

Other Governmental and Non-governmental Agencies Involved in Laboratory Safety

U.S. Environmental Protection Agency (EPA)

Microbial Products of Biotechnology: Final Rule (62 FR 17910)

The regulation under which the TSCA Biotechnology Program functions is titled "Microbial Products of Biotechnology; Final Regulation Under the Toxic Substances Control Act" (TSCA), published in the Federal Register on April 11, 1997. This rule was developed under TSCA Section 5, which authorizes the Agency to, among other things, review new chemicals before they are introduced into commerce. Under a 1986 intergovernmental policy statement, intergeneric microorganisms (microorganisms created to contain genetic material from organisms in more than one taxonomic genus) are considered new chemicals under TSCA Section 5. The Biotechnology rule sets forth the manner in which the Agency will review and regulate the use of intergeneric microorganisms in commerce, or commercial research.

Documents relevant to this rule can be found at the following web site: <http://www.epa.gov/oppt/biotech/pubs/biorule.htm>.

U.S. Nuclear Regulatory Commission (NRC)

10 CFR 31.11 – General license for use of byproduct material for certain in vitro clinical or laboratory testing. Link at: <http://www.nrc.gov/reading-rm/doc-collections/cfr/part031/part031-0011.html>.

U.S. Department of Transportation (DOT)

An infectious substance is regulated as a hazardous material under the DOT's Hazardous Materials Regulations (HMR; 49 CFR Parts 171-180). The HMR apply to any material DOT determines is capable of posing an unreasonable risk to health, safety, and property when transported in commerce. An infectious substance must conform to all applicable HMR requirements when offered for transportation or transported by air, highway, rail, or water.

DOT's Pipeline and Hazardous Materials Safety Administration (PHMSA) published a final rule on June 1, 2006, revising the requirements in the HMR applicable to the transportation of infectious substances. The new requirements became effective October 1, 2006. Changes under the new rule apply to parts 171, 172, 173, and 175 of the HMR and include the following:

- New classification system
- New and revised definitions
- Revised marking requirements
- Revised packaging requirements
- New shipping paper requirements
- New security plan requirements
- New carriage by aircraft requirements

A guide to these changes is available at: http://www.phmsa.dot.gov/staticfiles/PHMSA/DownloadableFiles/Files/Transporting_Infectious_Substances_brochure.pdf.

U.S. Department of Health and Human Services (HHS)

Centers for Disease Control and Prevention (CDC)

Biosafety Levels

Laboratory supervisors are responsible for ensuring that appropriate safety and health precautions are in place in the laboratory. Therefore, for each biosafety level, there are specific supervisory qualifications as assurance that laboratory workers are provided with effective supervision. Various types of specialized controls and equipment are used to provide primary barriers between the microorganism and the laboratory worker. These range from disposable gloves and other PPE to complex biosafety cabinets or other containment devices.

The laboratory director is specifically and primarily responsible for the safe operation of the laboratory. His/her knowledge and judgment are critical in assessing risks and appropriately applying these recommendations. The recommended biosafety level represents those conditions under which the agent can ordinarily be safely handled. Special characteristics of the agents used, the training and experience of personnel, and the nature or function of the laboratory may further influence the director in applying these recommendations.

The U.S. Department of Health and Human Services' (DHHS) Centers for Disease Control and Prevention (CDC) defines four levels of biosafety, which are outlined below. Selection of an appropriate biosafety level for work with a particular agent or animal study (see Animal Facilities) depends upon a number of factors. Some of the most important are the virulence, pathogenicity, biological stability, route of spread, and communicability of the agent; the nature or function of the laboratory; the procedures and manipulations involving the agent; the endemicity (restricted to a locality/region) of the agent; and the availability of effective vaccines or therapeutic measures.

CDC Summary of Recommended Biosafety Levels for Infectious Agents

Biosafety Level	Agent Characteristics	Practices	Safety Equipment	Facilities (secondary barriers)
BSL-1	Not known to consistently cause disease in healthy adults	Standard microbiological Practices	None	Open bench top sink
BSL-2	Associated with human disease, hazard from percutaneous injury, ingestion, mucous membrane exposure	Standard microbiological Practices Limited access Biohazard warning signs Sharps precautions Biosafety manual defining any needed waste decontamination or medical surveillance policies.	Class I or II biosafety cabinets (BSCs) or other containment devices used for all agents that cause splashes or aerosols of infectious materials Laboratory coats and gloves Face protection as needed	Open bench top sink Autoclave
BSL-3	Indigenous or exotic agents with potential for aerosol transmission; disease may have serious or lethal consequences	All BSL-2 practices Controlled access Decontamination of all waste Decontamination of laboratory clothing before laundering Baseline serum	Class I or II BSCs or other physical containment devices used for all open manipulations of agents Protective lab clothing and gloves Respiratory protection as needed	Open bench top sink Autoclave Physical separation from access corridors Self-closing, double-door access Exhaust air not recirculated Negative airflow in laboratory
BSL-4	Dangerous/exotic agents which pose high risk of life-threatening disease; aerosol-transmitted lab infections; or related agents with unknown risk of transmission	All BSL-3 practices Clothing change before entering Shower on exit All material decontaminated on exit from facility	All procedures conducted in Class III BSCs, or Class I or II BSCs in combination with full-body, air-supplied, positive pressure personnel suit.	BSL-3 plus: Separate building or isolated zone Dedicated supply and exhaust, vacuum, and decontamination systems Other requirements outlined in the text

NOTE: The following information has been adapted from *Biosafety in Microbiological and Biomedical Laboratories*, 5th Ed. (BMBL, 5th Ed.), which is published jointly by the U.S. Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH), and is available online at www.cdc.gov/od/ohs/biosfty/bmbl5/bmbl5toc.htm. Laboratory workers and supervisors are strongly urged to review this publication directly before engaging in any experimentation.

Biosafety Level 1 (BSL-1)

BSL-1 is appropriate for working with microorganisms that are not known to cause disease in healthy humans. BSL-1 practices, safety equipment, and facility design and construction are appropriate for undergraduate and secondary educational training and teaching laboratories, and for other laboratories in which work is done with defined and characterized strains of viable microorganisms not known to consistently cause disease in healthy adult humans. *Bacillus subtilis*, *Naegleria gruberi*, infectious canine hepatitis virus, and exempt organisms under the *NIH Recombinant DNA Guidelines* (<http://www4.od.nih.gov/oba/rac/guidelines/guidelines.html>) are representative of microorganisms meeting these criteria. Many agents not ordinarily associated with disease processes in humans are, however, opportunistic pathogens and may cause infection in the young, the aged, and immunodeficient or immunosuppressed individuals. Vaccine strains that have undergone multiple in vivo passages should not be considered avirulent simply because they are vaccine strains.

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

Biosafety Level 2 (BSL-2)

The facility, containment devices, administrative controls, and practices and procedures that constitute BSL-2 are designed to maximize safe working conditions for laboratory personnel working with agents of moderate risk to personnel and the environment. BSL-2 practices, equipment, and facility design and construction are applicable to clinical, diagnostic, teaching, and other laboratories in which work is done with the broad spectrum of indigenous moderate-risk agents that are present in the community and associated with human disease of varying severity. With good microbiological techniques, these agents can be used safely in activities conducted on the open bench, provided

the potential for producing splashes or aerosols is low. Hepatitis B virus, H1V, the salmonellae, and *Toxoplasma* spp. are representative of microorganisms assigned to this containment level.

Biosafety Level 2 is also appropriate when work is done with any human-derived blood, body fluids, tissues, or primary human cell lines where the presence of an infectious agent may be unknown. Laboratory personnel in the United States working with human-derived materials should refer to the U.S. Occupational Safety and Health Administration (OSHA) *Bloodborne Pathogens Standard* (OSHA 1991), available online at www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS7p_id=1005, for required precautions.

Primary hazards to personnel working with these agents relate to accidental percutaneous or mucous membrane exposures, or ingestion of infectious materials. Extreme caution should be taken with contaminated needles or sharp instruments. Even though organisms routinely manipulated at Biosafety Level 2 are not known to be transmissible by the aerosol route, procedures with aerosol or high splash potential that may increase the risk of such personnel exposure must be conducted in primary containment equipment, or in devices such as a biological safety cabinet (BSC) or safety centrifuge cups. Personal protective equipment (PPE) should be used as appropriate, such as splash shields, face protection, gowns, and gloves.

Secondary barriers such as hand washing sinks and waste decontamination facilities must be available to reduce potential environmental contamination.

Biosafety Level 3 (BSL-3)

BSL-3 is suitable for work with infectious agents which may cause serious or potentially lethal diseases as a result of exposure by the inhalation route. This may apply to clinical, diagnostic, teaching, research, or production facilities in which work is done with indigenous or exotic agents with potential for respiratory transmission, and which may cause serious and potentially lethal infection. *Mycobacterium tuberculosis*, St. Louis encephalitis virus, and *Coxiella burnetti* are representative of the microorganisms assigned to this level. Primary hazards to personnel working with these agents relate to autoinoculation, ingestion, and exposure to infectious aerosols.

At BSL-3, more emphasis is placed on primary and secondary barriers to protect personnel in contig-

uous areas, the community, and the environment from exposure to potentially infectious aerosols. For example, all laboratory manipulations should be performed in a BSC or other enclosed equipment, such as a gas-tight aerosol generation chamber. Secondary barriers for this level include controlled access to the laboratory and ventilation requirements that minimize the release of infectious aerosols from the laboratory.

Biosafety Level 4 (BSL-4)

BSL-4 practices, safety equipment, and facility design and construction are applicable for work with dangerous and exotic agents that pose a high individual risk of life-threatening disease, which may be transmitted via the aerosol route, and for which there is no available vaccine or therapy. Agents with a close or identical antigenic relationship to Biosafety Level 4 agents also should be handled at this level. When sufficient data are obtained, work with these agents may continue at this or at a lower level. Viruses such as Marburg or Congo-Crimean hemorrhagic fever are manipulated at Biosafety Level 4.

The primary hazards to personnel working with Biosafety Level 4 agents are respiratory exposure to infectious aerosols, mucous membrane or broken skin exposure to infectious droplets, and autoinoculation. All manipulations of potentially infectious diagnostic materials, isolates, and naturally or experimentally infected animals pose a high risk of exposure and infection to laboratory personnel, the community, and the environment.

The laboratory worker's complete isolation from aerosolized infectious materials is accomplished primarily by working in a Class III BSC or in a full-body, air-supplied, positive-pressure personnel suit. The BSL-4 facility itself is generally a separate building or completely isolated zone with complex, specialized ventilation requirements and waste management systems to prevent release of viable agents to the environment.

Animal Biosafety Levels

The CDC defines four biosafety levels for activities involving infectious disease work with experimental animals. These combinations of practices, safety equipment, and facilities are designated Animal Biosafety Levels 1, 2, 3, and 4, and provide increasing levels of protection to personnel and the environment.

Protocols using live animals must first be reviewed and approved by an Institutional Animal Care and

Use Committee (IACUC) or must conform to governmental regulations regarding the care and use of laboratory animals. Follow all appropriate guidelines for the use and handling of infected animals.

For more information, refer to Section V of the BMBL, 5th Ed., available online at www.cdc.gov/od/ohs/biosafety/bmbl5/bmbl5toc.htm.

National Institutes of Health (NIH)

The NIH Office of Biotechnology Activities (OBA) promotes science, safety, and ethics in biotechnology through advancement of knowledge, enhancement of public understanding, and development of sound public policies. OBA accomplishes its mission through analysis, deliberation, and communication of scientific, medical, ethical, legal, and social issues.

OBA fulfills its mission through four important programs:

- Recombinant DNA (RAC)
- Genetics, Health, Society (SACGHS)
- Dual Use Research (NSABB)
- Clinical Research Policy Analysis and Coordination (CRpac)

Links to each of the programs listed above are provided at the OBA website: <http://oba.od.nih.gov/oba/index.html>.

National Institute for Occupational Safety and Health (NIOSH)

The NIOSH **Pocket Guide to Chemical Hazards (NPG)** (available at: www.cdc.gov/niosh/npg) provides a source of general industrial hygiene information on several hundred chemicals/classes for workers, employers, and occupational health professionals. While the NPG does not contain an analysis of all pertinent data, it presents key information and data in abbreviated or tabular form for chemicals or substance groupings (e.g., cyanides, fluorides, manganese compounds) that are found in the work environment. The information contained in the NPG should help users recognize and control occupational chemical hazards.

Other Government Web Links for Access to Additional Information Concerning Laboratory Safety

The Animal Plant Health Inspection Service (APHIS), www.usda/aphis.gov

U.S. Department of Agriculture (USDA), www.usda.gov

National Institute for Occupational Safety and Health (NIOSH), www.niosh.gov