. In the virology laboratory, cycloheximide is used in Chlamydia re-feed media. Cycloheximide is inactivated by alkaline solutions (pH

>7.0). Aspirating cycloheximide-containing culture fluids into vacuum traps containing a 1:10 bleach solution will inactivate the chemical. Most soaps and detergents are alkaline, and these agents will also inactivate cycloheximide. 8.2.5. Dimethyl sulfoxide Dimethyl sulfoxide (DMSO) is used as a cryoprotectant when freezing cell cultures. DMSO is a powerful solvent and can penetrate skin and latex gloves. 8.2.6. Electron microscopy stains, fixatives, and buffers 8.2.7. Electron microscopy embedding media (Meth)acrylates and epoxy-based materials are frequently used to embed biological samples for electron microscopy. Epoxy products include Epon, Araldite, Spurr resin, and Maraglas. Formvar (polyvinyl formal) is used as a support film for electron microscopy grids and for making replicas. Many of these compounds are toxic, carcinogenic or potentially carcinogenic and are known to cause skin irritation, dermatitis, and skin sensitization. Consult individual MSDS documents for more information. 8.2.8. Ethidium bromide Ethidium bromide (EtBr) is a DNA intercalating agent that is commonly used as a nonradioactive marker for visualizing nucleic acid bands in electrophoresis and other gel-based separations. EtBr is a potent mutagen, toxic after acute exposure, and is an irritant to the skin, eyes, mouth and the upper respiratory tract. 8.2.9. Evans blue Evans blue is used as a counterstain during fluorescence microscopy. Evans blue powders and solutions are skin irritants, but there is no known flammability, carcinogenicity, or teratogenicity warning associated with this compound. 8.2.10. Guanidinium solutions Guanidinium chloride, guanidinium thiocyanate, and guanidinium isothiocyanate are chaotropic agents used to disrupt cells and denature proteins (particularly RNases and DNases) during nucleic acid extraction procedures. These chemicals are strong irritants, and eye exposure can result in redness, irritation and pain. They are toxic if ingested and may cause neurologic disturbances. If inhaled, guanidinium compounds can cause respiratory tract irritation coughing, and shortness of breath. 8.2.11. Neutral red Neutral red is a pH indicator and a vital stain used in some plaque assays. It may be harmful if swallowed, inhaled, or

absorbed through the skin and can cause irritation to the skin, eyes, and respiratory tract. 8.2.12. Merthiolate (thimerosal) Merthiolate, or thimerosal, is a mercury-containing antiseptic and antifungal agent used as a preservative in some laboratory solutions. Concentrated thimerosal is very toxic when inhaled, ingested, and in contact with skin. 8.2.13. Organic solvents 8.2.14. Sodium azide Sodium azide is a common preservative in many laboratory reagents, including monoclonal antibodies, buffers, and enzyme immunoassay reagents. 8.3.1. Cell lines 8.3.2. Cell culture practices Workers who handle or manipulate human or animal cells and tissues are at risk for possible exposure to potentially infectious latent and adventitious agents that may be present in those cells and tissues. CDC/National Institutes of Health recommended cell culture practices (1) include the following. 8.3.3. Biohazards associated with cell culture reading 8.3.4. Biohazards associated with liquid nitrogen use Liquid nitrogen can become contaminated when ampoules are broken in the dewar, and contaminants can be preserved in the nitrogen (23). These potentially infectious contaminants can contaminate other vials in the dewar and generate an infectious aerosol as the liquid nitrogen evaporates. Plastic cryotubes rated for liquid nitrogen temperatures are recommended for liquid nitrogen storage because they appear to be sturdier than glass ampoules and are less likely to break in the nitrogen. Glass ampoules are not recommended. Ampoules and cryotubes can explode when removed from liquid nitrogen creating infectious aerosols and droplets. See Section 3.9 for additional information. No amount of safety engineering can reduce the physical, chemical, and biological risks in a laboratory environment if personal precautions are not employed consistently and rigorously. All laboratory workers and visitors are responsible for following established procedures regarding personal precautions. Directors and supervisors should periodically review their biosafety responsibilities (1). 8.4.1. Biological safety cabinet 8.4.2. Personal protective equipment 8.4.3. Disinfection Disinfection guidelines for the general microbiology laboratory are applicable to the

virology laboratory (Section 3). Routine clinical laboratory testing may provide the first evidence of an unexpected bioterrorism event, and routine clinical specimens may also harbor unusual or exotic infectious agents that are dangerous to amplify in culture. Early recognition of these possible high-risk organisms is critical, as is adherence to all fundamentals of laboratory safety. Events that require intervention by a supervisor or laboratory director are listed (Table 10). Although the majority of events are caused by inadvertent actions and pose no risk, laboratory technologists and directors should be aware that multiple high-risk causes are possible. How the laboratory responds to these trigger events will depend upon whether the laboratory has a BSL-3 facility and the capabilities of the state and local laboratory response network (LRN). 8.7.1. Fluorescent antibody testing bench 8.7.2. Suspicious or unusual results 8.7.3. Nucleic acid testing Diagnostic electron microscopy can be a relatively simple and rapid method for morphologic identification of agents in a specimen. Electron microscopy procedures can serve as a general screen to detect novel organisms or organisms that have altered genetic or immunologic properties that render them undetectable by nucleic acid or immunoassay protocols (192). Electron microscopy laboratories share many of the physical, chemical, and biological hazards described for the virology laboratory but also have some unique features. 8.8.1. Flammable and combustible liquids The electron microscopy laboratory uses a wide variety of flammable solvents, and the use of open flames is discouraged (see Section 8.2.13). 8.8.2. X-ray hazards The electron microscope will generate dangerous levels of X-rays within the microscope as high-energy electrons strike the metal components. Modern electron microscopes have sufficient shielding and lead-impregnated glass viewing ports that minimize dangers to the operator. However, modifications to the instrument, adding and removing accessories, and some maintenance procedures can compromise the shielding. 8.8.3. Electrical hazards See Section 3.7 for information regarding routine electrical safety in the electron microscopy laboratory. 8.8.4. Chemical hazards Several heavy metal stains

and aggressive fixatives are used in the electron microscopy laboratory. See Section 8.2 and the MSDS materials provided by the manufacturers for guidelines for handling stains and fixatives. Embedding and filmmaking materials are chemical hazards, and many of these materials are dissolved in flammable organic solvents. 8.8.5. Cryogens and compressed gases The most commonly used cryogens used in the electron microscopy laboratory are liquid nitrogen and liquid helium. Compressed helium, CO and nitrogen are also used. Hazards and safety measures associated with these gases are summarized in Sections 3.8 and 3.9. 8.8.6. Specialized equipment The electron microscopy laboratory uses a number of specialized instruments whose use can be hazardous. For example, evaporators, freeze-driers, freeze-fracture, and sputter coater units use vacuum, and the vessels could implode. Implosion hazards are reviewed in Section 3.13.1. 8.8.7. Biological hazards The biological hazards of the electron microscopy laboratory are similar to those of the virology laboratory, and good laboratory practices must be followed. Several FDA-approved, rapid immunodiagnostic tests for viral antigens and antibodies are available. Originally designed for point-of-care or near point-of-care testing, many of these tests are being used for testing in clinical virology laboratories. The following biosafety recommendations are based upon CDC biosafety guidance for handling clinical specimens or isolates containing 2009-H1N1 influenza A virus (194). Molecular virology laboratories share many of the physical, chemical and biological hazards described for the virology laboratory, but they also present some unique hazards. 8.10.1. Electrical hazards See Section 3.7 for information regarding routine electrical safety in the molecular virology laboratory. Special high-voltage power sources are used in electrophoresis and nucleic acid sequencing equipment. 8.10.2. Ultraviolet light hazards 8.10.3. Chemical hazards The chemical hazards unique to the molecular virology laboratory include chloroform, ethidium bromide (Section 8.2.8) and guanidinium-based extraction reagents (Section 8.2.10). Avoid acute and long-term exposure to these. 8.10.4. Biological hazards The

biological hazards in the molecular virology laboratory are similar to those of the virology laboratory, and good laboratory practices must be followed. All specimens of human and animal origin tested by the chemistry, toxicology, or drug-testing laboratory may contain infectious agents. It is imperative to understand and minimize the risk of exposure to patient specimens through surface contact, aerosolization, or penetrating injury. Risk mitigation of laboratory-acquired infections is discussed in Sections 2 and 3. Automated analyzers frequently have added features to help reduce operator exposures, but they do not totally eliminate the potential for exposure. A common feature in newer systems is closed system sampling. To adequately assess the risk of active biohazards in analyzer effluents or processes, risk analysis should begin with assessment of procedures that occur prior to the use of specific analyzers. Sample preparation protocols may fully inactivate viruses and bacteria so that the risk of biohazardous aerosol generation in the analyzer effluent is essentially zero. One example is the use of protein-precipitation techniques or protein denaturing solvents in liquid chromatography, which would negate biohazard concerns in aerosols or effluents generated by the analyzer. 9.3.1. Graphite furnaces 9.3.2. Mass spectrometers Biosafety guidelines for the hematology laboratory are the same as those for the microbiology laboratory and are described in Section 3.1. See Section 3.2.1. 10.2.1. Standard operating procedures Standard operating procedures are described in Section 3.1.4. 10.2.2. Manual removal of sealed caps and specimen aliquotting/pipetting See Section 3.1.5. 10.2.3. Unfixed specimens Guidelines for personal precautions, including use of a BSC (Section 3.3), PPE (Section 3.2.1), and disinfection (Section 3.4) are described in Section 3. See Section 3.5 for guidelines for decontamination and disposal of laboratory waste. See Section 3.16. Whether automated or manual, procedures with the potential for producing specimen aerosols and droplets (e.g., stopper removal, vortexing, opening or piercing evacuated tubes, automatic sample dispensers) require either PPE or engineering controls designed to prevent exposures to infectious agents.

10.6.1. Waterbaths See Section 3.17.1. 10.6.2. Centrifuges See Section 3.17.2. 10.6.3. Automated hematology/hemostasis analyzers Automated analyzers frequently have added features to help reduce operator exposures, but these do not totally eliminate potentials for exposure. A common feature in newer systems is closed system sampling. See Sections 3.17.3, 9.1, and 11.6.3 for additional information. 10.6.4 Flow cytometers (see Section 3.17.3) Occupational exposures in a routine flow cytometry (FCM) laboratory arise either from sample handling or, more specifically, from aerosols and droplets generated by the flow itself. Flow cytometric applications, e.g., phenotypic analysis, calcium flux evaluations, and apoptosis measurements of unfixed cells, when performed using jet-in-air flow cytometers with extremely high pressure settings can expose operators to potentially hazardous aerosols. 10.6.5. Automated slide stainers 10.6.6. Total or semiautomated hematology test systems Consider used testing kits to be contaminated, and dispose of them appropriately in accordance with applicable local and state environmental regulations. 10.9.1. General recommendations (200–203) 10.9.2. Dirty versus clean areas in the laboratory See Section 3.16. 10.9.3. Pneumatic tube systems See Section 3.1.6. 10.9.4. Personal precautions See Section 3.2. 10.9.5 Disinfection of work space See Section 3.4.1. Regardless of the method, the purpose of decontamination is to protect the phlebotomist, the patient and the environment, and anyone who enters a patient room/drawing station or who handles materials that have been carried into or out of the patient room/drawing station. 10.9.6. Disinfecting patient room work areas and drawing stations See Section 3.4.1. 10.9.7. Documentation of training and competency assessment in phlebotomy Assessment includes knowledge of, and adherence to, any applicable hospital infection control policies/procedures in patient settings and the concept of Standard Precautions. Many infectious agents are transmitted through transfusion of infected blood; these include hepatitis B virus, hepatitis C virus, human immunodeficiency viruses 1 and 2, human T-cell lymphotropic viruses (HTLV-I and II), cytomegalovirus, parvovirus B19, West Nile virus , dengue virus,

trypanosomiasis, malaria, and variant Creutzfeldt-Jakob disease. The AABB provides information on transfusion-transmitted diseases as well, available at http://www.aabb.org/Pages/Homepage.aspx.

The Occupational Safety and Health Administration's (OSHA) Bloodborne Pathogen Standard, 29 CFR 1910.1030 must be adhered to in the blood bank laboratory (33). Guidelines for receiving and logging specimens and handling specimen containers are described in Section 3.1. Written procedures for blood bank include specific work practices and work practice controls to mitigate potential exposures. Standard operational procedures (SOPs) and procedure manuals are described in Section 3.1.4. 11.4.1. Unfixed specimens 11.4.2. Biological safety cabinet A Class II biological safety cabinet (BSC; see Section 3.3) is required for all aerosol-generating processes. 11.4.3. Personal protective equipment See Section 3.2.2. 11.4.4. Disinfection See Section 3.4. 11.4.5. Decontamination and disposal of laboratory waste See Section 3.5 for discussion, including a waste management plan. See Section 3.16. See Section 3.17. 11.6.1. Refrigerators and freezers For all refrigerators and freezers in the blood bank, establish a cleaning and maintenance protocol that will minimize contamination and extend the life of the equipment and also maintain the sophisticated cooling systems blood bank refrigerators require to provide uniform and quick temperature recovery when needed. (also see Section 3) Most newer blood bank laboratory refrigerators and freezers are stainless steel and have painted finishes and removable trays, which make cleaning and sanitizing an easier process. 11.6.2. Automated blood bank analyzers Automated or semi-automated instruments are now available that are adapted either to donor collection settings or patient transfusion settings. Although these instruments have the potential to replace much of the open bench testing in blood banks and donor collection settings, manual testing is still being used for some antibody detection and verification procedures and in smaller laboratories. All blood bank automated analyzers currently approved for use in the United States have added features to help reduce

operator exposures, but they have not totally eliminated potential for exposure. 11.6.3. Total or semiautomated test systems See Section 10.6.6. See Section 10.7. Donor collection and apheresis areas are considered patient care settings, and all applicable hospital patient care and infection control polices/procedures must be strictly adhered to. This section provides practical guidelines for work practices that minimize biosafety hazards from veterinary diagnostic specimens. Many of the biosafety practice guidelines for human clinical microbiology laboratories are applicable in veterinary diagnostic laboratories. Similar to human clinical microbiology laboratories, the nature of the work performed in veterinary diagnostic laboratories puts these laboratorians, too, at risk for laboratory-acquired infections. Sixty percent of infectious diseases in humans are due to multihost pathogens that move across species lines (206,207), and during the past 30 years, 75% of the emerging human pathogen diseases (e.g., West Nile virus fever, highly pathogenic avian influenza, Lyme disease) have been zoonotic, i.e., transmitted between humans and animals (208). All nonhuman diagnostic specimens are potentially infectious to humans, although the degree of risk is less so than with handling and examination of human diagnostic specimens. Potential infectious agents in human diagnostic specimens are by definition human pathogens. Conversely, not all potential infectious agents in animal diagnostic specimens are human pathogens. The key to managing biosafety risk in veterinary diagnostic laboratories depends not only upon good general biosafety practices but, more importantly, on a practical risk assessment of the "unknown" diagnostic specimen. In general, veterinary diagnostic laboratories use biosafety level (BSL)-2 practices and facilities for general veterinary diagnostic work and do practical risk assessment of incoming accessions to determine whether decreased (BSL-1) or increased (BSL-3) biosafety practices or facilities are warranted. Where biosafety risk and practices differ between handling of human and animal diagnostic specimens, those differences are highlighted in this section. 12.2.1. Risk classification Two classifications of risk groups

have been developed to facilitate the assessment of risk from various microbes and to recommend appropriate safety practices for the handling of those microbes (1). The World Organization for Animal Health (OIE) and World Health Organization (WHO) list four groups of biohazardous agents for humans and animals based upon level of risk and availability of effective treatment and prevention (Table 12) (209). CDC/National Institutes of Health (CDC/NIH) guidelines propose four biosafety levels and recommendations for appropriate containment practices for agents known to cause laboratory-acquired infections (Tables 12,13) (1). The two lists of risk groups are roughly equivalent, and neither makes allowance for persons who are particularly susceptible to infections by pre-existing conditions, such as a compromised immune system or pregnancy. In both risk group classification systems, increasing risk levels (numbers) imply increasing occupational risk from exposure to an agent and the need for additional containment for work with that agent. 12.2.2. Risk assessment See Section 2 for detailed risk assessment guidelines. See Section 3 for extensive and detailed biosafety guidelines generally applicable to all subdiscipline areas within a veterinary diagnostic laboratory. 12.3.1. Hand washing 12.3.2. Personal Protective Equipment 12.3.3. Staff training 12.3.4. Biological spill management 12.3.5. Immunization See Section 5 for detailed biosafety guidelines applicable to necropsy, surgical pathology, and histology working areas in a veterinary diagnostic laboratory. See Section 6. See Section 7. See Section 8. See Section 9. See Section 10. Biosafety guidelines to be followed when conducting molecular diagnostic testing (i.e., polymerase chain reaction [PCR]) or using rapid tests such as enzyme-linked immunosorbent assay (ELISA) can be specific to the particular testing being conducted. These are discussed in Section 3 and Sections 4, 5, 6, 7, 8 and 10, which deal with specific types of pathogens and testing. Section 8.10 provides the most thorough biosafety guidelines for molecular diagnostic testing. See Section 13 for detailed biosafety guidelines applicable to functions within a veterinary diagnostic laboratory

regarding storage, packaging and shipping of infectious or diagnostic specimens. See Section 15 for practical guidelines regarding biosafety training within a veterinary diagnostic laboratory. See Section 16 for guidelines regarding continual improvement of biosafety within a veterinary diagnostic laboratory. Infectious substances in a clinical microbiology laboratory are encountered as fresh and processed patient specimens, cultures and subcultures, stored isolates, and serum or plasma. Invariably, all of these substances must occasionally be stored in some form and for some length of time, and many of these substances will be manipulated, relocated, and otherwise touched by laboratory workers. Therefore, storage of infectious substances is an important and integral component of worker safety in clinical microbiology laboratories. Handle all stored infectious substances using Standard Precautions and aseptic technique. Organisms responsible for external contamination of the storage vial will remain viable during storage and can be transmitted by manipulating the vial. Note: The requirements and regulations governing the transport of infectious substances change frequently. Shippers are responsible for being aware of these changes, adhering to current regulations, obtaining permits in advance of shipping, and interpreting applicable regulations for themselves and their facilities. Persons shipping these substances are advised to check the web sites of the respective appropriate agencies. 13.2.1. Governing authorities and regulations 13.2.2. Importance of regulations The purpose of the regulations is to protect the public, emergency responders, laboratory workers, and personnel in the transportation industry from accidental exposure to the infectious contents of the packages. An important non–safety-related benefit of adherence to these regulations and requirements is minimizing the potential for damage to the contents of the package during transport and reducing the exposure of the shipper to criminal and civil liability associated with improper shipment of dangerous goods. 13.2.3. Exceptions 13.2.4. Specific regulations 13.2.5. U.S. Postal Service The U.S. Postal Service publishes its own regulations in the USPS Domestic Mail

Manual (96). The USPS regulations for mailing hazardous materials generally adhere to DOT regulations; however, consult the USPS Domestic Mail Manual for specific needs and requirements. 13.3.1. Classification All shipped goods must be classified using a three-step process to define dangerous goods that are shipped by commercial carriers. Classification allows the shipper to select the proper IATA packing instructions and directions to use, and provides information necessary to complete required documentation (a Shipper's Declaration for Dangerous Goods) if the substance is a Category A infectious substance. 13.3.2. Steps of classification 13.3.3. Category A infectious substances A Category A substance is "an infectious substance which is transported in a form that, when exposure to it occurs, is capable of causing permanent disability, or life-threatening or fatal disease to otherwise healthy humans or animals" (93). 13.3.4. Category B infectious substances A Category B substance is "an infectious substance that does not meet the criteria for inclusion in Category A" (93). Category B substances are not in a form generally capable of causing disability, life-threatening illness, or fatal disease. Category B substances must be assigned UN number UN3373 (Biological Substance, Category B). Following are examples of possible Category B substances: 13.3.5. Exempt human (or animal) specimens Exempt human or animal body site specimens are those for which there is "minimal likelihood there are pathogens present" (93). Examples of such specimens include urine or serum to be tested for glucose, cholesterol, hormone levels, prostate-specific antigen, and analytes used to evaluate heart and kidney function. 13.3.6. Exempt substances Many substances commonly encountered in clinical laboratories are exempt from strict infectious substance shipping requirements (Figure 2). Examples of such substances are 13.3.7. Patient specimens 13.3.8. Genetically modified organisms Genetically modified organisms usually meet either Category A or Category B criteria. If this is not the case, the organism must be classified as a "genetically modified microorganism" (Class 9, Miscellaneous Dangerous Goods) and packed and shipped as such. 13.3.9.

Biological products Virtually all commercially available biological products are exempt from regulations for packing and shipping infectious substances. Examples of biological products include bacterial typing sera, vaccines, bacterial antigens, antimicrobial agents, reagents for identifying bacteria, and reagents used in antimicrobial susceptibility testing. 13.3.10. Infected animal 13.3.11. Medical waste 13.5.1. Packing instructions and directions 13.5.2. Marking and labeling outer packages 13.5.3. Specific markings and labels The following list cites the situations requiring a marker or label, and the specific markings or labels for that situation. 13.6.1. Shipper's Declaration for Dangerous Goods 13.6.2. Emergency response telephone number 13.6.3. Airbills IATA carriers are required to prepare airbills to describe air cargo and accompany shipments in transit. Some dangerous goods shipments, such as Biological Substances Category B shipments, require preparation of this document but not a Shipper's Declaration. Specific preparation instructions are detailed in each IATA package instruction and in the "Documentation" section of the Dangerous Goods Regulations. Packaging must be leakproof when wet ice is used. Dry ice is a Class 9 dangerous good; it must be packaged according to PI 954, and its use requires completion of a Shipper's Declaration if it is used to ship a Category A substance. Note: Dry ice is an explosion hazard and must never be placed into a tightly sealed container. Dry ice must be placed outside the secondary container, and the outer packaging must permit the release of CO. The risk of acquiring a laboratory-associated infection (LAI) after physically contacting a microorganism (an "exposure") in the workplace is real, always present, and an integral part of working in a diagnostic laboratory, and in particular the clinical microbiology laboratory. The potential for an exposure exists whenever a laboratorian manipulates and transports microorganisms, processes and stores patient specimens, and operates instruments used in the process. Diagnostic laboratories can be safe places to work if standard and appropriate safe work practices and procedures are easily accessible, understood by employees, enforced, and followed. These

procedures are to be properly outlined in an exposure control plan and laboratory manuals. These plans are composed of essential elements related to preventing an exposure, and, equally important, they describe employer and employee involvement and responsibilities before and after an exposure. Appropriate actions taken after an exposure can greatly reduce or even eliminate the chance that an exposure will result in an LAI. Well-designed plans with the full support of the director and higher management can reduce workers' chances of exposures to microorganisms and can help ensure a culture of safety in diagnostic laboratories. 14.1.1. Exposure control plan 14.1.2. Documentation of potential exposures 14.1.3. Emergency response equipment and facilities 14.1.4. Immunizations The Advisory Committee on Immunization Practices, in addition to recommending immunization of health-care personnel with vaccines recommended for all adults (influenza, measles/mumps/rubella, varicella, and tetanus/diphtheria/pertussis), recommends meningococcal or hepatitis B vaccination for those at risk for occupational exposure (211,217,218). 14.1.5. Education of employees It is the responsibility of laboratory employees to do the following: 14.3.1. Determination of the extent of exposure 14.3.2. Documentation of exposures 14.3.3. Consultation with employee health clinicians The employee and the supervisor of an employee who has experienced a potential exposure are to contact the employee health physician or nurse and discuss the exposure. These clinicians are the persons most likely to provide advice regarding timely chemoprophylaxis and to able to administer appropriate antimicrobial agents. 14.3.4. Counseling exposed employees 14.3.5. Exposure to Mycobacterium tuberculosis 14.3.6. Exposure to Neisseria meningitidis 14.3.7. Exposure to bloodborne pathogens Biosafety education efforts begin even before an employee begins working in the laboratory. The employer must develop an accurate job description so that the employee understands the job responsibilities. Knowledge, skills, and abilities needed for the job are to be defined. Evaluate incoming employees to see if they meet these criteria. Develop a mentoring

plan and fill any training gaps before employees are placed in a position that would put them at risk for exposure. Evaluate and document the employees' competency before they are allowed to work independently. Educational opportunities to reinforce safe behaviors must be ongoing and supported by all levels of management and staff. In accordance with Occupational Safety and Health Administration (OSHA) requirements, education about the risks of exposure to infectious agents begins with a new employee's first orientation to the laboratory or assignment to technical work and is to be specific to the tasks the employee performs. Training must include an explanation of the use and limitations of methods that will reduce or prevent exposure to infectious materials. These include engineering controls, work practices, and personal protective equipment. Annual retraining for these employees must be provided within 1 year of their original training and should emphasize information on new engineering controls and practices. Annual safety training offers a chance to review key biosafety measures that may be forgotten during everyday work pressures. The responsibility for overseeing the safety education of laboratory personnel must be clearly assigned. This responsibility may be delegated to the biosafety officer or other staff member who has been given additional training through specialized courses or work experience and whose competency to perform the training has been verified. Because laboratory tests might be performed outside a traditional laboratory setting (e.g., doctor's office, outpatient clinic, community setting), these recommendations for training and education must be adapted to suit the employees performing the tests and the person who is overseeing them. Employee training can be accomplished by any of several methods, and nearly all of these can be adapted or combined to fit the needs of employees in a particular laboratory. There is no one "official" set of questions for an annual safety checklist. Although many common activities might be performed by all personnel, customize the list to reflect the actual job duties. Analyze each work station for the type of biosafety risks associated with it, and target the checklist to each of

these risks. If practical, ask individual laboratorians to draft their own checklists for the duties they perform, and have their list reviewed by their supervisor and safety officer. Employee training and competency assessment should be documented for the following: Integrate continuous quality improvement for biosafety with the continuous quality improvement for the entire laboratory. The 12 quality system essentials, as defined by the Clinical Laboratory Standards Institute, provide a comprehensive basis and reference for continuous quality improvement (222). More detailed and specific biosafety considerations have been listed for each of these elements (Table 17). We acknowledge the assistance of Tanya Graham, DVM, South Dakota State University, Brookings, SD; Larry Thompson, DVM, PhD, Nestle Purina Pet Care, St. Louis, MO; R. Ross Graham, DVM, PhD, Merrick and Company; Corrine Fantz, PhD, Emory University, Atlanta, GA; Thomas Burgess, PhD, and Quest Diagnostics, Tucker, GA. We appreciate the review and input into the document provided by the Office of Health and Safety, CDC; American Association of Veterinary Laboratory Diagnosticians; American Biological Safety Association; College of American Pathologists; American Society for Microbiology; Association of Public Health Laboratories; and subject matter experts at CDC. FIGURE 1. Risk assessment process for biologic hazards Alternate Text: The figure is a flow chart that presents the risk assessment process for a biologic hazard

TABLE 1. Laboratory activities associated with exposure to infectious agents Routes of exposure/transmission Activities/practices Ingestion/oral • Pipetting by mouth • Splashing infectious material • Placing contaminated material or fingers in mouth • Eating, drinking, using lipstick or lip balm Percutaneous inoculation/nonintact skin • 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 • 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 • 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 Micobiol Rev 1995;8:389–405 (18).

TABLE 2. Risk prioritization of selected routine laboratory tasks Task or activity Exposure risk Potential hazard Likelihood Consequence Risk rating Subculturing blood culture bottle Needle stick — percutaneous inoculation Likely Infection; medical treatment High Aerosols — inhalation Moderate Infection; medical treatment Medium Splash — direct contact with mucous membranes Moderate Infection; medical treatment High Centrifugation Aerosols — inhalation Likely Infection; medical treatment High Performing Gram stain Aerosols from flaming slides Moderate Colonization; infection Moderate Preparing AFB smear only Aerosols from sputum or slide preparation Likely Illness; medical treatment; disease High Performing catalase testing Aerosols — mucous membrane exposure Unlikely Colonization; infection Low AFB culture work-up Aerosols — inhalation Likely Illness; medical treatment; disease High Abbreviation: AFB = acid-fast bacillus.

TABLE 3. Example of job safety analysis for laboratorians working in diagnostic laboratories: hazards and controls Task or activity Hazards and recommended controls Potential hazard Engineering controls Administrative/work practices PPE Subculturing blood culture bottle Needle stick—percutaneous inoculation Safer sharps; retractable needles; puncture-resistant sharps container No recapping; immediate disposal into sharps container Gloves; gown or lab coat Aerosols—inhalation BSC or splash shield Work inside BSC or behind splash shield Face protection if not in BSC; gloves; gown or

lab coat with knit cuffs Splash—direct contact with mucous membranes BSC or splash shield

Work inside BSC or behind splash shield Face protection if not in BSC; gloves; gown or lab coat Centrifugation Aerosols—inhalation BSC; removable rotors; safety cups; O-rings on buckets; plastic tubes; splash shield Spin in BSC, or load and unload rotor in BSC; check O-rings and tubes for wear; no glass tubes; wait for centrifuge to stop before opening Face protection if not in BSC; gloves; gown or lab coat with knit cuffs Performing Gram stain Aerosols from flaming slides Slide warmer Air dry or use slide warmer Lab coat; gloves (optional) Preparing AFB smear only Aerosols from sputum or slide prep Work in BSC; sputum decontaminant; slide warmer Use slide warmer in BSC; dispose of slide in tuberculocidal disinfectant Lab coat; gloves Catalase testing Aerosols— mucous membrane exposure BSC; disposable tube Work in BSC or perform in disposable tube Lab coat; gloves; eye protection AFB culture work-up Aerosols—inhalation BSL-3 laboratory optimal; BSL-2 laboratory with BSC minimal All work in BSC using BSL-3 practices* Solid-front gown with cuffed sleeves; gloves; respirator if warranted Abbreviations:

PPE= personal protective equipment; BSC = biological safety cabinet; AFB = acid-fast bacillus; BSL = biosafety level.

* BSL-3 Practices include BSL-2 practice plus: restricted access; all work performed in a BSC (additional PPE); and decontamination of all waste before disposal.

TABLE 4. Summary of recommended biosafety levels (BSL) for infectious agents BSL Agents Practices Primary barriers and safety equipment Secondary barriers (facilities) 1 Not known to consistently cause diseases in healthy adults Standard microbiological practices None required Laboratory bench and sink required 2 • Agents associated with human disease • Routes of transmission include percutaneous injury, ingestion, mucous membrane exposure BSL-1 practice plus: • Limited access • Biohazard warning signs • "Sharps" precautions • Biosafety manual defining any needed waste contamination or

medical surveillance policies Primary barriers: • Class I or II BSC or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials PPE: • Protective laboratory clothing; gloves; respiratory protection as needed BSL-1 plus: • Autoclave available 3 • Indigenous or exotic agents with potential for aerosol transmission • Disease may have serious or lethal consequences BSL-2 practice plus: • Controlled access • Decontamination of all waste • Decontamination of laboratory clothing before laundering • Obtaining baseline serum from staff Primary barriers: • Class I or II BSC or other physical containment devices used for all open manipulation of agents PPE: • Protective laboratory clothing; gloves; respiratory protection as needed BSL-2 plus: • Physical separation from access corridors • Self-closing, double-door access • Exhaust air not recirculated • Negative airflow into laboratory Abbreviation:

BSC = biological safety cabinet; PPE = personal protective equipment.

TABLE 5. Comparison of biological safety cabinet characteristics BSC Class

Face velocity

Venting

Applications

Nonvolatile toxic chemicals and radionuclides

Volatile toxic chemicals and radionuclides

I 75 Outside or into the room through HEPA filter

Yes When exhausted outdoors*† II–A1 75 30% vented through HEPA filter back into the room or to outside through a canopy unit

Yes (minute amounts) No II–A2 100 Similar to II-A1, but has 100 lfpm intake air velocity Yes When exhausted outdoors (minute amounts)*† II–B1 100 Exhaust cabinet air must pass through a HEPA filter then through a dedicated duct to the outside.

Yes Yes (minute amounts)*† II–B2 100 No recirculation; total exhaust to the

outside through a HEPA filter Yes Yes (small amounts)*† III N/A Exhaust air passes through two HEPA filters in series and is exhausted to the outside via a hard connection.

Yes Yes (small amounts)*† Abbreviations:

BSC = biological safety cabinet; HEPA = high efficiency particulate air; lfpm = linear feet per minute Source: CDC/National Institutes of Health. Biosafety in microbiological and biomedical laboratories. 5th ed.

(1). * Installation may require a special duct to the outside, an in-line charcoal filter, and a spark-proof (explosion-proof) motor and other electrical components in the cabinet. Discharge of a Class I or Class II, Type A2 cabinet into a room should not occur if volatile chemicals are used.

† In no instance should the chemical concentration approach the lower explosion limits of the compounds.

TABLE 6. Air changes per hour (ACH) and time required for removal efficiencies of 99% and 99.9% of airborne contaminants* ACH Minutes required for removal efficiency† 99% 99.9% 2 138 207 4 69 104 6 46 69 12 23 35 15 18 28 20 7 14 50 3 6 400 <1 1 Source: Guidelines for preventing transmission of Mycobacterium tuberculosis. MMWR 2005 (46). * This table can be used to estimate the time necessary to clear the air of airborne Mycobacterium tuberculosis after the source patient leaves the area or when aerosol-producing procedures are complete.

† Time in minutes to reduce the airborne concentration by 99% or 99.9%.

TABLE 7. Possible parasite transmission in a health-care setting (diagnostic laboratory) Organism* Mode of transmission Comments Protozoa (intestinal) Entamoeba histolytica† (C) Accidental ingestion of infective cysts, trophozoites, oocysts or spores in food or water contaminated with fecal material; also direct transfer of stool material via fomites (fecal–oral transmission) Transmission becomes more likely when fresh stool

specimens are being processed and examined. Submission of fecal specimens in stool preservatives (commercially available vials) would decrease risks. Entamoeba dispar

(C) Entamoeba coli

(C) Entamoeba hartmanni

(C) Endolimax nana

(C) Iodamoeba bütschlii

(C) Blastocystis hominis† (C) Giardia lambliа† (C) Gloves, using capped centrifuge tubes and working in biological safety cabinet would decrease risk of acquiring

Cryptosporidium infections. Not recommended: Use of potassium dichromate

as collection fluid (not a fecal preservative) and use of sugar flotation on fresh stool. Dientamoeba fragilis† (T) Cryptosporidium

spp.†

(O) Cyclospora cayetanensis†

(O) Isospora belli†

(O) Microsporidia† (S) Protozoa (other body sites) Free-living amebae (Acanthamoeba, Naegleria, Balamuthia, Sappinia) Accidental inhalation of fluids containing organisms; accidental transmission of organisms to eyes via contaminated hands Gloves and transfer of liquid materials within a biological safety cabinet are recommended when working with cultures and patient specimens. Trichomonas vaginalis Accidental transmission of organisms to eyes, (e.g.) via contaminated aerosols or hands Same as for free-living amebae Helminths (intestinal) Enterobius vermicularis

(E) Inhalation/ingestion of infective eggs Very common in children, asymptomatic Strongyloides stercoralis

(IL) Skin penetration of infective larvae from stool material Exposure possible/likely when working with fresh stool cultures/concentrates for larval recovery Hymenolepis nana (E) Ingestion of infective eggs (fecal-oral) Ingestion of infective eggs

in fresh stool can lead to the adult worm in humans. Taenia solium

(E) Inhalation/ingestion of infective eggs could lead to cysticercosis. Exposure

very likely when working with unpreserved gravid proglottids (ink injection for speciation of worm). Blood/tissue protozoa Leishmania spp. Direct contact or inoculation of infectious material from patient lesion; accidental inoculation of material from culture or animal inoculation studies. Culture forms/organisms from hamster would be infectious. Trypanosoma spp. Same as for Leishmania

spp. Cultures, special concentration techniques represent possible means of

exposure. Plasmodium spp. Accidental inoculation could transmit any of the five species (P. vivax, P. ovale, P. falciparum, P. malariae, P. knowlesi) Blood should always be handled carefully; avoid open cuts. Toxoplasma gondii Inhalation/ingestion of oocysts in cat feces (veterinary situation); accidental inoculation of tachyzoites from tissue culture, tube of blood, animal isolation (mouse peritoneal cavity) Although many people already have antibodies to

Toxoplasma, indicating past exposure, laboratory incidents have been

documented in which illness was due to large infecting dose. Ectoparasites Pediculus spp. Specimens submitted on hair could be easily transmitted in the laboratory. Careful handling, fixation of the arthropods would prevent any potential problems with transmission. Sarcoptes scabiei Transmission via skin scraping or other means would be possible but unlikely. Careful handling, preparation of specimens with potassium hydroxide (KOH) tend to prevent any problems. Dipterous fly larvae (Myiasis) Transmission could occur anywhere. Protection from flies would solve the potential problem. Abbreviations:

C = cyst; T = trophozoite; O = oocyst; IL = infective larvae; E = egg; S =

spore * Not every possible parasite is included in the table; those mentioned represent the most likely transmission possibilities.

† Potentially pathogenic intestinal protozoa.

BOX 1. Potential exposures to laboratory-acquired parasitic infections Parenteral or aerosolization • Recapping a needle • Removing a needle from the syringe • Leaving a needle on the counter, point up • Dropping a syringe • Breaking hematocrit tube while pressing the end into clay • Performing venipuncture on agitated patient • Sudden animal movement during an inoculation procedure • Creation of aerosols during tapeworm proglottid injection • Creation of aerosols while working with cultures (bacteria, viruses, fungi, blood parasites, free-living amebae) Animal or vector bites • Bitten by an infected animal (e.g., mouse or hamster) • Bitten by infected mosquito or tick (e.g., mosquito colony) Skin exposure • Not wearing gloves during procedure • Failure to wear laboratory coat (closed sleeves, closed front over clothes) • Accidentally touching face or eyes during handling of infectious materials • Exposure of eyes, nose, or mouth to potential aerosols Ingestion • Mouth pipetting • Sprayed with inoculum droplets from coughing or regurgitating animal Other reasons for potential exposures • Working in disorganized laboratory bench setting • Working too fast • Failure to receive proper training • Assumption that agent is not infectious to humans • Assumption that agent(s) are no longer viable • Using defective equipment

TABLE 8. Resistance of parasites and other organisms to antiseptics and disinfectants (from most to least resistant) Type of organism Examples Prions Creutzfeldt-Jakob disease, Bovine spongiform encephalopathy Coccidia Cryptosporidium

spp. Microsporidial spores Enterocytozoon,

Encephalitozoon, Pleistophora, Trachipleistophora Bacterial spores Bacillus,

Clostridium difficile Mycobacteria Mycobacterium tuberculosis,

M. avium Cysts Giardia lamblia Small nonenveloped viruses Poliovirus

Trophozoites Acanthamoeba

Gram-negative bacteria (nonsporulating) Pseudomonas Fungi Candida,

Aspergillus Large nonenveloped viruses Enteroviruses, Adenovirus

Gram-positive bacteria Staphylococcus aureus, Enterococcus Lipid enveloped viruses

Human immunodeficiency virus, Hepatitis B virus

TABLE 9. 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 References Adenovirus Human kidney, pancreas, some adenovirus transformed cell lines, rhesus monkey kidney cells (130–134) 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) (135) Cytomegalovirus Kidney, human foreskin, monkey kidney cells (133,134,136) Epstein-Barr virus (EBV) Some lymphoid cell lines and EBV-transformed cell lines, human kidney (137) Hepatitis B virus Human blood, liver (138) Herpes simplex virus Human kidney (139,140) Herpesvirus group Monkey kidney cells (133,134) Human or simian immunodeficiency virus

Blood cells, serum, plasma, solid organs from infected humans or monkeys (141–143) HTLV-1 Human kidney, liver (144–147) Lymphocytic choriomeningitis virus

Multiple cell lines, mouse tissue (148–150) Mycoplasmas Many cell cultures (151) Myxovirus (SV5) Monkey kidney cells (133,152) Porcine parvovirus Fetal porcine kidney cells, trypsin preparations (153) Rabies virus Human cornea, kidney, liver, iliac vessel conduit (154–163) Simian adenoviruses Rhesus, cynomologous, and African green monkey kidney cells (133,164) Simian foamy virus

Rhesus, cynomologous, and African green monkey kidney cells (133,134,152,165) Simian virus 40 (SV40) Rhesus monkey kidney cells (135,166,167) Simian viruses 1–49 Rhesus monkey kidney cells (133,135,165) Swine torque teno virus Trypsin, swine-origin biological components (168) Squirrel monkey retrovirus Multiple cell lines, commercial interferon preparations (169,170) West Nile virus Human blood, heart, kidney, liver, lung, pancreas (171–191)

TABLE 10. Trigger events requiring supervisor or laboratory director notification or

intervention Event Typical causes High-risk causes Specimen processing/login bench Specimen brought in by law enforcement official with a chain-of-custody form Assault case workup Potential BT/BC specimen Suspect agent is on the Do Not Test/Do Not Process list Clerical mistake at order entry Might be from a patient with a high-risk infection Unusual (nonbiological) or unapproved specimen type or container Clerical mistake at order entry; inappropriate order • Powders, environmental samples, animal specimens, clothing, food samples, inanimate objects could contain BT/BC agents. • Might represent an attempt to introduce a BT/BC agent into the laboratory. Fluorescent antibody bench Dim staining when controls and other positive specimens stain normally Decreased antigen expression in cells Cross-reaction with another infectious agent Unusual staining pattern Added wrong antibody to well; antibodies ran together during incubation • Altered virus or genetic/antigenic variant • Cross-reaction with another agent Staining unusual cell types Added wrong antibody to well; antibodies ran together during incubation Infectious agent with altered host range; cross-reaction with another agent Cell culture bench CPE pattern and cell tropism are unusual Unusual/unexpected pathogen; BT/BC agent in specimen Familiar CPE pattern but in an unusual cell type Genetic drift; subspecies present

Unusual/unexpected pathogen; BT/BC agent in specimen Unexpected CPE/HAd pattern from the indicated specimen source Clerical error when entering source Unusual/unexpected pathogen; BT/BC agent in specimen Confirmation protocols do not work Genetic or antigenic drift Unusual/unexpected pathogen; BT/BC agent in specimen Nucleic acid testing Altered melting curve shape, too many peaks, altered T when controls and other patient curves are normal Genetic variation in agent; poor extraction; primer dimers Unusual/unexpected pathogen; more than one agent present; chimeric, recombinant or reassortant pathogen Change in the slope of the amplification curve Genetic variation in agent; poor extraction; specimen inhibition Unusual/unexpected pathogen; chimeric, recombinant or reassortant pathogen

Abbreviations:

BT = bioterrorism; BC = biocrime; CPE = cytopathic effects; HAd = hemadsorption;

Tmelting temperature.

TABLE 11. List of compounds incompatible with household bleach (sodium hypochorite)

Incompatible material*	Possible result from mixing
Acids and acidic compounds† such as: alum (aluminum sulfate) aluminum chloride ferrous or ferric chloride ferrous or ferric sulfate nitric acid hydrochloric acid (HCl) sulfuric acid hydrofluoric acid fluorosilicic acid phosphoric acid brick and concrete cleaners chlorinated solutions of ferrous sulfate	Release of chlorine gas, might occur violently.
Chemicals and cleaning compounds containing ammonia† such as: ammonium hydroxide ammonium chloride ammonium silicofluoride ammonium sulfate quaternary ammonium salts (quats) urea	• Formation of explosive compounds. • Release of chlorine or other noxious gases.
Organic chemicals and chemical compounds† such as: fuels and fuel oils amines methanol organic polymers propane ethylene glycol insecticides, solvents and solvent-based cleaning compounds	• Formation of chlorinated organic compounds. • Formation of explosive compounds. • Release of chlorine gas, may occur violently.
Metals§ such as: copper nickel vanadium cobalt iron molybdenum	Release of oxygen gas, generally does not occur violently. Could cause overpressure/rupture of a closed system.
Hydrogen peroxide	Release of oxygen gas, might occur violently.
Reducing agents such as: sodium sulfite sodium bisulfite sodium hydrosulfite sodium thiosulfate	

Evolution of heat, might cause splashing or boiling.

Oxidizing agents such as: sodium chlorite

Release of chlorine dioxide, chlorine, and oxygen gas. Increased rate as pH is lowered.

Avoid direct contact with sunlight or UV light

Release of oxygen gas, generally does not occur violently. Could cause overpressure/rupture of a closed system.

Source: The Chlorine Institute, Inc., Arlington, VA. Reprinted with permission.

* List is not all-inclusive.

† Some of these compounds can be found in common household, automotive, and industrial products, such as window, drain, toilet bowl, and surface cleaners, degreasers, antifreeze, and water treatment or swimming pool chemicals. Consult product labels, product manufacturers, sodium hypochlorite suppliers, or the Chlorine Institute for information.

§ Avoid piping and material handling equipment containing stainless steel, aluminum, carbon steel, chrome steel, brass, bronze, Inconel, Monel, or other common metals.

TABLE 12. OIE risk groups and CDC/NIH biosafety level (BSL) classifications Level Characterization OIE risk group 1 Unlikely to cause disease; not considered infectious 2 Moderate individual and low community risk; unlikely to cause serious disease or be transmitted; effective treatment and prevention available 3 High individual and community risk; causes serious infections but not readily transmitted; effective treatment and prevention usually available 4 High individual and community risk; readily transmitted and no effective treatment or prevention available CDC/NIH BSL Class 1 Well-characterized agents not known to consistently cause disease in healthy adult humans; minimal potential hazard to laboratory personnel and the environment 2 Agents of moderate potential hazard to personnel and the environment 3 Indigenous and exotic agents that cause serious or potentially lethal disease as a result of

exposure by the inhalation route 4 Dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease Abbreviations:

OIE = World Organization for Animal Health; NIH = National Institutes of Health Source: Adapted from Biosafety and biosecurity in the veterinary microbiology laboratory and animal facilities. In: OIE manual for diagnostic tests and vaccines for terrestrial animals, 6th Edition. 2008 (209); and CDC/National Institutes of Health. Biosafety in microbiological and biomedical laboratories. 5th ed. 2007 (1).

TABLE 13. CDC/NIH BSL practices and equipment BSL Practices Safety equipment and facilities 1 Standard microbiological practices None required 2 • BSL-1 practices • Limited access • Display biohazard signs • Sharps precautions • Staff trained with pathogens • Safety manual available • BSC used for specimen processing and work producing aerosols or splashes • PPE (coats, gloves, face shields) as needed • Autoclave available 3 • BSL-2 practices • Controlled access • Collect baseline serum from personnel • BSL-2 equipment/facilities • BSC used for work with all specimens and cultures • PPE (gowns and masks) as needed • Negative pressure airflow • Self-closing double doors • Exhaust air not recirculated 4 • BSL-3 practices • Change clothing before entering • Shower on exit • Decontaminate all waste on exit • BSL-3 equipment/facilities • Separate building or facility • BSC and full-body, air-supplied positive pressure suit for all procedures • Specialized ventilation and decontamination system Abbreviations:

NIH = National Institutes of Health; BSL = biosafety level; BSC = biological safety cabinet; PPE = personal protective equipment. Source: Adapted from CDC/National Institutes of Health. Biosafety in microbiological and biomedical laboratories. 5th ed. 2007 (1).

BOX 2. Examples of common zoonotic microorganisms in risk groups 2 and 3* that might be present in the veterinary diagnostic laboratory Group 2 • Viruses: Influenza

viruses types A, B, C; Newcastle disease virus; parapoxvirus (Orf); West Nile virus • Bacteria:

Alcaligenes spp., Arizona spp., Campylobacter spp.,

Chlamydophila psittaci (nonavian), Clostridium tetani,

Clostridium botulinum, Corynebacterium spp.,

Erysipelothrix rhusiopathiae, Escherichia coli,

Haemophilus spp., Leptospira spp.,

Listeria monocytogenes, Moraxella spp.,

Mycobacterium avium, Pasteurella spp.,

Proteus spp., Pseudomonas spp., Salmonella spp.,

Staphylococcus spp., Yersinia enterocolitica,

Yersinia pseudotuberculosis • Fungi: Aspergillus fumigatus,

Microsporum spp., Trichophyton spp.,

Blastomyces dermatitidis (tissues), Coccidioides immitis (tissues),

Cryptococcus neoformans, Histoplasma capsulatum (tissues),

Sporothrix schenkii Group 3 • Viruses: Rabies virus; equine encephalomyelitis virus (eastern, western, Venezuelan); Japanese encephalitis virus; louping ill virus • Bacteria:

Bacillus anthracis, Burkholderia mallei,

Brucella spp., Chlamydophila psittaci (avian strains only),

Coxiella burnetii, Mycobacterium bovis • Fungi: Blastomyces dermatitidis spores (cultures only),

Coccidioides immitis spores (cultures only),

Histoplasma capsulatum spores (cultures only) Source: Adapted from OIE manual of diagnostic tests and vaccines for terrestrial animals, 6th edition. 2008 (209).

* As defined by the World Organization for Animal Health (see Table 12).

BOX 3. High-consequence livestock pathogens and select agents Livestock African

horse sickness virus African swine fever virus Akabane virus Avian influenza virus (highly pathogenic) Bluetongue virus (exotic) Bovine spongiform encephalopathy Camel pox virus Classic swine fever virus Foot-and-mouth disease virus Goat pox virus Japanese encephalitis virus Lumpy skin disease virus Menangle virus Mycoplasma capricolum subspecies Mycoids small colony (MmmSC) (contagious bovine pleuropneumonia) Peste des petits ruminants virus Rinderpest virus Sheep pox virus Swine vesicular disease virus Vesicular stomatitis virus (exotic)—Indiana subtypes VSV-IN2, VSV-IN3 Virulent Newcastle disease virus US Department of Agriculture/Department of Health and Human Services overlap agents Bacillus anthracis Brucella abortus Brucella melitensis Brucella suis Burkholderia mallei Burkholderia pseudomallei Hendra virus Nipah virus Rift Valley fever virus Venezuelan equine encephalitis virus Source: Adapted from USDA/APHIS select agent and toxin list, 2010. (http://www.aphis.usda.gov/programs/ag_selectagent/ag_bioterr_toxinlist).

TABLE 14. Rabies pre-exposure prophylaxis guide — United States, 2008 Risk category Nature of risk Typical populations Pre-exposure recommendations Continuous Virus present continuously, often in high concentrations. Specific exposures likely to go unrecognized. Bite, nonbite, or aerosol exposure. Rabies research laboratory workers; rabies biologics production workers. Primary course. Serologic testing every 6 months; booster vaccination if antibody titer is below acceptable level.* Frequent Exposure usually episodic, with source recognized, but exposure also might be unrecognized. Bite, nonbite, or aerosol exposure. Rabies diagnostic laboratory workers, cavers, veterinarians and staff, and animal-control and wildlife workers in areas where rabies is enzootic. All persons who frequently handle bats. Primary course. Serologic testing every 2 years; booster vaccination if antibody titer is below acceptable level.* Infrequent (greater than population at large) Exposure nearly always episodic with source recognized. Bite or nonbite exposure. Veterinarians and animal-control staff working with terrestrial animals in areas where rabies is uncommon to rare. Veterinary

students. Travelers visiting areas where rabies is enzootic and immediate access to appropriate medical care including biologics is limited. Primary course. No serologic testing or booster vaccination. Rare (population at large)* Exposure always episodic with source recognized. Bite or nonbite exposure. Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test. A booster dose should be administered if the titer falls below this level. U.S. population at large, including persons in areas where rabies is epizootic. No vaccination necessary. Source: CDC. Human rabies prevention — United States, 2008. MMWR 2008 (212). * Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test. A booster dose should be administered if the titer falls below this level.

TABLE 15. Types and classifications of IATA division 6.2 infectious substances Type of infectious substance IATA classification Category A substance Category A Category B substance Category B* Patient specimen Meets Category A criteria

Category A Meets Category B criteria

Category B Does not meet Category A or B criteria Exempt human or animal specimen Exempt human or animal specimen Exempt human or animal specimen Genetically modified microorganism Meets Category A criteria

Category A Meets Category B criteria

Category B Does not meet Category A or B criteria Genetically modified organism Exempt substance None Biological product†

None Infected animal†

None Medical waste† None Abbreviation:

IATA: International Air Transport Association * The proper shipping name for Category B substances is Biological Substance, Category B. †Substance is not addressed in detail in these guidelines. FIGURE 2. Algorithm for classifying infectious substance for shipment Alternate Text: The figure is a flow chart that presents the

process for classifying an infectious substance for shipment.

TABLE 16. Summary of packing requirements for exempt human specimens, Category B substances, and Category A substances Packing requirement Specimen/substance Exempt human specimens* Category B† Category A§ Inner containers Leakproof primary and secondary containers Yes Yes Yes Pressure-resistant primary or secondary container —¶ Yes Yes Absorbent between primary and secondary containers** Yes Yes Yes List of contents between secondary container and outer package — Yes Yes Positively sealed primary container — No Yes Outer container Rigid outer packaging — Yes Yes Strict manufacturing specifications None†† Few Many Name and number of responsible person — Yes§§ Yes Markings and labels Yes¶¶ Less More Quantity limits for either passenger or cargo aircraft Maximum for each primary container — 1 L (1 kg) 50 mL (50 g) Total maximum for outer package — 4 L (4 kg) 50 mL (50 g) Documentation Shipper's Declaration for Dangerous Goods — No Yes Emergency response telephone number — No Yes Costs Cost of labor and materials to pack substance Least More Most

*

The International Air Transport Association (IATA) and the US Department of Transportation (DOT) provide only minimal standards (i.e., no detailed and numbered packing instructions) for packing and shipping exempt human specimens.

† Packing instructions 650.

§ Packing instructions 620.

¶ Requirement not specified by IATA or DOT. **

Not required for solid substances such as tissue and solid agar media cultures or slant.

†† IATA states that this should be "of adequate strength for its intended capacity, mass, and intended use."

§§ May be placed either on the outer package or on the air waybill.

¶¶ Only "Exempt Human Specimen" or "Exempt Animal Specimen" is required. FIGURE

3. A completely labeled outer package. The primary container inside the package contains a Biological Substance, Category B infectious substance and is packed according to PI 650 Abbreviation: PI = packing instructions. Alternate Text: The figure is a diagram of a shipping package with the appropriate labeling for a Category B infectious substance.

FIGURE 4. A completely labeled outer package. The primary container inside contains a liquid Category A infectious substance and is packed according to PI 620 Abbreviation: PI = packing instructions. Alternate Text: The figure is a diagram of a shipping package with the appropriate labeling for a liquid Category A infectious substance.

TABLE 17. Quality system essentials (QSE), definition, and related biosafety considerations QSE no. QSE Definition Biosafety considerations 1 Organization Organizational structure of responsibility is defined. Clear reporting structure is established for 24/7 reporting of safety incidents. Each staff member knows whom to consult for biosafety reporting at all times. A chain of responsibility for overall compliance leads directly to the head of the organizational unit. 2 Documents and records Process and procedure documents are written and maintained. All incidents and "near misses" are recorded. All safety practices and policies are written, reviewed and approved and available on all shifts to all personnel and management. Document control ensures that the most current policies are in use and available. Vaccination records and safety training records are appropriately completed, maintained and easily recovered. 3 Facilities and safety The physical environment and space are appropriate for the work being done. Facilities are designed and constructed with safety controls and minimize the risk of injury and occupational illness. Safe work practices are followed at all times. 4 Personnel Laboratory personnel follow prescribed policies and procedures according to their job descriptions. Personnel have received appropriate

safety training at orientation, annually, and when their duties change. Documentation of biosafety training and continuous education is maintained in their personnel file and linked to their annual review. Training requirements are part of the annual resource planning process. 5 Equipment Instruments and equipment are used appropriately to carry out laboratory functions. All biohazard risks associated with operating instruments are clearly defined in SOPs. Personnel are aware of procedures to decontaminate equipment prior to maintenance or being decommissioned. 6 Purchasing and inventory Processes and procedures for purchasing necessary supplies and materials are adhered to. Appropriate safety supplies (masks, gloves, gowns, biohazard disposal bags and containers) and vendors are identified and documented. Sufficient inventory of safety supplies is available so that personnel do not compromise their personal safety or the safety of others. 7 Process control Workflow is defined to meet customer expectations and ensure the quality of the service. Biohazard risks associated with operational procedures are clearly defined and referenced in SOPs. Regulatory standards are met and procedures are mapped out with quality and safety as priority goals. 8 Information management Flow of information is effective and complies with legal and regulatory requirements. Reporting of incidents and responses back to the employee are documented. Retention of documents meets legal requirements. 9 Occurrence management Information that results from laboratory errors or other events is identified and analyzed.

All noncompliance with established safety procedures and policies is documented. All incidents are reported to Employee Health; all "near-misses" are recorded so that systems can be improved. A reporting mechanism exists to enable reports to be categorized to type of error so that corrective actions can be established. 10 Assessment Effectiveness of the of the system is assessed. Audits of the biosafety risks and policies are performed annually to initiate improved methods and engineering controls.

11 Customer service Expectations of the customer are met or exceeded. The requirements for biosafety are met and personnel are satisfied with policies, work practices and engineering controls to protect them. Biological samples, reagents and other items shipped to reference laboratories ("customers") are clearly labeled for biosafety hazards.

12 Process Improvement Systemic review of processes identifies areas for improvement.

Systematic review of occurrence reports as well as risks and interventions informs management planning for systematic improvements. Abbreviation: SOP = standard operating procedure.

Source: Adapted from Clinical and Laboratory Standards Institute. Application of a quality management system model for laboratory services; approved guideline—third edition (CLSI document GP26-A3) 2004 (222). Blue Ribbon Panel for Issues of Clinical Laboratory Safety Kathleen G. Beavis, MD, College of American Pathologists, Chicago, Illinois; Ellen Jo Baron, PhD, Stanford, California; William R. Dunn, MS, Greater New York Hospital Association Regional Laboratory Task Force, New York, New York; Larry Gray, PhD, American Society for Microbiology, Cincinnati, Ohio; Bill Homovec, MPH, American Clinical Laboratory Association, Burlington, North Carolina; Michael Pentella, PhD, Association of Public Health Laboratories, Iowa City, Iowa; Bruce Ribner, MD, Atlanta, Georgia; William A. Rutala, PhD, Chapel Hill, North Carolina; Daniel S. Shapiro, MD, Burlington, Massachusetts; Lisa A. Skodack-Jones, MT, Salt Lake City, Utah; Christine Snyder, American Society for Clinical Laboratory Science, Helena, Montana; Robert L. Sunheimer, MS, American Society for Clinical Pathology, Syracuse, New York; Christina Z. Thompson, MS, American Biological Safety Association, Greenfield, Indiana. CDC Staff: Nancy L. Anderson, MMSc; Rex Astles, PhD; D. Joe Boone, PhD; David S. Bressler, MS; Roberta Carey, PhD; Casey Chosewood, MD; Mitchell L. Cohen, MD; Judy Delaney, MS; Thomas L. Hearn, DrPH; Kathleen F. Keyes, MS; Davis

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