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Chapter 5: Rethinking Mitigation Measures

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Abstract

Once a facility is constructed, risk managers have several tools to mitigate biorisks identified in the risk assessment. They can decide to eliminate the risk or substitute it; they can use equipment to mitigate risks, such as biosafety cabinets, badge readers, or personal protective equipment (PPE); they can decide who will have access and execute the work; and they can change work practices and administrative controls. Although these are all elements that should be considered at the time of design of a facility, they are also the same tools available to adjust the mitigations as needed to accommodate changes in mission. Risk managers must understand the menu of options that can be used to mitigate risks because, no matter how well planned a facility was, the mission will inevitably evolve and risk mitigations will need to be re-evaluated.

Introduction

Current western occupational hygiene literature recognizes a hierarchy of mitigation controls as elimination, substitution, engineering controls, administrative controls, practices and procedures, and personal protective equipment, each having various advantages and disadvantages (DiNardi, S.R., 1997; NIOSH, 2010; OSHA,

2014). Engineering controls are sub-divided into primary and secondary controls: primary controls are safety and security equipment, while secondary controls refer to the facility (see Chapter 4). Primary engineering controls include the equipment used in the laboratory to protect laboratory personnel and/or prevent accidental release, or intentional removal of biohazardous materials from the laboratory. Examples of this equipment include biosafety cabinets (BSC), chemical fume hoods, access controls (e.g., keys, cipher locks, badge swipes, and biometric readers), alarms (e.g., fire alarms, low oxygen sensors, motion sensors, and door open alarms) and other specialized equipment. Administrative controls can include policies, such as decisions about which personnel will conduct work, and training. Practices and procedures codify the expected behaviors of personnel. For example, expectations for waste handling should be captured in a documented procedure. Another standard practice in a bioscience facility is the use of mechanical pipettors instead of mouth pipettors. Personal protective equipment (PPE) is equipment worn by personnel and designed to reduce their exposure and protect them from injury. Common PPE in bioscience facilities includes goggles, gloves, lab coats, and respirators.

Gressel advocates that elimination and substitution merit particular attention in this hierarchy because these options not only increase the level of protection to the worker and the work environment, but also may result in mitigation approaches that are less expensive and require less maintenance (Gressel, M. 2005). Similarly, Soule explains how elimination and/or substitution frequently offer the most

effective solution to an industrial-hygiene problem (Soule, R. D., 2001). From a biorisk management perspective, the benefits of elimination or substitution need to be weighed against any scientific impacts. For example, there is an active debate over the benefits of retaining Variola major virus for research. The World Health Organization (WHO) has decreed that research on live Variola major virus must have public health benefits and not simply enhance scientific understanding (Butler 2011). After eradication of smallpox in 1980, WHO and member countries readily agreed to consolidate the remaining virus isolates in two laboratories to eliminate the biosafety and biosecurity risks at all other institutions. For work with the only other eradicated virus, Rinderpest, the World Organisation for Animal Health (OIE) lifted the moratorium on research with live virus and implemented a process for reviewing research proposals against three criteria to determine if the scientific benefits outweigh the biorisks (OIE, July 2013). These two examples showcase elimination as a risk reduction strategy, but many times substitution of a less pathogenic strain also can substantially reduce the risks while yielding good science. However, it is critical to ensure that the substitution option is actually less risky than the original process. In 2004, the Children's Hospital Oakland Research Institute believed they were working with nonviable vegetative cells of *Bacillus anthracis* Ames strain as a substitute for the pathogenic material. When it was discovered that the specimen had not actually been inactivated, eight personnel had to receive post-exposure chemoprophylaxis for prevention of inhalational anthrax (MMWR 2005).

When elimination or substitution of hazards is not feasible or may not provide comprehensive solutions to the risk, engineering controls are often implemented to reduce the risk. The phrase "hierarchy of controls" leads many to believe that engineering controls are the most important aspect of biorisk management. However, engineering controls are often misused and as such can provide a false sense of safety or security. Nevertheless, this is a common misperception and, as a result, some laboratories are designed entirely around engineering controls, neglecting other equally important control elements such as administrative controls, standard operating procedures (SOP), and the use of personal protective equipment (PPE). The level of implemented engineering control should be proportionate to the risk and should work in conjunction with other controls to optimize overall risk mitigation. Furthermore, disproportionate reliance on engineering controls to reduce laboratory risks can lead to overdesign of facilities and/or exorbitantly high operation, maintenance, and sustainability costs (see Chapter 4). Instead of being the single point of control, engineering controls should be approached as one aspect of a mitigation strategy that blends engineering controls with other elements such as, elimination, substitution, administrative controls (including training and mentoring), SOPs, and PPE. There are many risk factors and risk mitigation strategies that need to be considered when choosing the appropriate mitigation measures, including but not limited to: agent characteristics, endemicity, population susceptibility, availability of prophylaxis and/or treatment, availability of trained and experienced personnel, and availability of resources. This

is why the risk assessment (Chapter 3) is the crucial first step in selecting situation-specific mitigation measures.

Readers should rely on standard industrial hygiene, biosafety, and biosecurity texts for specific technical details on mitigation measures for bioscience institutions (WHO 2004, WHO 2006, BMBL 2009, Plog 2012). However, we argue that these cornerstone references are best used as a "menu of options" for selecting biorisk mitigation measures and not simply a checklist to implement measures based on default biosafety levels. Historically, the design and implementation of mitigation measures have been based upon the biosafety level (BSL) of the laboratory (e.g. BSL 1, 2, 3, or 4). The WHO states that "biosafety level designations are based on a composite of the design features, construction, containment facilities, equipment, practices and operational procedures required for working with agents from the various risk groups …. The biosafety level assigned for the specific work to be done is therefore driven by professional judgment based on a risk assessment" (WHO 2004). The use of the AMP model builds on this approach, further enabling professional judgment in identification and implementation of specific mitigation measures based on a thorough risk assessment rather than relying on the pre-defined solution sets of "biosafety levels." Using the biosafety level method to identify mitigation measures to be used is certainly better than no method at all, but a more strategic and technical approach to implement control measures would be to use a situation specific risk assessment to more effectively allocate limited resources and reduce risks. By using the AMP model to select mitigation measures

to address the identified risks, an institute does not necessarily have to use all of the elements in the hierarchy of controls but, rather, can rely on assessment and performance to help ensure that risk is reduced to an acceptable level. The effectiveness of mitigation control measures selected must also be evaluated on the feasibility and practicality to implement and sustain the measures.

Case Study: Challenges Mitigating Biorisks – Texas A & M University

Although many laboratories successfully implement measures to mitigate their biorisks, we believe the following case study is instructive as a source of lessons learned. On April 20, 2007, Texas A & M University (TAMU) in College Station, Texas received a cease and desist order from the US Centers for Diseases Control and Prevention (CDC) for any and all manipulations and storage of *Brucella abortus*, *Brucella melitensis*, and *Brucella suis* (Kaiser, 2007; Weyant, 2007). On June 30, 2007, the CDC expanded the cease and desist order to include all work with select agents and toxins while CDC conducted a "comprehensive review" to determine if TAMU met the standards for handling select agents (Schnirring, 2007) and delineated specific violations related to lapses in specific mitigation measures. In addition, the principal investigator of the *Brucella* laboratory was suspended.

These unprecedented cease and desist orders stemmed from TAMU's failure to report to CDC two cases of exposure to select agents in 2006. The first exposure occurred in February 2006 to a lab worker who had cleaned a Madison Aerosol Chamber that had contained *Brucella* in a biosafety level-3 laboratory in the School

of Veterinary Medicine. The lab worker subsequently developed brucellosis and recovered after treatment with antibiotics. One month later, three other workers from the TAMU Medical School tested positive for antibodies to *Coxiella burnetii*, the bacterium that causes Q fever, but did not develop the illness. TAMU admitted that it had failed to report both incidents in a timely fashion. Five laboratories in the School of Veterinary Medicine and the Medical School with 120 workers were closed. According to the CDC, this was the first time an entire university's select agent program was suspended.

These incidents raise the following questions: How did these events occur at a highly respected and well-funded university? What safeguards were in place? Were biosafety/biosecurity good laboratory work practices, standard operating procedures, administrative controls, personnel management, record keeping, incident response planning, and biorisk management in place?

The CDC report of August 31, 2007 indicated that TAMU had an inadequate biosafety and biosecurity program—violations occurred with primary biosafety and biosecurity equipment, administrative controls (especially with regard to personnel management) and procedures, and personnel management. These violations to the Select Agent Regulations (42 CFR 73) included over 25 institutional violations, as well as over 45 violations attributed to the specific principal investigator's research, laboratories, and employees. For example, safety equipment was not used properly: the Madison Aerosol Chamber used for animal studies opened directly into a

research laboratory with no primary containment barriers, clearly highlighting the absence of a system that systematically evaluated the performance of the risk mitigation measures. TAMU was also cited for failing to report a release from containment.

TAMU had difficulty implementing mitigation measures that intersected primary controls and administrative controls. At least seven incidences of unauthorized access to select agents also occurred because the primary engineered access controls either did not work properly or the associated administrative controls for personnel management policies regarding who was authorized to have access were missing or not performing properly. Other specific administrative control failures documented by CDC included:

- Failure to obtain approval for select agent work prior to experiments being conducted with both *Brucella spp.* and nine *Coxiella burnetti* aerosolization experiments. This was a clear failure to implement or verify performance of administrative controls for work planning and authorization;
- Individuals with the greatest access to laboratories and animal rooms did not meet proper medical entry requirements. No effective medical surveillance program was in place. This is another administrative controls failure regarding personnel management.
- TAMU's approved certificate of registration did not match the list of individuals provided by the PIs. Yet another failure in the administrative controls for personnel and work approvals.

- TAMU lacked training records for individuals with approved access and no documentation on formal training programs for individuals who worked in the laboratories of the PIs. Documented performance was lacking for training and other administrative controls.
- The security plan did not adequately address transfer of select agents or toxins. There was no documentation that a security plan had been designed in accordance with a site-specific risk assessment. Assessment was critically absent from the development of the security administrative controls.

TAMU did not use an AMP approach for developing and implementing procedures and practices. CDC cited them for inadequate administrative controls for preventing exposure (SOPs, routine maintenance) and waste handling procedures. CDC also noted inventory discrepancies and deemed institutional inventory oversight for select agents inadequate. Utilizing the assessment and performance components of the AMP model could have helped TAMU develop more appropriate SOPs for these key activities.

Each cited deficiency could have been avoided. Instead, TAMU had to pay $1 million in fines for the violations (Schnirring, 2008) so that the university could resume its biodefense research. The large monetary penalty set a new standard of accountability for all research institutions that conduct work on biological select agents. However, the most significant impact was related to the publicity the incidents generated for TAMU, which tarnished the university's reputation and

likely negatively impacted TAMU's failed attempt to win approval for a major new federal laboratory: the National Bio and Agro-Defense Facility.

Using AMP to Strengthen Mitigations

So, how can these types of negative impact be avoided? And, how do you apply AMP to optimize the implementation of the mitigation measures that can be adjusted after a facility is built as the science changes? Institutions must make decisions about what primary controls to employ, which people perform what activities, what practices and procedures to implement, and what PPE to require.

Primary engineering controls

Primary engineering controls are an integral component of biorisk management that can substantially mitigate biorisks, when used in accordance with a comprehensive risk assessment and a solid understanding of how the performance of these controls will be monitored and maintained. There is also a critical interplay between the primary engineering controls, the procedures, and the personnel. As an example, we will discuss some of these relationships between mitigation measures for the biological safety cabinet (BSC). The BSC (Kruse 1991) is a common and critical primary engineered control for reducing the risk of cross contamination (product protection), reducing the risk to the worker of an aerosol or droplet exposure, and reducing the risk to the environment of an aerosol exposure – but only if it is installed, maintained, and used correctly. If there are air drafts from

heating or air conditioning, personnel movements, doors opening and closing, or other sources of air drafts, the performance of the BSC will suffer. In fact, if a procedure that creates aerosols is being conducted in a BSC, the amount of aerosolized organisms that escape from the BSC is directly proportional to the velocity of the cross draft (Rake 1978). Some types of BSCs must be hard ducted to the building exhaust, while others can be installed without any connection into the facility ventilation system. It is important to understand these differences since they impact laboratory procedures, including when the BSC is not in use, handling failure modes, and the ability to work with any chemicals.

The National Sanitation Foundation (NSF) / American National Standards Institute (ANSI) Standard 49 establishes independent performance criteria for BSCs (NSF/ANSI 49). The US Biosafety in Microbiological and Biomedical Laboratories (BMBL 2009) recommends that laboratories certify their BSCs against this standard before being placed into service, after being relocated, and annually to ensure proper functioning for what is a critical primary control of biohazard risks for most laboratories. However, Kruse et al. document examples of improperly certified BSCs and how these primary controls did not perform as intended and inadvertently failed to mitigate the risks in the ways the facilities assumed. In one example, the protective covering of the filter for shipping of the BSC had not been removed so air was not filtered and exhausted properly. Instead, air blew out of the front of the BSC into the worker, yet the BSC had been tested and certified four times over several

years (Kruse 1991.). To address this personnel competence failing of the certifiers, NSF started a program to accredit BSC certifiers in 1993 (BMBL 2009).

The level of protection depends on the mechanical performance of the primary engineering control device as well as good laboratory work practices (Kruse 1991). If the personnel who use the BSCs do not understand and follow the correct procedures for conducting work inside the BSCs and decontaminating the BSCs afterwards, the BSCs will likely not mitigate the risks properly, even when the BSCs are properly selected, installed, and functioning correctly as verified by certification. Poorly trained workers often use the air intake grill of BSC as part of the work surface covering the grill with absorbent pad or microfuge tube holders or other equipment being used in the cabinet. These items disrupt the protective airflow. In this case, the worker may assume that certain protection is offered, does not attempt to augment the protection with additional PPE, and proceeds with the procedure. If the worker were aware that the containment aspects of the BSC were hindered, (s)he might choose to find an alternate mitigation strategy or choose not to perform the procedure. There are many other best practices for working in a BSC that a worker must be willing to follow if the risks are to be mitigated as planned even if, in doing so, additional time is required.

Standard operating procedures

Despite the plethora of engineered controls available to a bioscience institution, the success of these controls depends primarily on individual workers using the controls as designed. Standard operating procedures (SOPs) are the primary tool to achieve this outcome. These instructional documents are designed to guide "different people doing one thing the same way and achieving the same outcome" (Kaufman, 2009). SOPs generally aim to achieve a single or small outcome (e.g., how to correctly wash hands). Examples of SOPs one might expect to see in a bioscience laboratory include but are not limited to: (1) entering/exiting laboratory; (2) donning/doffing PPE; (3) instrument operating procedures [PCR, centrifuge, autoclave, etc.]; (4) use of biosafety safety cabinets; (5) emergency response; (5) hand washing; (6) waste segregation, management, and disposal; (7) inventory control; and (8) experiment specific activities. These SOPs should be based upon a robust risk assessment of the activities being conducted, the biological agent(s) involved, and the specific primary and secondary engineering controls that are in place for the given facility. The BMBL and WHO LBM list specific practices and procedures by biosafety level. Yet, practices and procedures are the mitigation measures that can be the most responsive to changing risks, thus default practices and procedures tied to biosafety levels should not automatically be used. In 2004, while Severe Acute Respiratory System (SARS) virus was still quite new and had not appeared in Belgium, Herman and colleagues analyzed the laboratory acquired infections in Singapore and China to inform a risk assessment for different diagnostic protocols (Herman 2004). They then used this data to guide the establishment of SOPs, including work with inactivated clinical specimens because

such specimens might still contain infectious RNA and for storage of positive clinical samples. They also developed other risk-based recommendations for a series of other practices and procedures for handling SARS virus.

Practices and procedures should be accessible to all relevant laboratory staff, and these must be evaluated and validated to ensure that individuals understand and can physically accomplish the procedure. As with other elements of the biorisk management system, the performance of all practices and procedures should be reviewed regularly and when changes occur. To consistently measure the ongoing effectiveness of a practice or procedure, systematic observation of behaviors by biorisk management officers can be used in addition to self-reporting or reporting by co-workers.

Gidley Amare argues that SOPs are fundamental elements of an effective management system that "help cultivate transparent functions, implement error prevention measures and facilitate corrective actions, and transfer knowledge and skill" (Amare 2012). Although practices and procedures should define how personnel actions fit into the biorisk management framework, persuading individuals to implement standard practices and procedures can be challenging. Amare explains how some personnel feel that standardization of procedures and practices "diminishes their importance at work and so are unwilling to share their knowledge and skills…..Some workers feel insecure in their position if everybody knows their skills and knowledge." The potential perceived impact of SOPs on job

status and job security highlights the importance of the people – the scientists, technicians, administrators, support staff, and others – in the biorisk management system.

Personnel

How should management encourage appropriate behavior among the staff towards biorisk management? How should management monitor personnel reliability? Personnel management throughout the lifecycle of the employee is often disconnected from the biorisk management program when it should be an integral part of the program. Institutions need to recruit the appropriate individuals who have the necessary technical skills, but also need to create an environment where the staff members embrace biorisk management. Other members of the workforce support the vision demonstrated and communicated by their leaders including management, biorisk management advisors, and principal investigators which can and will influence adoption of biorisk management practices. But, Burman and Evans argue that fundamentally, leadership is the key to affecting a safety culture (Burman and Evans 2008). From the authors' personal experience, when a Director attends a biorisk management training course with their workforce instead of just mandating it for the subordinates demonstrates leadership's commitment and vision better than a memo could ever communicate. The UK Health and Safety Executive identified five indicators of safety culture from the investigation of rail accidents (Human Engineering 2005) including leadership, two-way

communication, employee involvement, learning culture, and attitude towards blame. We believe these same factors are fundamental elements in creating a resilient biorisk management culture.

If an institution is successful in creating an impactful biorisk management culture, employees will not feel threatened by the institute's SOPs, will accept the need for and not circumvent the engineered controls, and will understand the purpose for not conducting work before receiving authorization. Institutional management needs to assess positions to define the reliability and skills needed, and the subsequent recruitment practices should be commensurate with that assessment and level of risk. Institutions must make decisions about new and current employees' reliability for the position. This can include evaluating trustworthiness, physical competence, mental competence, emotional stability, financial stability, and the ability to uphold obligations to safety, public health, national security, and scientific integrity.

Once an individual is hired, the risk-based approach to personnel management must extend to training (see Chapter 6), support, and career development. The American Association for the Advancement of Science (AAAS) published a report (Berger 2014) that discusses strategies for mitigating personnel security risks that touch on all aspects of the employee lifecycle, such as hiring, access, employee behaviors, training, personnel actions, and visitors. The report encourages bioscience institutions to rely on performance goals for employees to encourage ownership

and a sense of individual responsibility and other mechanism to build trust and transparency in addition to more traditional background screening methods and employee assistance programs. In this report, AAAS articulates the elements of personnel security as adherence to security protocols, technical competence, adherence to safety, scientific responsibility, and occupational health and well-being. When human behaviors depart from these norms, personnel can pose a safety or security concern either from malice or disregard (Greitzer 2013). In most cases of betrayal or attack by an employee, that employee exhibited serious personnel problems in the preceding months or year; thus, proactive action to address the anxiety or stress may have prevented the incident (Shaw 2005). Additionally, missteps in an employee's scientific responsibilities can negatively impact an institute's reputation and funding. They may also be indicators of the potential for additional misconduct that could lead to safety or security problems. In one of the most comprehensive analyses of scientific misconduct, Daniele Fanelli determined that "on average 2% of scientists admit to have falsified research at least once and up to 34% admit other questionable research practices" (Fanelli 2009). Individuals with admittedly questionable practices in research may disregard the biorisk management practices and pose a risk to the institution and others.

The challenges of personnel, engineering controls, and procedures also converge for visitors. Whether it is the certifier for the BSC or an employee's family member, an institution must assess the risks, develop specific mitigation measures (typically procedural), and validate those measures before admitting any visitor into the

institution. The maintenance of laboratory equipment may require visiting technicians to enter the laboratory. Granting access to these technicians may increase the likelihood for theft of material, and also increase the biosafety risk to the individual or environment. Institutions should establish a process to verify the visitor's credentials, ensure material is secured, escort visitors so they are monitored, and decontaminate the laboratory or equipment to be serviced. Equally important is requiring visitors to check out when they leave for the day to ensure accountability for all persons within the facility. For any persons who may require extended access to perform work, additional controls should be enforced, as with employees, including verification of the person's knowledge, skills, and abilities, and employment and education history.

Eliminating safety and security conflicts

Verifying performance of the system used to mitigate the identified risks will also ensure that conflicts between biosafety and biosecurity are resolved. Do primary engineered controls for security interfere with life safety? Security bars on windows may eliminate an emergency exit route if they do not have emergency release devices installed that allow the bars to be opened from the inside. Personnel also need to be aware of and understand how to use the release devices. Do the access controls operate correctly under the relevant procedures? Primary engineered controls for access can include lock and key, badge swipe, fingerprint reader, or retinal scanner, among others. However, a worker who is wearing gloves cannot use

a fingerprint scanner. A physical key or badge may need to be decontaminated if these items are used in a setting where they could become contaminated. Goggles or face shields can interfere with some types of eye scanners. In these cases, the point of access control could be moved, depending on the facility layout and workflows, or a different type of access control equipment could be utilized. It is crucial to consider and balance both biosafety and biosecurity aspects when making decisions about how to mitigate the identified risks. Furthermore, appropriate mitigation measures need to be based on what the infrastructure can support and sustain. For example, personnel can get trapped in the laboratory if the power goes out and there is not an alternate mechanism to open the door or reliable uninterruptible power supply for the locking mechanism.

Case Study: Different Solution Paths to Working with Ebola Virus

Since its 1976 discovery as the causative agent of an outbreak in what is now the Democratic Republic of the Congo, Ebola virus has been designated a risk group 4 agent by WHO, the European Centers for Disease Control, and the US CDC, among others. As a result of this designation, researchers traditionally only handle Ebola virus in a biosafety 4 level laboratory. However, an outbreak that began in Guinea in December 2013 has mushroomed into the largest outbreak of Ebola Virus Disease to date with active transmission in Guinea, Liberia, and Sierra Leone (as of October 2014). Travelers have imported isolated cases into Mali, Nigeria, Senegal, and the United States. The magnitude of the outbreak coupled with concerns over the possibility of additional exported cases has led several leading public health

agencies to release updated guidance for handling specimens suspected of containing Ebola virus to provide recommendations to non-biosafety level 4 laboratories to safely handle Ebola virus (WHO 2014, PHAC 2014, CDC 2014a).

The new guidelines have many commonalities that focus on implementing specific mitigation measures to match specific facets of the risks associated with handling Ebola virus samples. These guidelines all focus on mitigating the risks of exposure and emphasize the need for risk assessments to identify all possible sources of sprays, droplets, and splashes. The CDC interim guidelines suggest laboratory staff test specimens in a "certified class II Biosafety cabinet or Plexiglass splash guard with PPE to protect skin and mucous membranes" (CDC 2014a). This recommendation combines primary controls to contain droplets created during laboratory procedures with the usage of PPE to mitigate the risks of splashes and other releases from the primary controls. They highlight the risk associated with having laboratory staff work in unfamiliar PPE and this could inadvertently result in exposure during doffing (CDC 2014b). Personnel must be evaluated for their ability and comfort level in executing new protocols to handle Ebola virus. The Public Health Agency of Canada suggests designating specific personnel for work with suspected samples and limiting access to those individuals. Notably, the new guidelines for working with Ebola virus do not instruct laboratories to physically change their facilities, but rather to review and adjust their primary controls, administrative controls, personnel, and PPE to handle the potential new risk of a suspected Ebola virus sample.

In a set of questions and answers for "How U.S. Clinical Laboratories Can Safely Manage Specimens from Persons Under Investigation for Ebola Virus Disease," CDC describes why following protocols for bloodborne pathogens will sufficiently address the risks of clinical labs that handle Ebola virus – even though the CDC itself only works with Ebola virus in a biosafety level 4 laboratory (CDC 2014b). The CDC explains this difference in terms of the risks associated with the different activities conducted since CDC's Ebola researchers grow large quantities of viral stocks for subsequent testing of potential vaccines and treatments while clinical laboratories primarily process small amounts that are inactivated early in the testing process.

Summary

In this chapter, we maintain that it is not sufficient for bioscience institutions to simply rely on technical documents such as the US Biosafety in Microbiological and Biomedical Laboratories, WHO Laboratory Biosafety Manual, and the WHO Biorisk Management: Laboratory Biosecurity Guidance (WHO 2006) for choosing appropriate mitigation measures. To optimize the use of risk mitigation measures, institutions need to embrace flexible, creative thinking about using tools from across the hierarchy of controls to address their specific risks with appropriate biosafety and biosecurity —both in implementing their day-to-day mission and in adapting to disease outbreaks and other mission or situational changes. As the TAMU case illustrates, even a sophisticated institution can encounter serious gaps in their mitigation measures due to a compliance mindset that fails to examine the

assessment and performance of chosen mitigation measures. The Ebola outbreak shows how a facility may need to adapt its risk mitigation measures without the luxury of building a new secondary barrier (laboratory). Elimination and substitution of the hazards should be first considerations in any mitigation strategy. In many cases, innovative use of elimination and/or substitution can also greatly improve the science. The risk of testing for HIV has been significantly reduced through the development of dried blood spot tests that do not need viable virus while, concurrently, this advance in technology has improved the ability to do HIV surveillance in developing countries since a cold chain is no longer required for the samples (Solomon 2002). However, elimination or substitution may not always be feasible to achieve the scientific mission; the applicability of these control measures needs to be re-evaluated regularly as the scientific state of art advances. But, when elimination or substitution is not appropriate or sufficient, facilities can adjust their primary controls, administrative measures, procedures, and PPE to develop multiple strategies to mitigate their biorisks.

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