

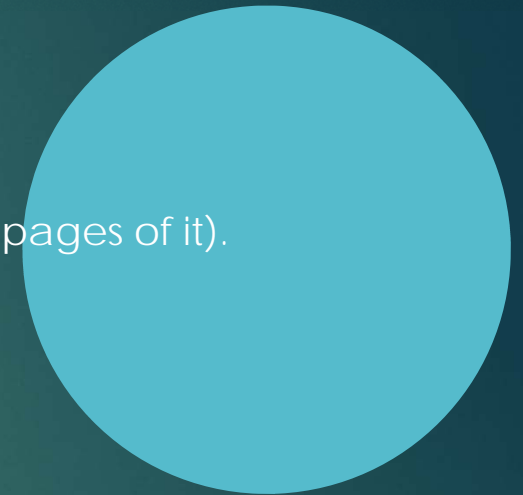
What's changed in BMBL6 (and when will see it)?

PAUL MEECHAN

MABSA BIOSAFETY VIRTUAL SYMPOSIUM

Start with the elephant...

- ▶ The manual has been translated into a publishable and electronically readable form
 - ▶ The “printers proof” has been reviewed and edited (all 600 pages of it).
 - ▶ GPO ready to print hard copy
- ▶ So, the electronic version?
 - ▶ Need to finish a “508” compliant version
 - ▶ Will post all sections at once
 - ▶ May be out after hard copy printed



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).

Specifics- Section II and III

▶ Section II-**Biological Risk Assessment**

▶ The section has been revised to:

1. Emphasize the need for inclusion of a broad range of stakeholders;
2. Note the role of risk assessment as part of an ongoing risk management process;
3. Link the positive culture of safety to the recurring risk management process.

▶ Risk management process have been revised to form a six step cycle.

▶ Section III-**Principles of Biosafety**

▶ Minor revision to emphasize the overlapping hierarchy of controls

Specifics- Section IV

- ▶ Removed “should” and “must” from recommendations.
- ▶ Part A (Standard Microbiological Practices) significantly revised to include most items common to any biosafety level.
 - ▶ Safety manual now recommended.
 - ▶ Glove recommendations have been moved to Part A.
 - ▶ Expanded language regarding sharps is provided in Part A.
 - ▶ General recommendations regarding decontamination and waste handling are now included here.
 - ▶ Mouth pipetting is still explicitly banned.
- ▶ At ABSL-2 and above, the recommendation for decontaminating laboratory waste in Part B (Special Practices) recommends the process be validated.
- ▶ In Part C, there is now a recommendation that respiratory protection be considered as part of the risk assessment at BSL-2 and above and, if needed, staff enrolled in a properly constituted respiratory protection program.

Section IV- continued

- ▶ Specific recommendations are provided for the removal of viable organisms from containment are now provided at BSL-3, instead of only at BSL-4.
- ▶ Facility-specific recommendations are retained in Part D (Laboratory Facilities).
 - ▶ A recommendation for adequate illumination has been added to Part D for all biosafety levels
 - ▶ BSC recommendations are in Part D. Class IIC BSCs are included in the recommendations.
 - ▶ Communications systems between the lab and outside are now recommended 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.

Specifics- Section V

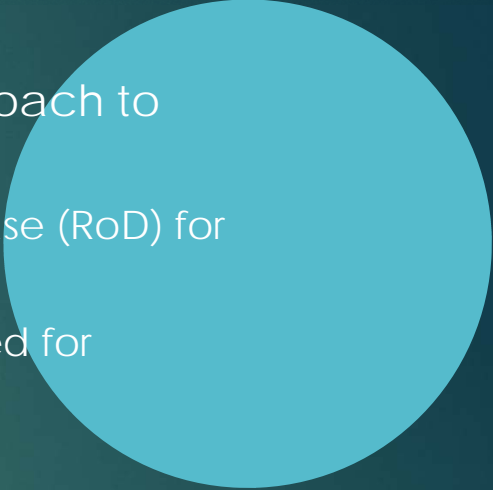
- ▶ Section V
 - ▶ Basic structure as in Section IV- the two sets of contributors were asked to help align the sections.
 - ▶ Section V is for laboratory animal research- the animals are capable of being confined based on risk assessment. Loose housed or penned animals should use ABSL-X Ag recommendations in Appendix D.
 - ▶ A recommendation that the risk assessment consider animal allergens if research animals are present has been added to Part A for all biosafety levels.
 - ▶ Separating animal containment facilities from the general traffic and away from exterior walls to minimize the impact of the external environment temperatures is recommended at all containment levels.
 - ▶ For ABSL-4 suit facilities, specific information is provided regarding facility recommendations if open housed animals will be held in the facility.

Specifics- Section VI

- ▶ 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.

Specifics- Section VII



- ▶ 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.
- 

Specifics- Section VIII Introduction



- ▶ 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.
- ▶ Subsections were reviewed and updated with current information regarding the agent and mitigation. Only changes beyond that will be noted.
- ▶ All agent summaries now note that a CDC import permit is required and a USDA import permit may be required.

Section VIIIA- Bacterial agents

- ▶ *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)

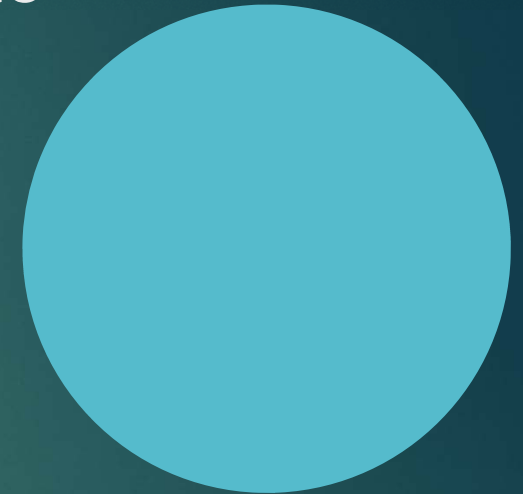
Section VIII B- Fungal agents



- ▶ Added *Blastomyces gilchristii* to *Blastomyces dermatitidis* agent summary.
- ▶ Removed *Cryptococcus neoformans* and Dermatophytes agent summaries.
- ▶ Created new table for miscellaneous molds and added *Cryptococcus neoformans* to table.

Section VIIC- Parasitic agents and Section VIID- Rickettsial agents

- ▶ Updated agent information for both sections.



Section VIII E- Viral agents

- ▶ *Herpesvirus simiae* renamed *Macacine alphaherpesvirus 1*.
- ▶ Significant revision of Influenza agent summary, including information regarding A(H1N1)pdm09.
- ▶ Poliovirus updated to reflect GAP III 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.

Section VIII F- Arboviruses and Related Zoonotic Viruses

- ▶ Elimination of recommendation for 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.

Section VIII G- Toxin agents and Section VIII H- Prion diseases


- ▶ Updated agent information for both sections.



Appendix A



▶ Appendix A

- ▶ 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



▶ Appendix B

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

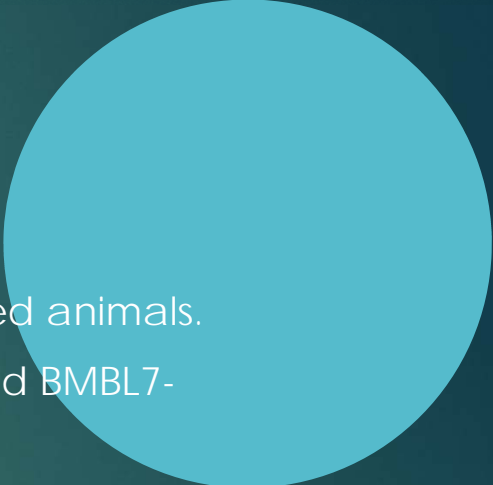
▶ Appendix C

- ▶ 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. Too late to be added to this edition.

Appendix D



▶ Appendix D

- ▶ 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 tables

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
<i>Actinobacillus spp</i>	<i>A. pleuropneumonia</i>	3	3,4,5	2	2	2	2Ag-3Ag	
<i>Aeromonas spp</i>	<i>A. hydrophila</i> , <i>A. salmonicida</i>	5	3,8	2	2	2	2Ag	
<i>Anaplasma spp</i>	<i>A. centrale</i> , <i>A. marginale</i> , <i>A. phagocytophilum</i>	1a	2,4	2	2	2	2Ag	
<i>Arcobacter spp</i>	<i>A. butzleri</i> , <i>A. cryaerophilus</i> , <i>A. skirrowii</i>	1,2,3,10b	1,8	2	2	2	2Ag	
<i>Bacillus spp</i>	<i>B. anthracis</i> , <i>B. cereus</i>	1-10	2,3,8	1-3	2-3	2-3	2Ag-3Ag	Y

Appendix E

▶ Appendix E

- ▶ 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> (Mar 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 on state of the art.
- ▶ **Appendix H- Working with Human, Non-Human Primate (NHP), and Other Mammalian Cells and Tissues**
 - ▶ Updated with current information on state of the art.
- ▶ **Appendix I- Guidelines for Work with Toxins of Biological Origin**
 - ▶ Updated with current information on state of the art.
- ▶ **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.

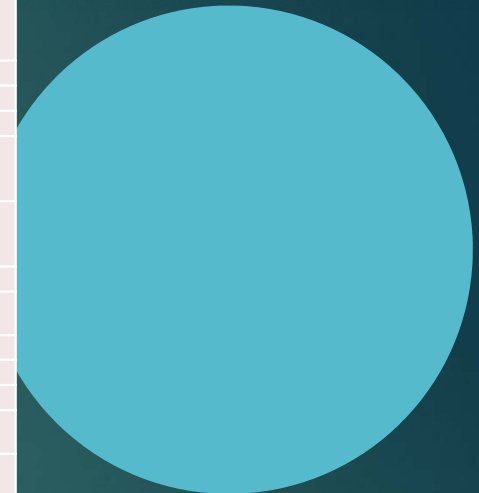
Appendix K

▶ 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 a number of inactivation processes.

Appendix K tables

Table 1: Advantages of physical inactivation			
	Heat	Ionizing radiation	Light (UV-C)
Efficacy	Broad	Broad	Inactivates viruses, Gram-positive and Gram-negative bacteria
Applicability	Broad	Broad	Broad
Residual toxicity	Low	None	None
Cost			Low cost
Structural maintenance		Proteins; 3-D structure preserved	Most proteins
Penetration	Complete, depending on length of treatment	Inactivation of denser materials	Surface
Resistance		None observed	None observed
Ease of use	Simple and convenient		Short exposure time
Table 2: Disadvantages of physical inactivation			
	Heat	Ionizing radiation	Light (UV-C)
Acute Toxicity	Thermal burns possible	High toxicity	May damage exposed skin
Structural maintenance	Limited due to denaturation of proteins; may damage agent's ability to produce immune response		DNA intrastrand crosslinks limit use for PCR and transcription assays
Cost		High cost	
Penetration	Limited by access of all material to steam or dry heat; trapped air may serve as insulation		Limited by capacity of light; impacted by opaqueness of liquid, proportion of suspended particles, soluble and insoluble materials, and distance from UV source
Ease of use		Regulatory, security constraints (irradiator); long exposure times	



Appendices L and M

▶ 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

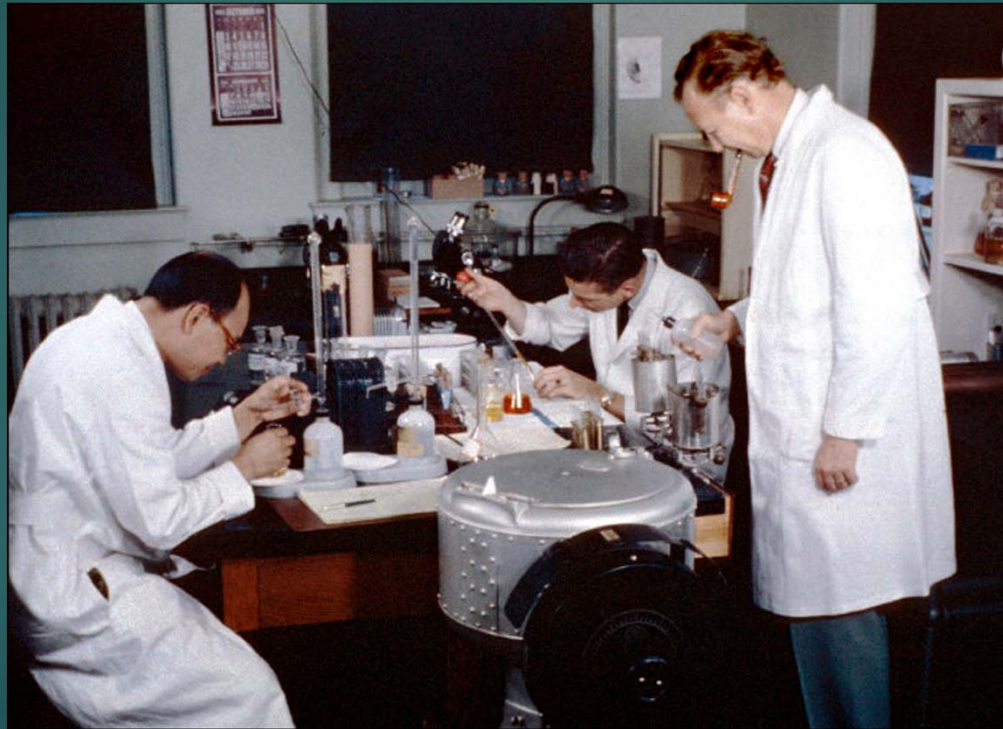
- ▶ Written to provide biosafety guidance to large-scale (>10 liter) facilities.
- ▶ Emphasizes the use of risk assessment and the unique hazards posed by large scale fermentation and purification and the potential issues surrounding balancing biosafety and Good Manufacturing Practices (GMP).

Appendix N

▶ Appendix N- Clinical Laboratories

- ▶ This new appendix was written to provide biosafety guidance to clinical laboratories. It 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 are also identified 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.
- ▶ It is not a replacement for Section IV.

Labs evolve



<http://phil.cdc.gov/Phil/home.asp>

Remaining Appendices



- ▶ **Appendix O- Acronyms**
 - ▶ Updated to reflect current terms.
- ▶ **Glossary**
 - ▶ New addition to BMBL. Key terms defined as used within the BMBL.
- ▶ **Resources**
 - ▶ Appendix removed and relevant content reassigned to sections and appendices that remain in text.

What happens now?



- ▶ Finish the printers' proof and provide to GPO.
- ▶ Revise 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.
- ▶ BMBL7 is an open question.
 - ▶ Your input to NIH and CDC is key. It is expensive and time consuming to produce a version.

And the color is...?

- ▶ You'll find out when it's published.
- ▶ We did some mock ups...and most failed.

- ▶ Need to recognize the hard work done by Rob Weyant and Jeff Potts after I left CDC. Not possible to do without their help and the help of Mallory Pomales and Shaina Mangino.

Biosafety in Microbiological and Biomedical Laboratories

5th Edition



Centers for Disease Control and Prevention
National Institutes of Health