May 25, 2016

Steering Committee and Editorial Board Members
Biosafety in Microbiological and Biomedical Laboratories (BMBL)
National Institutes of Health (NIH)
Centers for Disease Control and Prevention (CDC)

Dear Steering Committee and Editorial Board Members:

The Association of Public Health Laboratories (APHL) and the American Society for Microbiology (ASM) would like to thank you and the National Academy of Sciences, Engineering, and Medicine for convening the May 12, 2016 workshop, Soliciting Stakeholder Input for a Revision of Biosafety in Microbiological and Biomedical Laboratories (BMBL), 5th Edition. Prior to and during this workshop, APHL provided comments on behalf of its member laboratories, mainly local and state governmental laboratories conducting tests of public health significance. The ASM requested that its membership provide comments and also had a representative participate in the workshop and provide comments. Since its inception, the BMBL has been the standard for biosafety for research, academic, private clinical, and public health laboratories across the country. Although the BMBL is the most comprehensive biosafety guideline available, there are currently areas pertaining to diagnostic clinical and public health laboratories that are missing or are inconsistent with current practice.

In addition to the specific and detailed comments provided during the workshop, (see enclosure), APHL and ASM recommend the following:

- **Need for Clinical and Public Health Laboratory Representation:** Due to the recent biosafety lapses that have been widely reported as well as biosafety concerns that have been raised in clinical and public health laboratories dealing with emerging infectious diseases (Ebola and Zika), APHL and ASM strongly recommend that the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) revise the BMBL to better integrate and strengthen the practices of the clinical and public health diagnostic laboratories. Further, we recommend that a practicing clinical and public health laboratory official be included as members of both the Steering Committee and the Editorial Board for the BMBL. Inclusion of both clinical and public health experts with strong diagnostic laboratory backgrounds will be essential to provide technical guidance on the enhancements necessary in the next edition of the BMBL.

- **Need for Risk Assessment Prior to the Assignment of Biosafety Level:** One example of a critical lapse currently in the current BMBL is the assignment of high consequence or emerging pathogens to biosafety levels without a rigorous risk assessment. Page 238 of the BMBL 5th edition states, “Clinical specimens from persons suspected of being infected with one of the agents listed in this summary (i.e. Risk Group 4) should be submitted to a laboratory with a BSL-4 maximum containment facility.” This statement does not reflect the current practice in public health laboratories. While it is understood that the above statement is intended to be a suggestion of best practices, it is not always construed that way, and during a public health emergency any delay in response could lead to disastrous consequences. The revised BMBL
should not implicitly or explicitly link agents to biosafety levels. While high consequence and emerging pathogens demand appropriate containment, the level of containment should be determined after performing a risk assessment. Although many hemorrhagic fevers (such as Ebola) certainly warrant caution, the concentration of infectious material found in any specimen and the procedures to be performed, among other considerations, should influence what mitigation measures are selected. A clinical specimen that may contain Ebola can be inactivated safely within a Biological Safety Cabinet (BSC) in a Biosafety Level 3 (BSL-3) laboratory for downstream real time polymerase chain reaction (PCR) analysis. This procedure deserves different and appropriate mitigations compared to propagating large quantities of Ebola for animal experiments in research laboratories.

- **Include recommendations on working with unknown clinical samples:** While the current BMBL provides strong recommendations for working with known samples, it offers little guidance for controlling the biosafety risks associated with unknown clinical samples.

- **Include guidelines for working with potential mixed samples:** In addition to working with unknown samples, clinical and public health laboratories often receive samples that may contain more than one pathogen. For example, a sample that is suspected to contain Zika virus may also contain Chikungunya virus—both arboviruses circulate in the same geographical area—but they currently fall in two distinct risk groups.

- **Include guidelines for pathogen inactivation:** As noted above, many specimens suspected of containing high consequence pathogens are initially inactivated for further downstream molecular testing thus rendering the sample safe to be worked with in a lower containment level. This may not be the case for experiments performed in research laboratories. Unfortunately, the BMBL has no performance guidelines on appropriate methods for validating inactivation protocols or acknowledging their limits of detection. Such standard guidance could help prevent future mishaps whether in the clinical, public health or research laboratories.

- **Include clinical guidance for all agent summary statements:** While many of the agent summary statements provide guidance for clinical specimens under the section, *Laboratory Safety and Containment Recommendations*, others do not. This is particularly true for many of the viruses. All pathogens such as Ebola, Chikungunya and Zika viruses that have a potential public health impact should have a separate agent summary sheet.

Should you have any questions about these recommendations, please contact APHL’s Manager, Biosafety and Biosecurity, Mr. Brit Hart at brit.hart@aphl.org or 240-485-2702. Thank you again for this opportunity to contribute to the revision of the BMBL 5th Edition. We look forward to working with you and other stakeholders to strengthen the BMBL to meet the needs of clinical and public health laboratories.

Sincerely,

Michael Pentella, Ph.D., D(ABMM)
Chair, APHL Biosafety and Biosecurity Committee
Director, Bureau of Laboratory Sciences
William A. Hinton State Laboratory Institute (Massachusetts State Public Health Laboratory)