

Ask the Experts

John H. Keene

Biohaztec Associates, Midlothian, Virginia

Do you have a biosafety question and you're not sure who to ask? Send your questions to the "Ask the Experts" column and I'll get them answered for you. Drawing from my own experience or that of other experts in the field, we'll try to compile a thorough and comprehensive answer to your question. Please e-mail your questions to jkeene@biohaztec.com or Co-Editor Barbara Johnson at barbara_johnson@verizon.net or Co-Editor Karen B. Byers at karen_byers@dfci.harvard.edu.

Shortcuts Not an Option When it Comes to Risk Assessment and Biosafety Manuals

Why is the performance of a risk assessment so important?

It is apparent that we have concentrated our risk assessments based on the pathogenicity of organisms for man, and in some cases animals, but is this the real basis of risk assessment? It is true that the original reasoning for the biosafety levels, as defined in the Centers for Disease Control and Prevention/National Institutes of Health (CDC/NIH) *Biosafety in Microbiological and Biomedical Laboratories* (BMBL) was to minimize the potential for the risk of occupationally acquired infections in laboratory workers. Unfortunately, biosafety professionals and Principal Investigators have tended to look at the risk assessment process in light of the BMBL only, and have not examined the overall picture of potential risk to laboratory workers and the environment (the community, including plant and animal exposure). This shortsighted view of risk assessment could result in serious liability for an institution, especially since the recommended guidelines in the BMBL are minimal guidelines for the protection of workers against possible exposure.

The primary objective of physical containment should be to confine organisms in order to reduce the potential for exposure of laboratory workers, persons outside the laboratory, and the environment to organisms which have been determined to be hazardous to one or more of these entities. Any risk assessment should be based on a realistic evaluation of the potential for the agent in question to cause any problems should it be released in any way or form from the laboratory.

Different conditions require different procedures and containment requirements. For example, an experiment to study the pathogenicity of a fungus that causes infection in wheat might have an entirely different risk assessment if performed in the middle of Manhattan, New York, as opposed to the same research being per-

formed in Manhattan, Kansas. It is critical to perform a realistic assessment of the potential damage caused should the organism escape from the laboratory. This seems at times, to be a difficult concept to understand for a researcher who does not view the agent as pathogenic, but rather, as a tool to study a specific metabolic pathway, or to produce a protein, particularly when that researcher has "always used this organism and never had a problem."

Sometimes the experiment must be modified for reasons other than the potential for release of infectious agents. I recall a particular instance when a researcher came to me with a new recombinant *Bacillus* species that carried the gene for making the external coat protein of a particularly dangerous viral pathogen. He wanted to put this organism into a fermenter and produce large quantities of the viral antigen. The risk assessment began with the question: "Does the recombinant *Bacillus* form spores?" His answer was "No, well at least not many." The next question posed was, "Then it does form spores to some extent?" To which he answered, "Well, yes." The answer to the following question was problematic: "What antibiotic was used to select for this particular organism?" "Oh, that's easy; it is resistant to antimegasus (fictional antibiotic to protect the innocent)." This particular answer also completed the risk assessment and the final determination was that you can't put this organism into the fermenter in this fermentation plant.

Now, there was actually no danger of infection from this organism, either as the *Bacillus* itself, or from the protein that it produced, but there was a concern on the part of the fermentation plant operator. It so happened that "antimegasus" was the main product for this particular facility, and the antibiotic was the major antibiotic used when people were allergic to a similar antibiotic produced in other facilities. From a corporate standpoint, it was not feasible to take the risk to put a spore-forming bacillus, resistant to "antimegasus" and carrying the gene for production of a pathogenic virus coat protein, in this particular fermentation plant. The risk of release of the spore-former with its viral coat protein, along with its concomitant contamination of the company's "cash cow," was not acceptable. Therefore, the experiment was not allowed to continue and the researcher went back to the drawing board to develop a similar organism that was not resistant to the antibiotic in question.

Physical containment begins with the realistic review of the potential danger, and is achieved through the use of specifically designed laboratory practices, containment equipment, and special laboratory design. There are no shortcuts and each risk assessment is unique to the facil-

ity in which the work is to be performed. No matter how much you may want to do it, you cannot use someone else's risk assessment.

Does anyone out there have a biosafety manual I can use/copy/plagiarize?

Simply copy the BMBL word-for-word and your work is done. Wrong! The BMBL publication is by definition "guidelines" and minimal guidelines at that. Each facility and each laboratory within the facility is a unique entity, and the biosafety manual that serves the facility, or laboratory must be equally unique. This concept fits with the concept of risk assessment discussed above. It is important for the biosafety manual to reflect the needs of the risk assessment. The BMBL is the skeleton upon which you and the PI place the meat of the specific safety requirements for the laboratory. Those requirements are based on the potential for release of an organism, or its product to the environment, and the hazard to workers associated with performing the specific protocols in the specific laboratory.

Do you want to build a good biosafety manual? If so, start with the BMBL; then take each section and determine how you are going to specifically meet those require-

ments within your laboratory while performing your particular protocol. For example, the BMBL states that access to the laboratory must be controlled while experiments are being performed. Your manual should indicate that access to the laboratory is controlled by placing appropriate signage at the door to the laboratory prior to initiating work with the agents, and must be enforced by laboratory personnel working in the laboratory. Note that the BMBL states what should be done; the safety manual states how you will do it in your laboratory.

The days of starting an experiment that was just dreamed up without significant planning on the part of the PI and the lab staff are long over. If we are going to have to develop a protocol for conducting an experiment, then we should take the time to complete the risk assessment and to develop appropriate safety protocols to match. Safe operation is not only good for lab workers; it improves the science and the experiment.

Remember, the biosafety manual is not a static document that is developed, put on the shelf, and never looked at again. It is a dynamic document that must change as the experiments progress and protocols change. It is work, but it is work well worth doing.

Biosafety Tips

Karen B. Byers

Dana-Farber Cancer Institute, Boston, Massachusetts

Biosafety Tips brings you practical approaches to biosafety or "news you can use." If you are looking for a useful and sensible solution to a biocontainment problem, or perhaps a reference to help convince a skeptical researcher of the need for caution, this is the place to look. In this column, I share biosafety insights for managing a variety of workplace situations. I welcome feedback and suggestions for future topics. Please e-mail any comments or suggestions to karen_byers@dfci.harvard.edu or to Co-Editor Barbara Johnson at barbara_johnson@verizon.net.

Brucella Outbreak in Clinical Microbiology Laboratories

An overview of laboratory-associated infections reported in the past 75 years is published in the Chapter entitled "Epidemiology of Laboratory-Associated Infections" (Harding & Byers, 2006). The source literature on these infections provides detailed case reports that are useful for training purposes. *Biosafety Tips* in Volume 12,

Number 1, summarized reports of laboratory-acquired infections with *Neisseria meningitidis* in clinical microbiologists. In every case, a single microbiologist was infected through droplet, or aerosol transmission from routine identification procedures conducted on the open bench. This column describes a report in the *Journal of Clinical Microbiology* of an airborne Brucella outbreak in 31% of the clinical microbiology staff of a community hospital (Staszkiwicz et al., 1991) and two publications (Sue et al., 1989; Ruben et al., 1991) that describe secondary cases of Brucella infection.

Background

Brucella is a zoonotic pathogen and, outside of the laboratory, presents an occupational risk for farmers, veterinarians, and abattoir workers. Approximately 200 cases of human brucellosis are reported annually in the U.S. In Michigan, where this outbreak occurred, eight cases were reported between 1983 through 1987 (Staszkiwicz et al., 1991).