National Institutes of Health
Office of Management

Biosafety in Microbiological and Biomedical Laboratories (BMBL)

6th Edition

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National Institutes of Health
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

History

- First published in 1984
- Last revision was completed in 2009
- Document has been a joint publication between the Centers for Disease Control (CDC) and National Institutes of Health (NIH)
- Each subsequent revision as built upon the advances in biomedical sciences as well as building and engineering principles
- Established as performance-based guidelines

Revision Process

- As needed with no ongoing review
- Email submission for comments
- In process since mid-2015
- Town hall run by National Academy of Science (NAS)
- Lead authors identified in late 2015/early 2016 for the 29 sections/appendices

What's Changed

- More emphasis on risk assessment. The entire book is a set of best practices, but they may or not fit your needs/activities or your institution's risk tolerance
- To reiterate; it's not a set of regulations (there are no BMBL police)
- New appendices have been added: Large Scale, Sustainability, Clinical Laboratories, Inactivation
- Otherwise, the order has not changed (the new appendices are at the back of the manual)

Section II and Section III

Biological Risk Assessment

- Emphasize the need for inclusion of a broad range of stakeholders
- Note the role of risk assessment as part of an ongoing risk management process
- Link the positive culture of safety to the recurring risk management process
- Introduction of a six-step cycle

Principles of Biosafety

- Minor edits with emphasis on overlapping hierarchy of controls

Section IV

Laboratory Biosafety Level Criteria

- Removed “should” and “must” from recommendations
- Part A (Standard Microbiological Practices) significantly revised to include most items common to any biosafety level
  - Safety manual
  - Glove recommendations
  - Expanded sharps language
  - Decontamination and waste handling
  - Mouth pipetting

Declarative Statements

Current language: “The laboratory supervisor must enforce the institutional policies that control access to the laboratory”

New language: “The laboratory supervisor enforces the institutional policies that control safety in and access to the laboratory”

Section IV (continued)

Laboratory Biosafety Level (BSL) Criteria

- At BSL-2 and above, validating decontamination of laboratory waste in Part B (Special Practices)
- In Part C, if respiratory protection is considered as part of the risk assessment at BSL-2 and above, staff enrolled in a properly constituted respiratory protection program
- Removal of viable organisms from containment are now provided at BSL-3, instead of only at BSL-4

Section IV (continued)

Laboratory BSL Criteria

- Facility-specific recommendations are retained in Part D (Laboratory Facilities)
  - Adequate illumination has been added to Part D for all biosafety levels
  - BSC recommendations are in Part D
  - Communications systems between the lab and outside at BSL-3 and BSL-4
  - At BSL-3 and BSL-4, facilities are tested annually or after significant modification to ensure operational parameters are met

Section V

Animal Biosafety Level (ABSL) Criteria

- Considerable effort on harmonization with lab criteria
- Laboratory animals which are capable of being confined based on risk assessment
- Risk assessment considers animal allergens if research animals are present
- Separating animal containment facilities from the general traffic
- For ABSL-4 suit facilities, specific information is provided regarding facility recommendations if open housed animals will be held in the facility

Section VI

Principles of Laboratory Biosecurity

- Additional supporting material identified, including ISO35001, Executive Order (EO) 13546, and Global Health Security Agenda EO 13747
- Section now differentiates between Agricultural biosecurity and Laboratory biosecurity

Section VII

Occupational Health

- Overhauled to emphasize the need for a risk-based approach to providing occupational health support to laboratories
  - Introduces the use of Risk of Exposure (RoE) and Risk of Disease (RoD) for post-exposure risk assessment
  - Matrix is similar to “Probability” vs “Consequences” table used for biological risk assessment

Section VIII

Agent Summary Statements

- New overarching introduction notes the applicability of additional resources for agent information
  - Public Health Agency of Canada's Pathogen Safety Data Sheets;
  - Control of Communicable Diseases Manual;
  - Manual of Clinical Microbiology; and
  - ABSA International's Risk Group Database

- Agent summaries now note that a CDC import permit is required

- Subsections were reviewed and updated with current information regarding the agent and mitigation

Agent Summaries

Bacteria

- *B. cereus* biovar *anthracis* added to *B. anthracis* agent summary
- *Clostridium botulinum*- removed information regarding toxins and refer the reader to Section VIII-G: Toxin Agents
- New agent summaries added:
  - *Clostridioides* (formerly *Clostridium*) *difficile*
  - *Staphylococcus aureus* (Methicillin Resistant, Vancomycin Resistant, or Vancomycin Intermediate)

Fungal

- Added *Blastomyces gilchristii* to *Blastomyces dermatitidis* agent summary
- Removed *Cryptococcus neoformans* and Dermatophytes agent summaries

Agent Summaries (Continued)

Virus

- *Herpesvirus simiae* renamed *Macacine alphaherpesvirus 1*
- Significant revision of Influenza agent summary, including information regarding A(H1N1)pdm09
- Poliovirus updated to reflect GAPIII requirements
- Poxvirus agent summary revised to note that requests to lower containment for recombinant poxviruses (e.g., TROVAC, ALVAC) must be obtained from the NIH Office of Science Policy
- Rabies Virus and related lyssaviruses agent summary now has a table for recommended containment levels for a number of lyssaviruses
- SARS-CoV agent summary now has information regarding MERS

Agent Summaries (Continued)

Arbovirus

- Elimination of HEPA filtration for any viruses used at BSL-2
- Table generated for viruses to be handled at BSL-3 containment and with HEPA filtration of exhaust
- Reduction in recommended containment for West Nile and St. Louis encephalitis viruses to BSL-2
- Central European tick-borne encephalitis viruses (TBEV-CE subtype) now recommend BSL-3 containment, provided all at-risk personnel are immunized
- Arbovirus list rearranged and simplified. Family and genus provided; requirement for HEPA filtration moved to new table
- Arthropod-only arbovirus table added

Appendix A

Primary Containment

- Harmonized with NSF/ANSI 49-2018 Standard where possible, particularly with definition of HEPA and ULPA filtration and exhaust alarm requirement for canopy-connected Class II Type A cabinets
- Updated terminology to reflect current use (e.g., canopy)
- Updated to include information on C cabinets
- Recommendations provided for institutions which choose to allow ultraviolet lights (UV) in BSCs

Appendices B & C

Decontamination & Disinfection

- Updated to identify U.S. regulations surrounding disinfectants (FIFRA, etc.). Revised table of selected chemical disinfectants to clarify relationship between concentration and activity level

Transportation

- Updated to reflect changes in contacts at regulatory agencies and international and U.S. regulations

  *Have been made aware that DOT will now require “hands on” training for certification

Appendix D

Agricultural Animals and Animals that are Loose-Housed or in Open Penning

- Significant changes
- Now “ABSL-XAg” and includes 2Ag and 4Ag
- Defined when “Ag” is used- for loose-housed or open-penned animals
- USDA intends to develop ABC between release of BMBL6 and BMBL7- will serve as agricultural complement to BMBL

Appendix D

- No agent summaries- tables of agents and recommended containment
- Tables for Bacteria, and Molds, Nematodes, Trematodes, Cestodes, Protozoa, and Ectoparasites, Viruses, Toxins, and Prions

Genus	Agent(s)	Hosts[1]	Routes[2]	Stability[3]	In vitro Containment	In vivo Containment	In vivo Ag Containment	Other Regs
Actinobacillus spp	*A. pleuropneumonia*	3	3,4,5	2	2	2	2Ag-3Ag	
Aeromonas spp	*A. hydrophila, A. salmonicida*	5	3,8	2	2	2	2Ag	
Anaplasma spp	*A. centrale, A. marginale, A. phagocytophilum*	1a	2,4	2	2	2	2Ag	
Arcobacter spp	*A. butzleri, A. cryaerophilus, A. skirrowii*	1,2,3,10b	1,8	2	2	2	2Ag	
Bacillus spp	*B. anthracis, B. cereus*	1-10	2,3,8	1-3	2-3	2-3	2Ag-3Ag	Y

Appendix E

Arthropod Containment

- The appendix references the revision of the Guidelines and provides a web link to the 2019 version
- Thanks to the American Committee of Medical Entomology (ACME), a subcommittee of the American Society of Tropical Medicine and Hygiene (ASTMH) for their hard work on the update
- The update is located at: http://doi.org/10.1089/vbz.2018.2431

  (March 2019 edition of *Vector-Borne Zoonotic Diseases)*

Appendices F -J

Appendix F- Select Agents and Toxins

- Updated to clearly identify the key elements of the Select Agent regulations as bullet points

Appendix G- Integrated Pest Management

- Updated with current information

Appendix H- Working with Human, Non-Human Primate (NHP), and Other Mammalian Cells and Tissues

- Updated with current information

Appendix I- Guidelines for Work with Toxins of Biological Origin

- Updated with current information

Appendix J- NIH Oversight of Research Involving Recombinant Biosafety Issues

- Updated to reflect changes in NIH rDNA guidelines, including the removal of RAC approval for human gene therapy experiments

Appendix K

Inactivation and Verification

- Written in consultation with the Division of Select Agents and Toxins (DSAT), CDC
- Provides risk-based guidance on how to validate and verify inactivation procedures (chemical and physical)
- Conforms to Select Agent guidance for inactivation and verification but goes beyond it for inactivation verification of lower risk organisms
- Also provides tables listing the advantages and disadvantages of inactivation processes

Appendix L

Sustainability

- Created to provide guidance for both existing laboratories and new facilities regarding means to save water and energy and reduce waste
- Specific examples of methods to reduce energy usage are provided
- International freezer challenge- https://www.freezerchallenge.org/
- Some items may or may not work for you (composting bedding, or chilled beams)

Appendix M

Large Scale Biosafety

- Written to provide biosafety guidance to large-scale (>10 liter) facilities
- Emphasizes the use of risk assessment and the unique hazards posed by large scale fermentation and purification and the potential issues surrounding balancing biosafety and Good Manufacturing Practices (GMP)

Appendix N

Clinical Laboratories

- Emphasizes the use of risk assessment and the hierarchy of controls to minimize the risk from clinical samples, which may contain unknown pathogens. The appendix also identifies key “trigger points” in the clinical laboratory process where high-risk activities or potential pathogens can be identified. Key risk points and recommendations for mitigation are provided
- Sample trigger points:
  - Growth from sterile sites (e.g., blood, cerebrospinal fluid [CSF], body fluid);
  - Poor growth after 48-72 hours incubation;
  - Growth only on chocolate agar or better growth on chocolate agar compared to sheep blood agar (SBA); and/or
  - Any culture with filamentous mold growth

Additional Content

Acronyms (Appendix O)

- Updated to reflect current terms

Glossary

- Key terms defined as used within the BMBL

Resources

- Appendix removed and relevant content reassigned to sections and appendices that remain in text

Current Status

- CDC Printing Office
- Electronic version to be fully 508 compliant
- Notify stakeholders when each version is available
- NIH is providing an email box for errata
  - We intended to do electronic updates and an errata page that can be appended to the hard copy, but no updates to the hard copy
  - BMBLComments@mail.nih.gov

- BMBL7 is an open question
  - Your input to NIH and CDC is key. It is expensive and time consuming to produce a version

Thank you

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