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Comparative Analysis of the Fourth and Fifth Editions of *Biosafety in Microbiological and Biomedical Laboratories* Section IV (BSL2-4)

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Abstract

We developed a matrix of changes between Section IV of the current and former editions of Biosafety in Microbiological and Biomedical Laboratories (BMBL), focusing on biosafety levels two, three, and four (BSL2, BSL3, and BSL4). Citations containing multiple statements were subdivided into individually addressable statements and statements with similar/identical scope were aligned, allowing for a precise comparative analysis. In addition, statements were categorized for further analysis based on the subject of the change, the type of change, and the outcome of the change. Although the Fifth Edition of BMBL (BMBL5) proved to be a close facsimile of its predecessor, we identified 375 total changes, including 165 novel statements not addressed in the former edition. Over 65% (110) of these changes were found in statements pertaining to BSL4 containment. In our study, we further examine these edition differences and identify key areas where those entities responsible for compliance with these new recommendations may wish to focus their efforts.

Introduction

First introduced in 1984, BMBL is an advisory document recommending best practices for the safe conduct of work in biomedical and clinical laboratories. Since its inception, it has become one of the most frequently used codes of practice in biosafety, and an authoritative reference for: the development of laboratory policies and procedures, the construction of new laboratories, and the renovation of existing laboratories (U.S. Department of Health and Human Services, 1999). Over the past two decades, periodic updates have been made to the BMBL to “refine guidance based on new knowledge and experiences and to address contemporary issues that present new risks that confront laboratory workers and the public health” (U.S. Department of Health and Human Services, 2007). In February 2007, a consortium of individuals from the Centers for Disease Control and Prevention (CDC) and National Institutes of Health (NIH) released the fifth edition of the BMBL, which contained a number

of revisions and additions from the former, including:

- Added guidance on laboratory biosecurity and risk assessment.
- Added guidance on agricultural Biosafety Level 3 (BSL3-Ag) laboratories.
- Revisions and additions to agent summary statements.
- Expanded guidance on a number of topics, including decontamination, sterilization, occupational medicine, and immunization.

We report here the development of a change matrix identifying content changes to Section IV (Laboratory Biosafety Level Criteria) between the Fourth Edition of BMBL (BMBL4) and BMBL5, focusing specifically on BSL2-4.

Methods

The Laboratory Biosafety Level Criteria sections from BMBL4 and BMBL5 were analyzed and a matrix of changes was developed for BSL2-BSL4. The PDF version of BMBL5, released in November 2007 and available at www.cdc.gov/od/ohs/biosfty/bmb15/BMBL_5th_Edition.pdf, was used for this analysis. Both sections were transferred electronically to a Microsoft Excel spreadsheet and separated by citation. Citations containing multiple statements were further subdivided into individually addressable statements to facilitate a detailed comparative analysis independent of simple structural and format differences not affecting meaning. BMBL4 statements were then reorganized and horizontally aligned with BMBL5 statements having a similar or identical scope. The original BMBL4 citations were preserved for cross-referencing. Each statement, or statement pair, was then systematically categorized based on subject, change type, and outcome, for further analysis.

Based upon observed trends in BMBL topics and laboratory commonalities, the following 17 biosafety-related subjects were determined and then assigned to each statement, or statement pair:

- Access
- Biological Safety Cabinet (BSC) design
- BSC exhaust
- BSC usage
- Decontamination

- Doors/Windows
 - Exposures (lab-related accidents/illnesses)
 - Immunization/Serum Collection
 - Laboratory construction
 - Laboratory furnishings (seating, furniture, carpeting)
 - Laboratory ventilation (filtration, vacuums)
 - Miscellaneous (food, cosmetics, pest control)
 - Personal Protective Equipment (PPE)
 - Sharps (glassware, needles, syringes)
 - Signage
 - Sinks/Eyewashes/Fountains
 - Techniques (pipetting, animal use, storage, transfer)
 - Training/Policies/Standardized Operating Procedures
- Six change types, defined below, were then assigned

to the data:

- No change—the statement scopes are identical; any rewording or reorganization does not affect meaning or potential interpretation.
- Not currently addressed—the BMBL4 statement is not addressed in BMBL5.
- Not previously addressed—the BMBL5 statement was not addressed in BMBL4.
- Rewording—the statement scopes are similar; however, the change affects meaning or potential interpretation.
- Scope expansion—the statement scopes are similar; however, the BMBL5 statement has been further expanded to include additional details.
- Scope generalization—the statement scopes are similar; however, the BMBL5 statement has been further generalized to be more all-encompassing.

Finally, three change outcomes were assigned to the data: those requiring only a change in documentation (such as recommendations for the establishment of written manuals), those requiring a change in practice (such as guidance on infectious waste decontamination procedures), and those requiring a facility change (such as guidance on laboratory ventilation requirements). The change matrix tool uses a basic Microsoft Excel filter function to allow users to sort the data based on the aforementioned categorizations as well as by BSL. We are providing the change matrix tool electronically to interested individuals free of charge upon request. In addition, a brief summary of major changes is presented herein.

Results

An excerpt of the change matrix covering the BSL2 subsection only is shown in Figure 1. For a complete change matrix covering BSL2-4, please contact the author via e-mail at ccrews@constellagroup.com or visit the ABSA web site at www.absa.org/word/BMBLChangeMatrix.xls where the change matrix tool has been posted. This file allows the user to filter and sort the various BMBL statements based on the criteria relevant to a particular laboratory situation. Five hundred twelve total

statement/statement pairs were identified following the subdivision of citations and realignment of BMBL4 statements with similar/identical scope. Of this total, 375 unique changes were identified. Fifty-six percent (211) of these changes were identified as BSL4 statements whereas 26% (97) were identified as BSL3 changes and 18% (67) were identified as BSL2 changes. These results are summarized in Figure 2.

Forty-five percent (166) of the total changes were identified as being unique to BMBL5 (not addressed in the previous edition); 66% of the changes unique to BMBL5 (110) were identified as BSL4 statements; 15% (56) of the total changes were identified as being unique to BMBL4 (not addressed in the current edition); 16% (61) of the total changes were identified as scope generalizations, and 13% (50) were identified as scope expansions. Twelve percent (44) of the total changes were identified as rewordings affecting the statement's meaning. Figure 3 is a summary of the percent of total changes by type.

Figure 4 summarizes the number of changes by subject. The three most frequent subjects for change are decontamination (62, 17%), laboratory ventilation (47, 13%), and personal protective equipment (PPE) (58, 16%). Other notable areas of change include biological safety cabinet (BSC) exhaust (26, 7%), laboratory construction/layout (35, 9%), sharps (25, 7%), and training/standard operating procedures (25, 7%).

Forty-seven percent (177) of the total number of changes between the two BMBL editions are practice changes, whereas 37% (140) are facility changes and 16% (58) are documentation changes. Seventy-one percent (99) of facility changes and 54% (95) of practice changes were identified at BSL4 changes. These data are summarized in Figure 5.

Figure 6 shows a concise summary of the major changes between the fourth and fifth editions of BMBL Section IV. The biosafety levels pertinent to each change, as well as to all applicable BMBL citations are documented. The summary focuses on major practice and facility changes that we have subjectively determined to have a high impact based upon a number of criteria, including: the immediacy of the safety concern, the level of resources required to comply with the change, and the severity of the consequences of non-compliance. The summary is intended to be a quick resource to assist biosafety professionals in concentrating their efforts on specific areas, and is not intended to be definitive or official reference material.

Discussion

Although the BMBL is not intended as a regulatory document, in some circumstances, compliance with the BMBL has been legally mandated. For biosafety professionals tasked with ensuring facility compliance with the BMBL, keeping abreast of changing guidance poses a

Figure 1

A change matrix comparing 4th and 5th editions of *Biosafety in Microbiological and Biomedical Laboratories*, Section IV. This figure only presents BSL2 changes. For a complete change matrix covering BSL2-4, please contact the author via e-mail at ccews@constellagroup.com or visit the ABSA web site at www.absa.org/word/BMBLChangeMatrix.xls where the change matrix tool has been posted.

| Item # | BSL | Subject | BMBL-4 Section | BMBL-4 | BMBL-5 Section | BMBL-5 (PDF version) | Change Type | Outcome |
|----------------------------------------------|------|------------|----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|---------|
| Biosafety Level 2 | | | | | | | | |
| A. Standard Microbiological Practices | | | | | | | | |
| 1 | BSL2 | Access | BMBL4: A1 | Access to the laboratory is limited or restricted at the discretion of the laboratory director when experiments are in progress. | BMBL5: A1 | The laboratory supervisor must enforce the institutional policies that control access to the laboratory. | Rewording | PC |
| 2 | BSL2 | Decon. | BMBL4: A2 | Persons wash their hands after they handle viable materials, after removing gloves, and before leaving the laboratory. | BMBL5: A2 | Persons must wash their hands after working with potentially hazardous materials and before leaving the laboratory. | Rewording | PC |
| 3 | BSL2 | Misc. | BMBL4: A3 | Eating, drinking, smoking, handling contact lenses, and applying cosmetics are not permitted in the work areas. | BMBL5: A3 | Eating, drinking, smoking, handling contact lenses, applying cosmetics, and storing food for human consumption must not be permitted in laboratory areas. | Expansion | DC |
| 4 | BSL2 | Misc. | BMBL4: A3 | Food is stored outside the work area in cabinets or refrigerators designated for this purpose only. | BMBL5: A3 | Food must be stored outside the laboratory area in cabinets or refrigerators designated and used for this purpose. | No Change | NC |
| 5 | BSL2 | Techniques | BMBL4: A4 | Mouth pipetting is prohibited; | BMBL5: A4 | Mouth pipetting is prohibited; | No Change | NC |
| 6 | BSL2 | Techniques | BMBL4: A4 | mechanical pipetting devices are used. | BMBL5: A4 | mechanical pipetting devices must be used. | No Change | NC |
| 7 | BSL2 | Sharps | BMBL4: A5 | Policies for the safe handling of sharps are instituted. | BMBL5: A5 | Policies for the safe handling of sharps, such as needles, scalpels, pipettes, and broken glassw are must be developed and implemented. | Expansion | DC |
| 8 | BSL2 | Sharps | | | BMBL5: A5 | Whenever practical, laboratory supervisors should adopt improved engineering and work practice controls that reduce risk of sharps injuries. | NPA | DC |
| 9 | BSL2 | Sharps | BMBL4: B8 | A high degree of precaution must always be taken with any contaminated sharp items, including needles and syringes, slides, pipettes, capillary tubes, and scalpels. | BMBL5: A5 | Precautions, including those listed below, must always be taken with sharp items. These include: | No Change | NC |
| 10 | BSL2 | Sharps | BMBL4: B8-a | Needles and syringes or other sharp instruments should be restricted in the laboratory for use only when there is no alternative, such as parenteral injection, phlebotomy, or aspiration of fluids from laboratory animals and diaphragm bottles. | | | NCA | DC |
| 11 | BSL2 | Sharps | BMBL4: B8-b | Only needle-locking syringes or disposable syringe-needle units (i.e., needle is integral to the syringe) are used for injection or aspiration of infectious materials. | | | NCA | DC |
| 12 | BSL2 | Sharps | | | BMBL5: A5-a | Careful management of needles and other sharps are of primary importance. | NPA | DC |
| 13 | BSL2 | Sharps | BMBL4: B8-b | Used disposable needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal | BMBL5: A5-a | Needles must not be bent, sheared, broken, recapped, removed from disposable syringes, or otherwise manipulated by hand before disposal. | Generalization | PC |
| 14 | BSL2 | Sharps | BMBL4: B8-b | rather, they must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal. | BMBL5: A5-b | Used disposable needles and syringes must be carefully placed in conveniently located puncture-resistant containers used for sharps disposal. | No Change | NC |
| 15 | BSL2 | Sharps | BMBL4: B8-b | Non-disposable sharps must be placed in a hard-walled container for transport to a processing area for decontamination, preferably by autoclaving. | BMBL5: A5-c | Non-disposable sharps must be placed in a hard-walled container for transport to a processing area for decontamination, preferably by autoclaving. | No Change | NC |
| 16 | BSL2 | Sharps | BMBL4: B8-c | Syringes which re-sheath the needle, needleless systems, and other safety devices are used when appropriate. | | | NCA | DC |
| 17 | BSL2 | Sharps | BMBL4: B8-d | Broken glassw are must not be handled directly by hand, but must be removed by mechanical means such as a brush and dustpan, tongs, or forceps. | BMBL5: A5-d | Broken glassw are must not be handled directly. Instead, it must be removed using a brush and dustpan, tongs, or forceps. | No Change | NC |
| 18 | BSL2 | Sharps | BMBL4: B8-d | Containers of contaminated needles, sharp equipment, and broken glass are decontaminated before disposal, according to any local, state, or federal regulations | | | NCA | DC |
| 19 | BSL2 | Sharps | BMBL4: B8-a | Plasticw are should be substituted for glassw are whenever possible. | BMBL5: A5-d | Plasticw are should be substituted for glassw are whenever possible. | No Change | NC |
| 20 | BSL2 | Techniques | BMBL4: A6 | All procedures are performed carefully to minimize the creation of splashes or aerosols. | BMBL5: A6 | Perform all procedures to minimize the creation of splashes and/or aerosols. | No Change | NC |
| 21 | BSL2 | Decon. | BMBL4: A7 | Work surfaces are decontaminated on completion of work or at the end of the day and after any spill or splash of viable material with disinfectants that are effective against the agents of concern. | BMBL5: A7 | Decontaminate work surfaces after completion of work and after any spill or splash of potentially infectious material with appropriate disinfectant. | No Change | NC |
| 22 | BSL2 | Decon. | BMBL4: A8 | All cultures, stocks, and other regulated wastes are decontaminated before disposal by an approved decontamination method such as autoclaving. | BMBL5: A8 | Decontaminate all cultures, stocks, and other potentially infectious materials before disposal using an effective method. | Rewording | PC |
| 23 | BSL2 | Decon. | | | BMBL5: A8 | Depending on where the decontamination will be performed, the following methods should be used prior to transport: | No Change | NC |
| 24 | BSL2 | Decon. | BMBL4: A8 | Materials to be decontaminated outside of the immediate laboratory are placed in a durable, leakproof container and closed for transport from the laboratory. | BMBL5: A8-a | Materials to be decontaminated outside of the immediate laboratory must be placed in a durable, leak proof container and secured for transport. | No Change | NC |
| 25 | BSL2 | Decon. | BMBL4: A8 | Materials to be decontaminated off-site from the facility are packaged in accordance with applicable local, state, and federal regulations before removal from the facility. | BMBL5: A8-b | Materials to be removed from the facility for decontamination must be packed in accordance with applicable local, state, and federal regulations. | No Change | NC |

NPA = Not Previously Addressed; NCA = Not Currently Addressed; DC = Documentation Change; FC = Facility Change; PC = Policy/Procedural Change; NC = No Change

Figure 1 (Con't.)

| Item # | BSL | Subject | BMBL-4 Section | BMBL-4 | BMBL-5 Section | BMBL-5 (PDF version) | Change Type | Outcome |
|-----------------------------|------|--------------------------------|----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|---------|
| 26 | BSL2 | Signage | BMBL4: B3 | A biohazard sign must be posted on the entrance to the laboratory when etiologic agents are in use. | BMBL5: A9 | A sign incorporating the universal biohazard symbol must be posted at the entrance to the laboratory when infectious agents are present. | Rewording | FC |
| 27 | BSL2 | Signage | BMBL4: B3 | Appropriate information to be posted includes the agent(s) in use, the biosafety level, the required immunizations, the investigator's name and telephone number, any personal protective equipment that must be worn in the laboratory, and any procedures required for exiting the laboratory. | BMBL5: A9 | Posted information must include: the laboratory's biosafety level, the supervisor's name (or other responsible personnel), telephone number, and required procedures for entering and exiting the laboratory. | Generalization | DC |
| 28 | BSL2 | Signage | BMBL4: B3 | Appropriate information to be posted includes the agent(s) in use | BMBL5: A9 | Agent information should be posted in accordance with the institutional policy. | Rewording | FC |
| 29 | BSL2 | Misc. | BMBL4: A9 | An insect and rodent control program is in effect. | BMBL5: A10 | An effective integrated pest management program is required. See Appendix G. | Expansion | PC |
| 30 | BSL2 | Training/SOPs | BMBL4: B7 | The laboratory director ensures that laboratory and support personnel receive appropriate training on the potential hazards associated with the work involved, the necessary precautions to prevent exposures, and the exposure evaluation procedures. | BMBL5: A11 | The laboratory supervisor must ensure that laboratory personnel receive appropriate training regarding their duties, the necessary precautions to prevent exposures, and exposure evaluation procedures. | Rewording | PC |
| 31 | BSL2 | Training/SOPs | BMBL4: B7 | Personnel receive annual updates or additional training as necessary for procedural or policy changes. | BMBL5: A11 | Personnel must receive annual updates or additional training when procedural or policy changes occur. | No Change | NC |
| 32 | BSL2 | Training/SOPs | | | BMBL5: A11 | Personal health status may impact an individual's susceptibility to infection, ability to receive immunizations or prophylactic interventions. Therefore, all laboratory personnel and particularly women of child-bearing age should be provided with information regarding immune competence and conditions that may predispose them to infection. | NPA | PC |
| 33 | BSL2 | Training/SOPs | | | BMBL5: A11 | Individuals having these conditions should be encouraged to self-identify to the institution's healthcare provider for appropriate counseling and guidance. | NPA | PC |
| B. Special Practices | | | | | | | | |
| 34 | BSL2 | Access | BMBL4: B1 | Access to the laboratory is limited or restricted by the laboratory director when work with infectious agents is in progress. In general, persons who are at increased risk of acquiring infection, or for whom infection may have serious consequences, are not allowed in the laboratory or animal rooms. For example, persons who are immunocompromised or immunosuppressed may be at increased risk of acquiring infections. The laboratory director has the final responsibility for assessing each circumstance and determining who may enter or work in the laboratory or animal room. | | | NCA | PC |
| 35 | BSL2 | Access | BMBL4: B2 | The laboratory director establishes policies and procedures whereby only persons who have been advised of the potential hazards and meet specific entry requirements (e.g., immunization) may enter the laboratory. | BMBL5: B1 | All persons entering the laboratory must be advised of the potential hazards and meet specific entry/exit requirements. | Generalization | PC |
| 36 | BSL2 | Immunization/ Serum Collection | BMBL4: B4 | Laboratory personnel receive appropriate immunizations or tests for the agents handled or potentially present in the laboratory (e.g., hepatitis B vaccine or TB skin testing). | BMBL5: B2 | Laboratory personnel must be provided medical surveillance and offered appropriate immunizations for agents handled or potentially present in the laboratory. | Expansion | PC |
| 37 | BSL2 | Immunization/ Serum Collection | BMBL4: B5 | When appropriate, considering the agent(s) handled, baseline serum samples for laboratory and other at-risk personnel are collected and stored. Additional serum specimens may be collected periodically, depending on the agents handled or the function of the facility. | BMBL5: B3 | Each institution must establish policies and procedures describing the collection and storage of serum samples from at-risk personnel. | Generalization | DC |
| 38 | BSL2 | Training/SOPs | BMBL4: B6 | Biosafety procedures are incorporated into standard operating procedures or in a biosafety manual adopted or prepared specifically for the laboratory by the laboratory director. | BMBL5: B4 | A laboratory-specific biosafety manual must be prepared and adopted as policy. | Generalization | DC |
| 39 | BSL2 | Training/SOPs | BMBL4: B6 | Personnel are advised of special hazards and are required to read and follow instructions on practices and procedures. | | | NCA | DC |
| 40 | BSL2 | Training/SOPs | | | BMBL5: B4 | The biosafety manual must be available and accessible. | NPA | PC |
| 41 | BSL2 | Training/SOPs | | | BMBL5: B5 | The laboratory supervisor must ensure that laboratory personnel demonstrate proficiency in standard and special microbiological practices before working with BSL-2 agents. | NPA | PC |
| 42 | BSL2 | Techniques | BMBL4: B9 | Cultures, tissues, specimens of body fluids, or potentially infectious wastes are placed in a container with a cover that prevents leakage during collection, handling, processing, storage, transport, or shipping. | BMBL5: B6 | Potentially infectious materials must be placed in a durable, leak proof container during collection, handling, processing, storage, or transport within a facility. | Generalization | PC |
| 43 | BSL2 | Decon. | BMBL4: B10 | Laboratory equipment and work surfaces should be decontaminated with an effective disinfectant on a routine basis, after work with infectious materials is finished, and especially after overt spills, splashes, or other contamination by infectious materials. | BMBL5: B7 | Laboratory equipment should be routinely decontaminated, as well as, after spills, splashes, or other potential contamination. | Generalization | PC |

NPA = Not Previously Addressed; NCA = Not Currently Addressed; DC = Documentation Change; FC = Facility Change; PC = Policy/Procedural Change; NC = No Change

Figure 1 (Con't.)

| Item # | BSL | Subject | BMBL-4 Section | BMBL-4 | BMBL-5 Section | BMBL-5 (PDF version) | Change Type | Outcome |
|---------------------------------------------------------------------------------|------|------------|----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|---------|
| 44 | BSL2 | Decon. | | | BMBL5: B7-a | Spills involving infectious materials must be contained, decontaminated, and cleaned up by staff properly trained and equipped to work with infectious material. | NPA | PC |
| 45 | BSL2 | Decon. | BMBL4: B10 | Contaminated equipment must be decontaminated according to any local, state, or federal regulations before it is sent for repair or maintenance or packaged for transport in accordance with applicable local, state, or federal regulations, before removal from the facility. | BMBL5: B7-b | Equipment must be decontaminated before repair, maintenance, or removal from the laboratory. | Generalization | PC |
| 46 | BSL2 | Exposures | | | BMBL5: B8 | Incidents that may result in exposure to infectious materials must be immediately evaluated and treated according to procedures described in the laboratory biosafety safety manual. | NPA | PC |
| 47 | BSL2 | Exposures | BMBL4: B11 | Spills and accidents that result in overt exposures to infectious materials are immediately reported to the laboratory director. | BMBL5: B8 | All such incidents must be reported to the laboratory supervisor. | No Change | NC |
| 48 | BSL2 | Exposures | BMBL4: B11 | Medical evaluation, surveillance, and treatment are provided as appropriate and written records are maintained. | BMBL5: B8 | Medical evaluation, surveillance, and treatment should be provided and appropriate records maintained. | No Change | NC |
| 49 | BSL2 | Techniques | BMBL4: B12 | Animals not involved in the work being performed are not permitted in the laboratory. | BMBL5: B9 | Animals and plants not associated with the work being performed must not be permitted in the laboratory. | No Change | NC |
| 50 | BSL2 | Techniques | | | BMBL5: B10 | All procedures involving the manipulation of infectious materials that may generate an aerosol should be conducted within a BSC or other physical containment devices. | NPA | PC |
| C. Safety Equipment (Primary Barriers and Personal Protective Equipment) | | | | | | | | |
| 51 | BSL2 | BSC usage | BMBL4: C1 | Properly maintained biological safety cabinets, preferably Class II, or other appropriate personal protective equipment or physical containment devices are used whenever: | BMBL5: C1 | Properly maintained BSCs (preferably Class II), other appropriate personal protective equipment, or other physical containment devices must be used whenever: | No Change | NC |
| 52 | BSL2 | BSC usage | BMBL4: C1-a | Procedures with a potential for creating infectious aerosols or splashes are conducted. These may include centrifuging, grinding, blending, vigorous shaking or mixing, sonic disruption, opening containers of infectious materials whose internal pressures may be different from ambient pressures, inoculating animals intranasally, and harvesting infected tissues from animals or embryonate eggs. | BMBL5: C1-a | Procedures with a potential for creating infectious aerosols or splashes are conducted. These may include pipetting, centrifuging, grinding, blending, shaking, mixing, sonicating, opening containers of infectious materials, inoculating animals intranasally, and harvesting infected tissues from animals or embryonate eggs. | Expansion | PC |
| 53 | BSL2 | BSC usage | BMBL4: C1-b | High concentrations or large volumes of infectious agents are used. Such materials may be centrifuged in the open laboratory if sealed rotor heads or centrifuge safety cups are used, and if these rotors or safety cups are opened only in a biological safety cabinet. | BMBL5: C1-b | High concentrations or large volumes of infectious agents are used. Such materials may be centrifuged in the open laboratory using sealed rotor heads or centrifuge safety cups. | Generalization | PC |
| 54 | BSL2 | PPE | BMBL4: C3 | Protective laboratory coats, gowns, smocks, or uniforms designated for lab use are worn while in the laboratory. | BMBL5: C2 | Protective laboratory coats, gowns, smocks, or uniforms designated for laboratory use must be worn while working with hazardous materials. | Expansion | PC |
| 55 | BSL2 | PPE | BMBL4: C3 | This protective clothing is removed and left in the laboratory before leaving for non-laboratory areas (e.g., cafeteria, library, administrative offices). | BMBL5: C2 | Remove protective clothing before leaving for non-laboratory areas (e.g., cafeteria, library, administrative offices). | No Change | NC |
| 56 | BSL2 | PPE | BMBL4: C3 | All protective clothing is either disposed of in the laboratory or laundered by the institution; it should never be taken home by personnel. | BMBL5: C2 | Dispose of protective clothing appropriately, or deposit it for laundering by the institution. | No Change | NC |
| 57 | BSL2 | PPE | BMBL4: C3 | | BMBL5: C2 | It is recommended that laboratory clothing not be taken home. | Rewording | PC |
| 58 | BSL2 | PPE | BMBL4: C2 | Face protection (goggles, mask, face shield or other splatter guard) is used for anticipated splashes or sprays of infectious or other hazardous materials to the face when the microorganisms must be manipulated outside the BSC. | BMBL5: C3 | Eye and face protection (goggles, mask, face shield or other splatter guard) is used for anticipated splashes or sprays of infectious or other hazardous materials when the microorganisms must be handled outside the BSC or containment device. | Expansion | PC |
| 59 | BSL2 | PPE | | | BMBL5: C3 | Eye and face protection must be disposed of with other contaminated laboratory waste or decontaminated before reuse. | NPA | PC |
| 60 | BSL2 | Misc. | BMBL4: A3 | Persons who wear contact lenses in laboratories should also wear goggles or a face shield. | BMBL5: C3 | Persons who wear contact lenses in laboratories should also wear eye protection. | Generalization | PC |
| 61 | BSL2 | PPE | BMBL4: C4 | Gloves are worn when hands may contact potentially infectious materials, contaminated surfaces or equipment. | BMBL5: C4 | Gloves must be worn to protect hands from exposure to hazardous materials. | Generalization | PC |
| 62 | BSL2 | PPE | | | BMBL5: C4 | Glove selection should be based on an appropriate risk assessment. | NPA | PC |
| 63 | BSL2 | PPE | BMBL4: C4 | Alternatives to powdered latex gloves should be available. | BMBL5: C4 | Alternatives to latex gloves should be available. | Generalization | FC |
| 64 | BSL2 | PPE | BMBL4: C4 | and they should not be worn outside the lab. | BMBL5: C4 | Gloves must not be worn outside the laboratory. | No Change | NC |
| 65 | BSL2 | PPE | | | BMBL5: C4 | In addition, BSL-2 laboratory workers should: | Generalization | PC |
| 66 | BSL2 | PPE | BMBL4: C4 | Gloves are disposed of when overtly contaminated, and removed when work with infectious materials is completed or when the integrity of the glove is compromised. | BMBL5: C4-a | Change gloves when contaminated, integrity has been compromised, or when otherwise necessary. | Generalization | PC |
| 67 | BSL2 | PPE | BMBL4: C4 | Wearing two pairs of gloves may be appropriate. | BMBL5: C4-a | Wear two pairs of gloves when appropriate. | No Change | NC |

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Figure 1 (Con't.)

| Item # | BSL | Subject | BMBL-4 Section | BMBL-4 | BMBL-5 Section | BMBL-5 (PDF version) | Change Type | Outcome |
|------------------------------------------------------|------|------------------|----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|---------|
| 68 | BSL2 | PPE | BMBL4: C4 | Hands are washed following removal of gloves. | BMBL5: C4-b | Remove gloves and wash hands when work with hazardous materials has been completed and before leaving the laboratory. | Expansion | PC |
| 69 | BSL2 | PPE | BMBL4: C4 | Disposable gloves are not washed, reused, or used for touching "clean" surfaces (keyboards, telephones, etc.). | BMBL5: C4-c | Do not wash or reuse disposable gloves. | Rewording | PC |
| 70 | BSL2 | PPE | | | BMBL5: C4-c | Dispose of used gloves with other contaminated laboratory waste. | NPA | PC |
| 71 | BSL2 | PPE | BMBL4: C4 | Hands are washed following removal of gloves. | BMBL5: C4-c | Hand washing protocols must be rigorously followed. | Generalization | PC |
| 72 | BSL2 | PPE | | | BMBL5: C5 | Eye, face and respiratory protection should be used in rooms containing infected animals as determined by the risk assessment. | NPA | PC |
| D. Laboratory Facilities (Secondary Barriers) | | | | | | | | |
| 73 | BSL2 | Doors/Windows | BMBL4: D1 | Provide lockable doors for facilities that house restricted agents. | BMBL5: D1 | Laboratory doors should be self-closing and have locks in accordance with the institutional policies. | Expansion | FC |
| 74 | BSL2 | Lab Construction | BMBL4: D2 | Consider locating new laboratories away from public areas. | | | NCA | DC |
| 75 | BSL2 | Sinks/Eyewash | BMBL4: D3 | Each laboratory contains a sink for hand washing. | BMBL5: D2 | Laboratories must have a sink for hand washing. | No Change | NC |
| 76 | BSL2 | Sinks/Eyewash | | | BMBL5: D2 | The sink may be manually, hands-free, or automatically operated. | NPA | FC |
| 77 | BSL2 | Sinks/Eyewash | | | BMBL5: D2 | It should be located near the exit door. | NPA | FC |
| 78 | BSL2 | Lab Construction | BMBL4: D4 | The laboratory is designed so that it can be easily cleaned. | BMBL5: D3 | The laboratory should be designed so that it can be easily cleaned and decontaminated. | Expansion | PC |
| 79 | BSL2 | Lab Furnishings | BMBL4: D4 | Carpets and rugs in laboratories are inappropriate. | BMBL5: D3 | Carpets and rugs in laboratories are not permitted. | Rewording | FC |
| 80 | BSL2 | Lab Furnishings | BMBL4: D6 | Laboratory furniture is capable of supporting anticipated loading and uses. | BMBL5: D4 | Laboratory furniture must be capable of supporting anticipated loads and uses. | No Change | NC |
| 81 | BSL2 | Lab Construction | BMBL4: D6 | Spaces between benches, cabinets, and equipment are accessible for cleaning. | BMBL5: D4 | Spaces between benches, cabinets, and equipment should be accessible for cleaning. | No Change | NC |
| 82 | BSL2 | Lab Construction | BMBL4: D6 | Bench tops are impervious to water and are resistant to moderate heat and the organic solvents, acids, alkalis, and chemicals used to decontaminate the work surfaces and equipment. | BMBL5: D4-a | Bench tops must be impervious to water and resistant to heat, organic solvents, acids, alkalis, and other chemicals. | No Change | NC |
| 83 | BSL2 | Lab Furnishings | BMBL4: D6 | Chairs and other furniture used in laboratory work should be covered with a non-fabric material that can be easily decontaminated. | BMBL5: D4-b | Chairs used in laboratory work must be covered with a non-porous material that can be easily cleaned and decontaminated with appropriate disinfectant. | Rewording | FC |
| 84 | BSL2 | Doors/Windows | | | BMBL5: D5 | Laboratory windows that open to the exterior are not recommended. | NPA | FC |
| 85 | BSL2 | Doors/Windows | BMBL4: D10 | If the laboratory has windows that open to the exterior, they are fitted with fly screens. | BMBL5: D5 | How ever, if a laboratory does have windows that open to the exterior, they must be fitted with screens. | No Change | NC |
| 86 | BSL2 | BSC Exhaust | BMBL4: D7 | Install biological safety cabinets in such a manner that fluctuations of the room supply and exhaust air do not cause the biological safety cabinets to operate outside their parameters for containment. | BMBL5: D6 | BSCs must be installed so that fluctuations of the room air supply and exhaust do not interfere with proper operations. | No Change | NC |
| 87 | BSL2 | BSC Exhaust | BMBL4: D7 | Locate biological safety cabinets away from doors, from windows that can be opened, from heavily traveled laboratory areas, and from other potentially disruptive equipment so as to maintain the biological safety cabinets' air flow parameters for containment. | BMBL5: D6 | BSCs should be located away from doors, windows that can be opened, heavily traveled laboratory areas, and other possible airflow disruptions. | Generalization | FC |
| 88 | BSL2 | Lab Ventilation | | | BMBL5: D7 | Vacuum lines should be protected with High Efficiency Particulate Air (HEPA) filters, or their equivalent. | NPA | FC |
| 89 | BSL2 | Lab Ventilation | | | BMBL5: D7 | Filters must be replaced as needed. | NPA | PC |
| 90 | BSL2 | Lab Ventilation | | | BMBL5: D7 | Liquid disinfectant traps may be required. | NPA | FC |
| 91 | BSL2 | Sinks/Eyewash | BMBL4: D8 | An eyewash station is readily available. | BMBL5: D8 | An eyewash station must be readily available. | No Change | NC |
| 92 | BSL2 | Lab Construction | BMBL4: D9 | Illumination is adequate for all activities, avoiding reflections and glare that could impede vision. | | | NCA | DC |
| 93 | BSL2 | Lab Ventilation | BMBL4: D10 | There are no specific ventilation requirements. How ever, planning of new facilities should consider mechanical ventilation systems that provide an inward flow of air without recirculation to spaces outside of the laboratory. | BMBL5: D9 | There are no specific requirements on ventilation systems. How ever, planning of new facilities should consider mechanical ventilation systems that provide an inward flow of air without recirculation to spaces outside of the laboratory. | No Change | NC |
| 94 | BSL2 | BSC Exhaust | | | BMBL5: D10 | HEPA filtered exhaust air from a Class II BSC can be safely re-circulated back into the laboratory environment if the cabinet is tested and certified at least annually and operated according to manufacturer's recommendations. | NPA | FC |
| 95 | BSL2 | BSC Exhaust | | | BMBL5: D10 | BSCs can also be connected to the laboratory exhaust system by either a thimble (canopy) connection or a direct (hard) connection. | NPA | FC |
| 96 | BSL2 | BSC Exhaust | | | BMBL5: D10 | Provisions to assure proper safety cabinet performance and air system operation must be verified. | NPA | PC |
| 97 | BSL2 | Decon. | | | BMBL5: D11 | A method for decontaminating all laboratory wastes should be available in the facility (e.g., autoclave, chemical disinfection, incineration, or other validated decontamination method). | NPA | DC |

NPA = Not Previously Addressed; NCA = Not Currently Addressed; DC = Documentation Change; FC = Facility Change; PC = Policy/Procedural Change; NC = No Change

Figure 2

A graphical representation of the percent of total BMBL Section IV changes by Biosafety Level.

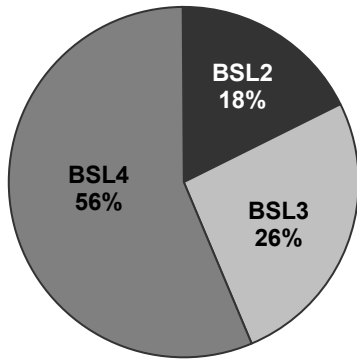


Figure 3

A graphical representation of the percent of total BMBL Section IV changes by type (n = 375).

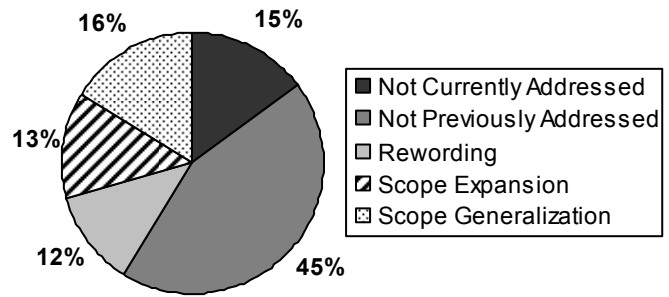


Figure 4

A comparison of the number of BMBL Section IV changes by subject. White bars indicate the three most common subjects for change.

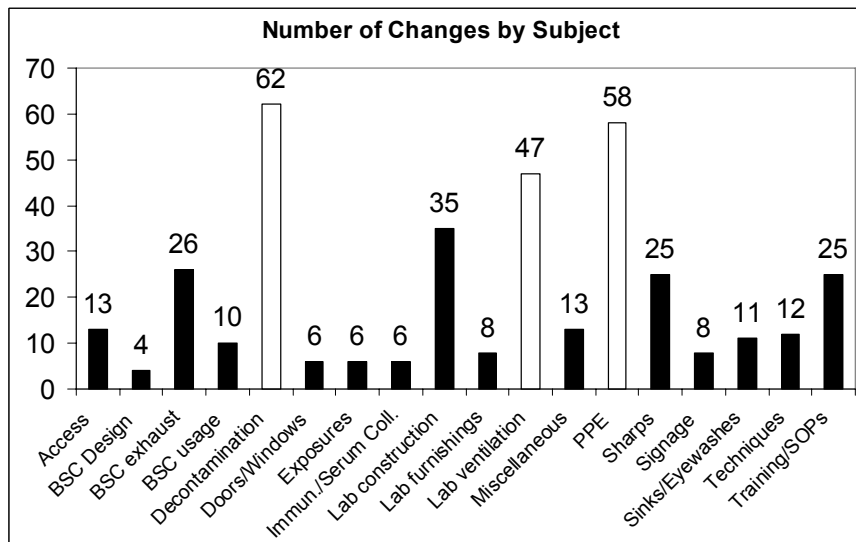


Figure 5

A graphical representation of the number of document, practice, and facility changes between the 4th and 5th editions of BMBL by biosafety level.

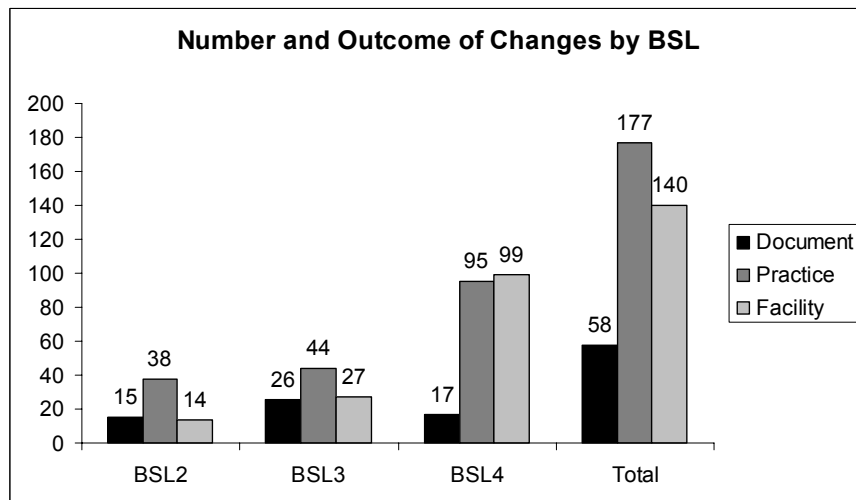


Figure 6

A summary of major changes between the 4th and 5th editions of BMBL Section IV, BSL2-BSL4.

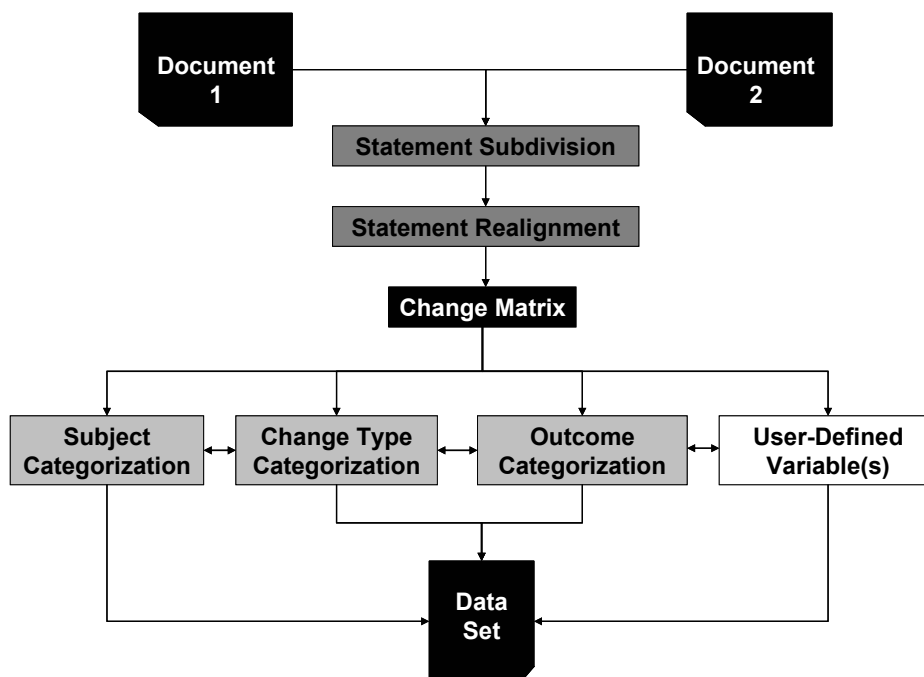
| Biosafety Level | Major Changes | Applicable BMBL Citations |
|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| BSL2, BSL3, BSL4 | The restriction of access to personnel who are at risk of acquiring infection is not addressed in BMBL5. BMBL5 states that all lab personnel should be provided with information regarding “immune competence and conditions that may predispose them to infection.” Lab personnel are also encouraged to self-identify. | BMBL4: BSL2 B1; BSL3 B2; BSL4 B1. BMBL5: BSL2 A11; BSL3 A11; BSL4 A11. |
| BSL2, BSL3 | “Laboratory personnel must be provided with medical surveillance.” | BMBL5: BSL2 B2; BSL3 B3. |
| BSL2, BSL3, BSL4 | “Incidents that may result in exposure to infectious materials must be immediately evaluated and treated according to procedures described in the laboratory biosafety safety manual.” | BMBL5: BSL2 B8; BSL3 B8; BSL4 B8. |
| BSL2 | “All procedures involving the manipulation of infectious materials that may generate an aerosol should be conducted within a BSC or other physical containment devices.” | BMBL5: BSL2 B10 |
| BSL2, BSL3, BSL4 | Enhanced guidance on eye and face protection use, decontamination and disposal (See Citations). | BMBL5: BSL2 C3; BSL3 C3; BSL4 C(A)3 |
| BSL2, BSL3, BSL4 | Enhanced guidance on glove selection, use, and disposal (See Citations). | BMBL5: BSL2 C4; BSL3 C4; BSL4 C(A)4, C(B)3, C(B)4 |
| BSL2 | “Vacuum lines should be protected with High Efficiency Particulate Air (HEPA) filters, or their equivalent. Filters must be replaced as needed. Liquid disinfectant traps may be required.” | BMBL5: BSL2 D7 |
| BSL2, BSL3, BSL4 | Enhanced guidance on Class II BSC exhaust (See Citations). | BMBL5: BSL2 D10; BSL3 D10; BMBL4: C(B)1, D(A)10, D(B)10. |
| BSL3 | “Laboratory doors must be self closing and have locks in accordance with the institutional policies.” | BMBL5: BSL3 D1 |
| BSL3 | “If the laboratory is segregated into different laboratories, a sink must also be available for hand washing in each zone.” | BMBL5: BSL3 D2 |
| BSL3 | Enhanced guidance on HEPA filtration of laboratory exhaust air (See Citation). | BMBL5: BSL3 D14 |
| BSL4 | “Mechanical pipetting devices must be used.” | BMBL5: BSL4 A4 |
| BSL4 | “The interior of the Class III cabinet as well as all contaminated plenums, fans and filters must be decontaminated using a validated gaseous or vapor method.” | BMBL5: BSL4 B7-b |
| BSL4 | Enhanced guidance on autoclave design and operation (See Citation). | BMBL5: BSL4 B10 |
| BSL4 (cabinet lab) | Enhanced guidance on Class III BSC design, exhaust, and usage in the cabinet laboratory (See Citation). | BMBL5: BSL4 C(A)1. |
| BSL4 (cabinet lab) | Enhanced guidance on personal and protective clothing usage and decontamination in the cabinet laboratory (See Citation). | BMBL5: BSL4 C(A)2. |
| BSL4 (cabinet lab); BSL4 (suit lab) | “An automatically activated emergency power source must be provided at a minimum for the laboratory exhaust system, life support systems, alarms, lighting, entry and exit controls, BSCs, and door gaskets. Monitoring and control systems for air supply, exhaust, life support, alarms, entry and exit, and security systems should be on an uninterrupted power supply (UPS).” | BMBL5: BSL4 D(A)1, D(B)1. |
| BSL4 (cabinet lab) | “All sinks in the room(s) containing the Class III BSC and the inner (dirty) change room must be connected to the wastewater decontamination system.” | BMBL5: BSL4 D(A)2 |
| BSL4 (cabinet lab); BSL4 (suit lab) | Enhanced guidance on liquid and gas services (See Citations). | BMBL5: BSL4 D(A)3, D(B)3. |

Figure 6 (Con't.)

| Biosafety Level | Major Changes | Applicable BMBL Citations |
|-------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| BSL4 (cabinet lab) | “Redundant supply fans are recommended. Redundant exhaust fans are required.” | BMBL5: BSL4 D(A)9 |
| BSL4 (cabinet lab) | “The design of the HEPA filter housing must have gas-tight isolation dampers; decontamination ports; and ability to scan each filter assembly for leaks.” | BMBL5: BSL4 D(A)9 |
| BSL4 (cabinet lab) | “Class III BSCs must be directly and independently exhausted through two HEPA filters in series.” | BMBL5: BSL4 D(A)9 |
| BSL4 (cabinet lab); BSL4 (suit lab) | “Access to the exit side of the pass-through shall be limited to those individuals authorized to be in the BSL-4 laboratory.” | BMBL5: BSL4 D(A)11, D(B)11. |
| BSL4 (cabinet lab); BSL4 (suit lab) | “Gas and liquid discharge from the autoclave chamber must be decontaminated. When feasible, autoclave decontamination processes should be designed so that over-pressurization cannot release unfiltered air or steam exposed to infectious material to the environment.” | BMBL5: BSL4 D(A)13; D(B)13 |
| BSL4 (cabinet lab); BSL4 (suit lab) | “Provisions for emergency communication and access/egress must be considered.” | BMBL5: BSL4 D(A)15, D(B)15. |
| BSL4 (suit lab) | “In the event of an emergency exit or failure of chemical shower system a method for decontaminating positive pressure suits, such as a gravity fed supply of chemical disinfectant, is needed.” | BMBL5: BSL4 D(B)1 |
| BSL4 (suit lab) | “Only laboratories with the same HVAC requirements (i.e., other BSL-4 labs, ABSL-4, BSL-3 Ag labs) may share ventilation systems if each individual laboratory system is isolated by gas tight dampers and HEPA filters.” | BMBL5: BSL4 D(A)9, D(B)9. |
| BSL4 (suit lab) | “Autoclaves that open outside of the laboratory must be sealed to the primary wall.” | BMBL5: BSL4 D(B)13 |

Figure 7

A flow chart representing the utility of the BMBL change matrix methodology for future BMBL and other regulatory and/or guidance document updates.



unique challenge since the revision summaries of rapidly and dramatically changing guidance documents are often scant or non-existent. The change matrix we have developed is intended to be a resource for biological safety officers, investigators, and others with a vested interest in biosafety to assist in the identification of the issues most pertinent to their facility or institution. Individual statements or statement pairs have been presorted based on a number of criteria therefore allowing the individual user the freedom to filter the data based on their specific needs. For instance, an individual primarily interested in facility changes affecting laboratory exhaust requirements may sort through the changes based on those specific criteria.

The change matrix we have created presents a systematic and streamlined methodology for identifying changes in the Laboratory Biosafety Level Criteria sections between the fourth and fifth editions of BMBL. An overview of this process is represented graphically in Figure 7. We believe this methodology can also be applied to future revisions as well as to other elaborate guidance documents where a precise awareness of changing guidance is crucial to safety and regulatory compliance. In addition, the organization of the matrix makes it possible for the

individual user to add additional criteria (e.g., level of resource investment) and search for them against existing criteria.

Authors' Note

The information contained herein does not necessarily represent the position of the federal government.

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