May 12, 2016 – Comments provided by the Association of Public Health Laboratories (APHL) on Revisions to the "Biosafety in Microbiological and Biomedical Laboratories (BMBL), 5th Edition"

On May 12, 2016, via funding from the National Institutes of Health, the National Academy of Sciences, Engineering, and Medicine convened the workshop, *Soliciting Stakeholder Input for a Revision of "Biosafety in Microbiological and Biomedical Laboratories*." Prior to and during this workshop, APHL provided the following comments to improve the Biosafety in Microbiological and Biomedical Laboratories (BMBL).

APHL Recommendations for Revisions to the BMBL

Section	Comment	Reason
General	Many of the bacterial specific guidance specify which biosafety level precautions to use based on the purpose (diagnostic vs. culture). This is not specified for viral work and should be.	Missing
General	The BMBL was written for research laboratories that (generally) know what agent they work with. Diagnostic laboratories generally don't know the agent; the purpose of their work is to identify the agent or to help explain the cause of the disease or malady. The BMBL really provides inadequate biosafety guidance for laboratories that must diagnose unknowns. Some hospitals and clinical laboratories in the US refused to test *suspect* Ebola samples because of the BMBL. The implications with a more ubiquitous infectious disease could be extremely challenging, even perhaps disastrous.	Missing
General	The risk assessment chapter needs to be rewritten. As it stands, it only articulates a hazard assessment – the identification of the various hazards in the laboratory. It also asserts that you should make a preliminary determination of the biosafety level following the agent hazard assessment, then a final biosafety level determination after considering procedure hazards. Then, you should evaluate staff proficiencies and the integrity of safety equipment. This is incomplete. A risk assessment should evaluate everything associated with a specific protocol before determining a set of effective mitigation measures.	

	Most importantly, this chapter omits these fundamental aspects of a risk assessment: a. Articulate everything that could go wrong during a particular activity or protocol – the risks b. Prioritize the risks based on a rigorous, repeatable evaluation of the risks: Likelihood x Consequences c. Demonstrate how the chosen mitigation measures focus on reducing the highest priority risks d. Describe the metrics that will be used to routinely (or constantly) evaluate the effectiveness of the chosen mitigation measures	
General	Although there is a universal understanding in the biosafety community that BSL-3 materials need to be properly inactivated before transferring to a lower BSL, the BMBL currently lacks any reference to the need for validated methods of inactivation protocols (other than for waste) in the BSL-3 guidelines, Additionally, there is no consensus on appropriate methods for validation of inactivation protocols or acknowledgement of the limitations (i.e., limits of detection) associated with validation procedures for viruses. ABSA, ASM, and APHL should work together to develop evidence-based best practices and expand guidance in the BMBL to clarify expectations (e.g., validation of inactivation methods) where appropriate. DSAT recently published draft guidance document on rendering samples free of select agents and toxins. Our institution noted some concerns with their guidance and expectations in the proposed select agent regulations, so DSAT should be involved in those discussions to ensure consistency.	
General	Additional guidance documents and standards (e.g., MMWR Guidelines for Human and Animal Diagnostic Labs and CLSI M29-A4 – Protection of Lab Workers from Lab Acquired Infection) have been developed specifically for the clinical and diagnostic lab setting. The guidance provided in these documents compared to the existing BMBL guidance needs to be considered as they update the BMBL. The needs of the clinical/diagnostic laboratories and types evidence-based best practices appropriate for those environments may differ from biomedical/research lab setting, so that needs to be considered as the next edition of the BMBL.	Missing
General	Biosafety needs to take a management systems approach which includes risk assessment, mitigation, and performance evaluation. This information is included in the CWA Biorisk Management Standards Document. The BMBL should incorporate how to interface with both of these documents.	
General	The BMBL basically says: define the BSL, then you're good to go. Biosafety achieved. What the bioscience community now needs – and what is missing from the BMBL – is an explanation that biosafety must be implemented within a management system. There must be a mechanism for creating metrics – in advance of the	

	work, based on the risk assessment – that defines how the effectiveness of the safety mitigation measures will be evaluated on a routine basis. This is often called "performance management." This concept is well engrained in medical diagnostic laboratories that must establish quality management systems – as well as other high-consequence industries. We do not sufficiently promote an analogous (or integrated) safety management system in the biosciences. We have no mechanisms to routinely collect information about what works and doesn't work, and to document unexpected events in the lab, near misses, accidents, etc. This data, which should be collected on a routine (continuous) basis, should be used to regularly update the risk assessment, and to modify and improve mitigation measures before an accident happens. This is absolutely key for the future of biosafety. The BMBL must articulate a management system concept to move biosafety out of the administrative basements of bioscience laboratories – and the perception that biosafety is only the responsibility of the designated "biosafety officer" – and to create a system that invests the entire scientific staff in the performance of the safety system.	
General	The recently released GAO report on High Containment Laboratories references six elements that they identified as key for managing these types of laboratories: Incident reporting, roles and responsibilities, training, inventory control, inspections, and reference to the BMBL. Each of these elements should be reviewed in the context of the GAO report and ensure that an adequate level of guidance is provided for high containment labs. Additionally, we would recommend that the role of the Biorisk Management Standard, which also provides guidance on each of these elements, should be clarified because institutions are now faced with two separate guidance documents…one a code of conduct that can be implemented with risk-based/performance-based approach, the other a voluntary management system that can help create structure to a program. It would be helpful to have a section that clarifies how both documents can be used to complement one another.	
General	With a good risk management system in place, the practice of blaming the scientist or technician who makes a mistake should end. As long as we believe that mistakes are only caused by individuals, we deny that the overarching system has a problem. Instead, we need to understand accidents as system accidents. In a complex environment, such as a bioscience laboratory, with many different people, processes, and technologies contributing to the success or failure of the laboratory's operations, any mistake is a reflection on the overall system that governs the work of the laboratory. An accident is an example of a series of small mistakes that likely have been made for a period of time that simply haven't yet resulted in an accident. It is critical for management to create an	

	environment that embraces and even rewards discussion about what doesn't work well in the laboratory. Until we eliminate the tendency of blame and finger-pointing, problems, near misses, and accidents will be hidden and denied. And the lessons to be learned from the events will be lost. And the accidents will continue because the system will not change. It is essential for the BMBL to promote routine laboratory hot washes that reveal the utility and value of all of the control measures, and identify new data that can contribute to revisions of the risk assessment. The BMBL should also encourage incentives and rewards for those laboratory staff who identify safety issues and improvements. Finally, the BMBL should articulate the concept of the system accident, and explicitly reject the notion that individuals should be blamed for laboratory accidents.	
General	The BMBL should have an updated online version where each section can be updated frequently based on new information which becomes available.	General
General	The current arrangement of chapters is not the most useful method of organizing the available information.	Organization
General	The concept that agents have defined biosafety levels (BSLs) is problematic, especially for the clinical/diagnostic laboratory community. Tightly linking agents to BSLs basically preclude the concept of a rigorous, activity-specific or protocol-specific risk assessment. Why do a risk assessment if biosafety is defined as the implementation of a BSL, and the agent tells you what BSL to use? The result is substantive risk assessments are often not conducted	
General	The BMBL and BSL concepts do not translate into low-resource environments. The international message sent by saying that it is only acceptable to work with microscopic amounts of Ebola in the US is in a BSL-4 is fitting in highly resourced countries, but in the middle of an outbreak in a low resource environment these recommendations are impractical. The BMBL is now an international document and must be able to manage biological risks wherever they occur—this is more evidence to push for a risk-based system of biosafety which can be applied internationally. It is also critical that the revision of the BMBL be aligned with the revision of the WHO's *Laboratory Biosafety Manual*, which apparently is moving away from the agent-based perspective.	
Section VIII-E	Bacterial agents are separated out by specific organism and each bacterium has its own section. This is not true for viruses where they are classified by family (ex: arbovirus, or viral hemorrhagic fevers). Many viruses in the same family have unique requirements and these should be noted.	Missing
Parasitology	Insectories need to be covered in more detail as a risk of infection. Appendix E covers it somewhat but insufficiently to consider lab acquired infections.	Missing
Parasitology	Airborne acquisition of Cryptosporidium parvum needs to be considered for respiratory infection. It is mentioned for GI illness	Missing

	but not for respiratory illness. There are references for respiratory infection in the immunocompromised and the possibility of lab acquired respiratory infection should be mentioned.	
Parasitology	Cyclospora cayetanensis is not considered with the GI pathogens.	Missing

Agent Specific BMBL Revisions

Francisella tularensis

Section	Comment	Reason (Missing, Out of Date, etc.)
Section VIII-A-Francisella tularensis (pg 138)	Type A and Type B strains are highly infectious, requiring only 10-50 organisms to cause disease: This is to clarify that the exposure route is significant in determining infectious dose. Requiring only 5-10 organisms by the respiratory route and 10^6-10^8 organisms by ingestion	Missing
Section VIII-A-Francisella tularensis (pg 138)	The incubation period varies with the virulence of the strain, dose and route of introduction but ranges from 1-4 days with most cases exhibiting symptoms in 3-5 days: The incubation period has been modified to range from 1-14 days	Incorrect
Section VIII-A-Francisella tularensis (pg 138)	In Natural Modes of Infection adjust language to: *Francisella tularensis* can survive in animal carcasses and organs up to 133 days and water for up to 90 days. Ingestion of contaminated water, food, animal tissues or fluids, inhalation of infective aerosols and bite of arthropods (deerfly, mosquito) and tick are the primary transmission modes in nature. Remove: Tick bites, handling or ingesting infectious animal tissues or fluids, ingestion of contaminated water or food and inhalation of infective aerosols are the primary transmission modes in nature.	Incorrect
Section VIII-A-Francisella tularensis (pg 138)	Direct contact of skin or mucous membranes with infectious materials, accidental parenteral inoculation Include: animal bite	Missing
Section VIII-A-Francisella tularensis (pg 138)	In Vaccine Section include: Vaccination for tularemia is not generally available in the United States, nor is it useful in the management of ill patients. A vaccine for tularemia was used in the past to protect laboratory workers, but it is not currently available.	Outdated

Clostridium

Section	Comment	Reason (Missing, Out of Date, etc.)
Section VIII-A-Neurotoxin Producing Clostridia Species pg 134	*Clostridium botulinum*, and rare strains of *C. baratii* and *C. butyricum* are anaerobic spore-forming species that cause botulism, a life-threatening illness Include: and some isolates of *C. argentinense (BoNT/G)*	Include:
Section VII-A-Neurotoxin Producing Clostridia Species pg 134	Spore-forming species that cause botulism, a life-threatening illness: *C. argentinense* is isolated from soil and not known to cause food borne illness.	Incorrect
Section VII-A-Neurotoxin Producing Clostridia Species pg 134	There has been only one report of botulism associated with handling of the toxin in a laboratory setting. However, concerns about potential use of the toxin as an agent of bioterrorism or biological warfare have led to increased handling of the substance by investigators studying mechanism of action and/or developing countermeasures to poisoning. Therapeutic use of BoNT is likely the predominant driver of "increased handling of the substance"	Outdated
Section VII-A-Neurotoxin Producing Clostridia Species pg 134	Botulism occurs when botulinum toxin is released into circulation following ingestion of preformed toxin: Ingestion of preformed toxin is not the only cause of "naturally" occurring botulism. For example, wound, infant botulism, and adult colonization are caused by an infection not ingestion of preformed toxin.	Inaccurate
Section VIII-A-Neurotoxin Producing Clostridia Species pg 134	Symptoms and even death are possible by accidental injection of botulinum toxin: This statement is also true for other routes of exposure to preformed toxin. Only including injection may lead the reader to think that BoNT exposure via other routes is less risky.	Inaccurate
Section VIII-A-Neurotoxin Producing Clostridia Species pg 134	In Wound Botulism, exposure to toxin is caused by introduction of spores into puncture wounds and *in situ* production [of toxin] by the organism.	Include rephrase "of toxin"

Section VIII-A-Neurotoxin Producing Clostridia Species pg 134	Although spore-forming, there is no known risk to spore exposure except for the potential for the presence of residual toxin associated with pure spore preparations: Unless the laboratory scientist is an "…adult[s] with a compromised gastrointestinal tract (GI), such as following GI surgery or long-term administration of antibiotics, may increase risk for intestinal infection and *in situ* production of toxin"	
Section VII-A-Neurotoxin Producing Clostridia Species pg 134	Additional primary containment and personnel precautions, such as those recommended for BSL-3, should be implemented for activities with a high potential for aerosol or droplet production, or for those requiring routine handling of larger quantities of the organism: Consider more specificity as to what is considered "larger"	Vague
Section VII-A-Neurotoxin Producing Clostridia Species pg 134	Select Agent Neurotoxin producing *Clostridia* species are select agents requiring registration with CDC and/or USDA for possession, use, storage and/or transfer. See Appendix F for additional information: Preformed BoNT in concentrations ≥0.5 mg are also regulated by the Federal Select Agent Program	Missing
Section VII-A-Neurotoxin Producing Clostridia Species pg 134	The vaccine section needs to be updated to remove the reference to available vaccinations. There is no currently available vaccine.	Outdated

Brucella species

Section VIII-A	Comment	Reason (Missing, Out of Date, etc.)
General	Agency summary statements, in general, need to be updated to include all relevant information needed in performing agent-specific risk assessments, as well as information relevant to post-exposure response. Therefore, the agents summary statement format should be modified to model Health Canada's MSDS format, or at least adopt relevant sections/topics from those documents that are not currently address consistently, including incubation period, communicability, infectious dose, Section IV – Viability (e.g., susceptibility to disinfectants, physical inactivation, and survival outside host), Section V – Medical (e.g.. post-exposure surveillance and follow-up, first aid/treatment, and prophylaxis).	Needs update to include additional information.
General	Agent summary statements need to be maintained electronically and referenced, separate from the published BMBL version if that still occurs, and have an approval process for updating and/or revising based on new information.	
Occupational Infections	Under "Occupational Infections" – references should be updated to reference more recent examples of both research and clinical associated lab infections involving Brucella if they exist.	
Occupational Infections	Consider addressing risk of RB51 vaccine or other vaccine strains if still handled by labs (e.g., for PT purposes).	
Lab Safety and Containment Recommendations	Under "Laboratory Safety and Containment Recommendations" – Review more recent literature to determine if most lab-associated cases still occur in research facilities from large quantity growth or placental tissue. Update as needed to reflect the highest risk exposure source associated with today's laboratories.	
Lab Safety and Containment Recommendations	Replace 1940 and 1991 references with more recent examples from the literature that reflect today's laboratory exposure risks.	
Lab Safety and Containment Recommendations	Describe current modes of transmission from both a clinical and research laboratory standpoint. Address known exposure risks as well as suspected exposure risks associated with new technologies in the lab (i.e., risk associated with automated equipment where research data doesn't exist to demonstrate whether or not there is aerosol and/or droplet exposure).	
Lab Safety and Containment Recommendations	Replace the recommendation for using "BSL-3 practices" for handling products of conception with the term "Aerosol/droplet precautions" or something similar which	

	specifically references practice #10 under BSL-3 special practices (i.e., the practice of no open handling or use of respiratory protection and containment devices where that cannot be achieved in the lab or for the particular operation). The term "BSL-3 practices" includes a number of other administrative requirements that may not be appropriate for that enhanced requirement. The term used for enhanced BSL-2 requirements should reflect the need for no open handling or use of droplet vs. respiratory protection depending upon the suspected agent and procedures involved.	
Lab Safety and Containment Recommendations	The reference to "products of conception" only should be expanded to blood and body tissues or cultures suspected of containing pathogenic Brucella until Brucella can be ruled out.	
Lab Safety and Containment Recommendations	Incorporate a section/description of the specific clinical/diagnostic tests/results that would serve as "triggers" for implementing "BSL-2 transmission precautions" until Brucella is ruled out, e.g., submitted as suspect Brucella case, culture is gram negative bacteria, biochemical test result, etc.	
Special Issues	Remove section on transfer unless specific importation/domestic transfer requirements related to Brucella species can be defined. The general guidance is of no value.	

Yersinia pestis

Section	Comment	Reason (Missing, Out of Date, etc.)
Section VIII-A-Yersinia pestis	BSL-3 practices should be used when working with Y. pestis. Wearing an N-95 or other respirator and face shield or safety glasses. This is due to the hazard posed from pneumatic plague.	Potentially higher level working practices
Section VIII-A-Yersinia pestis	Avoid using term microaerophlic: Most sentinel and LRN laboratories would not culture this organisms I special atmospheric conditions. Pestis is simply cultured aerobically	
Section VIII-A-Yersinia pestis	Rephrase: There are three biotypes of Y. pestis, all of which are virulent	Remove the extraneous information and move to natural modes of infection section
Section VIII-A-Yersinia pestis	Include: the disease manifestation of Y pestis infection is either in form of bubonic plague or pneumonic plague. IN the case of bubonic plague infective fleabites….etc.	
Section VIII-A-Yersinia pestis	Include: The outcome of this particular infection is the formation of dark-colored buboes (inflamed lymph nodes). It is important to note that bubonic plague is not transmitted person-to-person. The incubation period for bubonic plague ranges from two to six days.	
Section VIII-A-Yersinia pestis	Include Yersinia can be handled in BSL-2 however it is strongly recommended to use BSL3 practices for more robust safety precautions	Already mentioned this in Charlene's comment
Section VIII-A-Yersinia pestis	Recommend adding PPE which would include disposable gloves, lab coats, N-95 masks.	
Section VIII-A-Yersinia pestis	Define "additional containment for personal protective equipment"	Vague, explain.

Burkholderia

Section	Comment	Reason (Missing, Out of Date, etc.)
Section VIII-A-Burkholderia mallei and Burkholderia pseudomallei	Burkholderia mallei: The agent specific summary needs to be updated to include more recent references to laboratory related exposures such as Peacock EID 2008 in the occupational infection section.	Outdated
Section VIII-A-Burkholderia mallei and Burkholderia pseudomallei	Burkholderia pseudomallei: The agent specific summary should be updated to include additional risk factors such as alcohol abuse and kidney disease etc. in more recent publications.	Outdated

Hepatitis

Section	Comment	Reason (Missing, Out of Date, etc.)
Section VIII-E Hepatitis C Virus, pg 204-205	"These viruses are naturally acquired from a carrier during blood transfusion, vaccination, tattooing, or body piercing with inadequately sterilized instruments. Non-parenteral routes, such as domestic contact and unprotected (heterosexual and homosexual) intercourse, are also major modes of transmission." Injection drug use is the most common way that Hep C is acquired, and a major route for Hep B and this is not mentioned at all. Singling out "vaccination" as one means of infection is not a good approach. It would be better to say something such as "infection control breaches associated with medical procedures". We don't need to give people another misguided reason to fear vaccines! Although it can be acquired through blood transfusion, and this may have been a major route in the distant past, the risk is probably very, very low with the screening tests that we have today. CDC list the common and less common ways that HCV is acquired here: http://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#b1 CDC list of ways HBV is acquired: http://www.cdc.gov/hepatitis/hbv/hbvfaq.htm#treatment Suggest that this paragraph be revised to be more consistent with current knowledge of how HBV and HCV are acquired.	Outdated

Tuberculosis

Section	Comment	Reason (Missing, Out of Date, etc.)
Section VIII-A Tuberculosis	Under Mycobacterium tuberculosis complex surveillance, PPD skin testing is recommended. Add IGRA to this recommendation as an alternative for foreign-born individuals who have had BCG vaccine, and perhaps for others who are skin test positive but IGRA negative.	Missing
Section VIII-A Tuberculosis	Add species to the MTB complex---M. pinnipedii, M. caprae, M. orygis, M. canettii, M. mungi	Missing
Section VIII-A Tuberculosis	Under "Natural Mode of Infection"---"M. tb is the **predominant** etiologic agent of tuberculosis…" Currently states "M. tb is the etiologic agent…" Other members of the MTBC cause tuberculosis.	Vague
Section VIII-A Tuberculosis	Under "Containment Recommendations"-----Suggest adding that medical laboratories that perform minimal manipulation of positive cultures that may contain MTBC perform a risk assessment to determine the appropriate level of biosafety required. For example, working in a BSL2 facility using BSL-3 practices vs working in a BSL-3 facility.	Vague
Section VIII-A Tuberculosis	Under "Surveillance" add IGRAs as an alternative to the skin test.	Missing

Influenza

Section VIII-E Influenza	Comment	Reason (Missing, Out of Date, etc.)
Introduction	There are three types of influenza A (currently says “three serotypes”). Serotype may not be technically accurate.	Incorrect nomenclature
Natural Modes of Infection	“Transmission may also occur through direct contact since influenza viruses may persist for hours on surfaces” …Should this read “direct and indirect contact”? Direct for contact with sick patients and indirect for contact with fomites?	Vague phrasing

SARS-MERS/Emerging Highly-Pathogenic Coronaviruses

Section	Comment	Reason (Missing, Out of Date, etc.)
VIII-E-SARS Coronavirus	Consensus of the group on the conference call was that MERS and SARS should be grouped as “Novel Coronaviruses” or “Emerging Coronaviruses”	Since additional coronaviruses may emerge in the future, SARS and MERS safety could be applicable.
Natural Modes of Infection	Recommend that any updated information on spread and natural reservoir of SARS be included.	
Laboratory Safety and Containment Recommendations, Paragraph 5	States, “SARS-CoV propagation in cell culture and the initial characterization of viral agents recovered in cultures of SARS specimens must be performed in a BSL-3 facility using BSL-3 practices and procedures. Risk assessment may dictate the additional use of respiratory protection.” SMEs should review this guidance, and consider recommending the use of respiratory protection for SARS propagation activities.	Clarification needed

Chlamydophila pneumonia

Section VIII-A	Comment	Reason (Missing, Out of Date, etc.)
Introduction	Change *Chlamydia pneumoniae* to *Chlamydophila pneumoniae*	Genus name has changed
Natural Modes of Infection	While C. pneumonia is a common cause of respiratory infection, it is not often diagnosed.	Lack of diagnosis is missing from current statement
Laboratory Safety and Containment	Review statement about BSL-3 practices for activities with high potential for droplet or aerosol production and large quantities/concentrations. Most diagnostic lab experience would be with clinical specimens and handling at BSL2 (in a BSC) should be sufficient for C. pneumoniae.	May not accurately reflect commonly accepted practices.

Coxiella burnetii

Section VIII-D (Rickettsial Agents)	Comment	Reason (Missing, Out of Date, etc.)
Laboratory Safety and Containment	Need to include BSL recommendation for molecular methods, such as PCR	Missing
Special Issues – Vaccine	Review vaccine status	Potentially out of date
Special Issues – Select Agent	C. burnetii has been proposed to be removed from the select agent list	Out of date

Legionella pneumophila

Section VIII-A	Comment	Reason (Missing, Out of Date, etc.)
Introduction	There are more than 60 known species	Out of date (currently 48 species)

Bordetella pertussis

Section VIII-A	Comment	Reason (Missing, Out of Date, etc.)
Introduction	Consider mentioning heavy reliance on PCR for diagnosis	Missing
Special Issues: Vaccines	Vaccine info needs to be updated probably from The Pink Book. In addition, some statement should be made of the immunity induced by vaccination is not enduring.	Out of date

Hantavirus

Section VIII-E	Comment	Reason (Missing, Out of Date, etc.)
Occupational Infections	Documented laboratory-acquired infections have occurred in individuals working with hantaviruses Include mostly infected rats	Missing
Section VIII-E – Hantavirus: Natural Modes of infection	Include: 6 Hantavirus infection is most commonly acquired by inhalation of infectious aerosols and extremely short exposure time (5 minutes) has been shown to be infectious	Missing
Natural Modes of Infection	Include: Rodents shed copious amounts of virus from their saliva, urine, feces for months. Cats may become infected through contact with rodents and become a reservoir	Missing
Laboratory Safety and Containment Recommendations	Include: 7 However, exposure may also occur by fluid contact and needle stick.	Missing
Laboratory Safety and Containment Recommendations	Include: There is currently no vaccine or antiviral treatment for Hantavirus infections.	Missing
Laboratory Safety and Containment Recommendations	The use of a certified BSC is recommended for all handling of human body fluids when potential exists for splatter or aerosol Remove: when potential exists for splatter or aerosol	Out of Date
Section VIII-E – Hantavirus: Laboratory Safety and Containment Recommendations	Recommend BSL3 Practices, not BSL2	Incorrect
Section VIII-E – Hantavirus: Laboratory Safety and Containment Recommendations	Include: Potentially infected research tissue samples should be handled in a BSL-3 facility using BSL-3 practices, containment equipment and procedures.	Missing

Rickettsial agents

Section VIII-D Rickettsial agents	Comment	Reason (Missing, Out of Date, etc.)
Section VIII-D Rickettsial agents	Coxiella burnetii should be removed from under Rickettsial agents as they are far removed from rickettsiae	Missing
Occupational Infections	Q fever is the second most commonly reported LAI: (This is historical data up to 1976. More recent surveys shows Shigellosis to be the most common lab-acquired infections. CID 2009, 49:142-147)	Out of date
Natural Modes of Infection	wild mammals are natural hosts for Q fever (C. burnetti, not Q fever)	Incorrect terminology
Section VIII-D Rickettsial agents	The placenta of infected sheep may contain as many as 109 and organisms per gram of tissue and milk may contain 105 These are meant to be 10^9 and 10^5	Typos
Section VIII-D Rickettsial agents	BSL-2 practices and facilities are recommended for nonpropagative laboratory procedures, including serological Include PCR testing	Missing
Section VIII-D Rickettsial agents: Vaccine	Should include the Australian QVax vaccine	Out of date
Section VIII-D Rickettsial agents : Select Agent	Select Agent *R. prowazekii* and *R. rickettsia*-No longer Select Agents	Out of date

Bacillus anthracis

Section	Comment	Reason (Missing, Out of Date, etc.)
Section VIII-A *Bacillus anthracis*	" It is *believed* that very few spores (10 or less) are required for cutaneous anthrax" This statement should be updated reflecting data published from the 2001 Anthrax cases.	
Section VIII-A *Bacillus anthracis* Laboratory Safety and Containment Recommendations	"Efforts should be made to avoid production of aerosols by working with infectious organisms in a BSC. In addition, all centrifugation should be done using aerosol-tight rotors that are opened within the BSC after each run" This is best practice for working with any infectious agent. Are there any additional recommendations specific for anthrax? What about inactivation? Should all work be done in a hood? If this paragraph is specific for diagnostic work, it should say that. `	
Bacillus anthracis Laboratory Safety and Containment Recommendations	"BSL-2 practices, containment equipment, and facilities are recommended for activities using clinical materials and diagnostic quantities of infectious cultures." There is a major gap between what is recommended here and what the select agent program requires. According to this, we do not have to perform BA testing in our BSL3, but I think SA program will argue this.	

Bacillus anthracis Laboratory Safety and Containment Recommendations	"Workers who frequently centrifuge B. anthracis suspensions should use autoclavable aerosol-tight rotors. In addition, regular routine swabbing specimens for culture should be routinely obtained inside the rotor and rotor lid and, if contaminated, rotors should be autoclaved before re-use" This seems out of place here. Maybe include a section on decontamination of equipment and work surfaces. This is suggesting that you should do routine environmental monitoring for contamination. Should it only be for centrifuge? Or other equipment too?	
Bacillus anthracis Special Issues	"Worker vaccination is recommended for … 3) performing confirmatory testing for B. anthracis, with purified cultures… Vaccination is not recommended for workers involved in routine processing of clinical specimens or environmental swabs in general diagnostic laboratories." This seems contradictory. Says it is not needed in diagnostic labs. But is needed for confirmatory testing of cultures. So what about a public health laboratory (PHL)? There are very few PHLs that have anthrax vaccinated staff. Perhaps, discuss mitigation strategies to the risks.	
Bacillus anthracis Special Issues	"permit from USDA/APHIS/VS" Is this SA form 2? It should specify that.	

Pox Virus

Section	Comment	Reason (Missing, Out of Date, etc.)
Section VIII: Pox viruses General	This section should be updated to include information on ORF viruses.	
Pox Viruses *Occupational Infections* and *Laboratory Safety and Containment Recommendations*	Both of these sections should be updated to include information provided in the most recent ACIP recommendations for lab workers and poxviruses (published March 17, 2016 in MMWR).	
Other Considerations	The phone numbers provided needed to be updated. The latter phone number is no longer a CDC number.	

Brucella species

Section	Comment	Reason (Missing, Out of Date, etc.)
Section VIII-A: Bacterial Agents *Brucella species*	Twelve **Brucella* species have been described using epidemiologic and biological characteristics, although at the genetic level all brucellae are closely related. *B. melitensis* (natural host: sheep/goats), *B. suis* (natural host: swine), *B. abortus* (natural host: cattle), *B. canis* (natural host: dogs), *B. ceti* (natural host: marine mammals) and *B. inopinata* (natural host: unknown) **,*** have caused illness in humans exposed to the organism including laboratory personnel., + * Scholz HC, Revilla-Fernández S, Al Dahouk S, et al. *Brucella vulpis* sp. nov., isolated from mandibular lymph nodes of red foxes (*Vulpes vulpes*). Int J Syst Evol Microbiol. 2016;66:2090-2098. * *Scholz HC, Nöckler K, Göllner C, et al *Brucella inopinata* sp. nov., isolated from a breast implant infection. Int. J. Syst. Evol. Microbiol. 2010;60:801-808. *** Tiller RV, Gee JE, Lonsway DR, et al. Identification of an unusual *Brucella* strain (BO2) from a lung biopsy in a 52 year-old patient with chronic destructive pneumonia. BMC Microbiol. 2010;10:23. + Centers for Disease Control and Prevention. Laboratory-acquired brucellosis—Indiana and Minnesota, 2006. MMWR Morb. Mortal. Wkly. Rep. 2008;57:39–42.	
Select Agent	This section is likely to need updating prior to publication of the 6th edition of BMBL if new recommendations are accepted by the Federal Select Agent Program. *Brucella abortus* and *B. suis* may be removed from the list of select agents and *B. melitensis* may become a USDA-only regulated select agent.	
Section VIII-A: Bacterial Agents *Brucella species Natural Modes of Infection*	add raw cheese made from contaminated milk	
Section VIII-A: Bacterial Agents *Brucella species Laboratory Safety and Containment Recommendations*	Include, bone marrow, lymph nodes, liver and spleen, as tissues that can be infected.	

Section VIII-A: Bacterial Agents	"Cases have occurred in clinical laboratory settings from sniffing bacteriological cultures or working on open bench tops".30,++,+++ ++ Traxler RM, Lehman MW, Bosserman EA, et al. A Literature Review of Laboratory-Acquired Brucellosis. J Clin Microbiol. 2013;51(9):3055–3062. +++ Traxler RM, Guerra MA, Morrow MG, et al. Review of Brucellosis Cases from Laboratory Exposures in the United States in 2008 to 2011 and Improved Strategies for Disease Prevention. J Clin Microbiol. 2013;51(9):3132–3136.	