Applied Biosafety
Volume 26, Number 3, 2021

DOI: 10.1089/apb.20.0068

ORIGINAL ARTICLE

Considerations for Laboratory Biosafety and Biosecurity During the Coronavirus Disease 2019 Pandemic: Applying the ISO 35001:2019 Standard and High-Reliability Organizations Principles

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Abstract

Background: Risk assessment is a critical tool for evaluating emerging pathogens such as severe acute respiratory syndrome coronavirus 2 because of the limited available information about pathogens and the diseases they cause. Industries adopt unique frameworks for risk assessment, for example, the ISO 35001:2019 biorisk management for laboratories and other related organizations provide tools to identify, assess, control, and monitor risks associated with hazardous biological materials. Industries such as aerospace are known as high-reliability organizations (HROs) because these must balance high-risk operations with minimal catastrophic outcomes. HROs focus on five core principles: preoccupation with failure, reluctance to simplify, sensitivity to operations, resilience, and deference to expertise to evaluate and manage risk.

Results: In the present discussion, practices described in the ISO 35001 standard and the HRO model are applied to the current challenges faced by laboratories worldwide. Laboratories processing known or unknown coronavirus disease 2019 (COVID-19) samples, testing COVID-19 vaccine candidates, propagating severe acute respiratory syndrome-associated coronavirus-2, or validating diagnostic assays benefit from implementing such practices. Principles extrapolated from the HRO also help illustrate the importance of the end-to-end processes to ensure successful outcomes.

Summary: Workplace safety is enhanced by the involvement of all stakeholders, from top leadership to front-line workers. High-quality outcomes as measured by a lack of incidents, accidents, injuries, or near misses are the positive consequences of strictly following standard operating procedures and timely communication of risks and pitfalls. Adopting a systematic framework to identify and manage risks posed by emerging pathogens results in increased workplace safety and higher quality processes and products.

Keywords: ISO 35001:2019, SARS-CoV-2/COVID-19, biorisk management, CWA 15793:2011, APHL Competency Guidelines

Introduction

The ISO (International Organization for Standardization) 35001:2019 biorisk management for laboratories and other related organizations, herein ISO 35001, was released in November of 2019. The backbone of ISO 35001 was the CEN (European Committee for Standardization) Workshop Agreement (CWA) 15793:2011 Laboratory Biorisk Management.[1] ABSA International and other international biosafety associations (e.g., European Biosafety Association) have demonstrated their commitment to biorisk management through their early involvement with stakeholders in the development of the CEN Workshop Agreement

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15793:2011 and subsequent ISO committees that developed the ISO 35001:2019 standard. ABSA International employs these biorisk management principles in its Laboratory Accreditation Program standards as well as in its basic 40-h training course, *Principles & Practices of Biosafety*.

The comprehensive analysis and comparison between the CWA 15793 and ISO 35001 are beyond the scope of this article. The ISO 35001 standard establishes biorisk management principles by applying ISO's management system approach using a continual improvement model considering the context of the organization, leadership, planning, support, operations, performance evaluation, and improvement. Each principle benefits from a systematic approach to assess, control, and evaluate its progress through the Plan-Do-Check-Act (PDCA) system to ''achieve continual improvement of processes and products.'' The overarching goal of ISO 35001 is to mitigate the biosafety and biosecurity risks in the workplace and ultimately minimize laboratory-associated infections, inadvertent releases, or other incidents or accidents.[2]

Examples of how some countries address biorisk management include *guidance* provided by the U.S. Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) fifth edition of the *Biosafety in Microbiological and Biomedical Laboratories* (*BMBL*) relative to how to perform a collaborative risk assessment that includes multiple stakeholders.[3] In contrast, the Government of Canada's Canadian Biosafety Standard (CBS), Second Edition[4] *requires,* to be licensed, a documented overarching risk assessment for an entity utilizing infectious materials or toxins, as well as a documented local risk assessment for each task/laboratory involved and a documented biosecurity risk assessment. Similarly, the United Kingdom's Health and Safety Executive requires that employers have a risk assessment to identify *sensible measures to control the risks in the workplace*.[5]

In this discussion, practices described in the ISO 35001 standard and the HRO model are applied to the current challenges faced by laboratories worldwide, including public health laboratories, blood banks, research laboratories, veterinary laboratories, university laboratories, and pharmaceutical laboratories processing samples from patients suspected of or confirmed to have COVID-19. Various types of laboratories not directly involved in patient care such as those testing COVID-19 vaccine candidates, propagating severe acute respiratory syndrome-associated coronavirus (SARS-CoV)-2, or validating diagnostic assays may also benefit from such standards or models.

Laboratory Safety in the Age of a Novel Coronavirus

On January 30, 2020, the World Health Organization (WHO) declared the coronavirus disease 2019 (COVID-19) outbreak as a public health emergency of international concern.[6] COVID-19 is caused by a novel coronavirus initially reported in December 2019 in Wuhan, China, which bears a higher than 70% identity to the SARS-CoV causing SARS that was responsible for the global outbreak in 2002.[7] In April 2020, Stiles presented strategies to prevent worker exposure to SARS-CoV-2 in clinical and research laboratories as well as blood banks.[8] As laboratories adapt to the demands of processing COVID-19–related samples, some challenges faced by the leadership and workforce include:

At the engineering controls or secondary barriers level:

- Availability of primary containment such as biosafety cabinets, including maintaining current equipment certification;
- heating, ventilation, and air conditioning challenges to maintain and increase air changes per hour while using existing infrastructure;
- installation of additional transmission control barriers between workstations and, if applicable, in a way that is consistent with the equipment manufacturer's specifications; and
- availability of handwashing stations in adapted spaces for laboratory activities.

At the administrative control level:

- Comprehensive and complete risk assessment process that accounts for changes in personnel, process, and/or other changing conditions.
- Personnel and training:
  - Providing just-in-time and appropriate training;
  - ensuring that surge capacity personnel are provided with appropriate safety and security training, including pathogen-specific training;
  - training for use and doffing of personal protective equipment (PPE) such as gloves, gowns, Controlled Air Purifying Respirator (CAPR®), or Powered Air Purifying Respirator (PAPR);
  - maintaining staffing levels in the event of a positive employee and coworkers in quarantine;
  - considering increased risks to lone workers outside normal operating hours;
  - ensuring personnel adherence to established protocols including provisions for operating under emergent infectious diseases with high community transmission;
  - considering additional supervision under surge capacity conditions; and
  - planning for mental or physical health support for personnel responding to high-stress or high-volume events.
- Procedures
  - Standard operating procedures for novel products and techniques;

- validation of inactivation methods, especially when transferring samples from high-containment (Biosafety Level [BSL]-3) to lower containment levels;
- new reagents and diagnostic techniques for use at BSL-2 that may need to be validated by the manufacturer and the technicians or laboratory staff;
- ability to institute enhanced work practices and procedures (i.e., from BSL-3 in a BSL-2 facility, also known as BSL-2+ or BSL-2 enhanced) for noninactivated materials such as blood or upper respiratory specimens, tissues, autopsy specimens, stool, other body fluids, waste water, and effluent;
- ensuring availability of test components or other critical supplies (e.g., lysis buffer, swabs, and other consumables.) and equipment;
- maintaining an accurate and up-to-date inventory of critical supplies and components;
- maintaining an inventory management system to assure integrity and security of biological materials and chemicals, especially for samples known to contain SARS-CoV-2 or suspected of containing novel pathogens; and
- adapting to a shortage of supplies and reagents and prioritizing work.

- Disinfection and waste management:
  - Ensuring availability of disinfectants/sanitizers that are proven to be effective in inactivating novel pathogens in the laboratory and office area as well as documenting and making available chemical safety data sheets in accordance with national standards and
  - ensuring that appropriate disposal methods for regulated biological and hazardous waste are in place and can be adapted for large volumes of materials. These processes must be in accordance with local, regional, national, or international regulations.
- Occupational Health
  - Ensuring availability of occupational health surveillance to all workers;
  - additional physical and mental stress on the workforce when working beyond normal duty hours due to colleagues in isolation or quarantine;
  - symptom screening or administering questionnaires to staff before returning to the workplace, especially after a known illness; and
  - following applicable country-specific standards such as clinical clearance before N95 respirator fit testing or testing for hepatitis B antibody titers (respiratory protection standard and Bloodborne Pathogen Standard in the United States).
- Nonpharmacological preventive measures directly related to the pandemic:
  - Ensuring clear guidance for personnel as to what respiratory precautions are required. Examples include demarcation of work and clean zones, clear delineation of the purpose of and requirement for different face coverings in different risk settings, and making its use consistent with overall biocontainment initiatives and institutional policies;
  - the COVID-19 pandemic has strained the supply chain for PPE and other risk-reduction materials and, therefore, availability of prescribed equipment has been limited. In these instances, a rigorous risk assessment will drive the minimal PPE needed by adjusting the engineering controls;
  - wearing face covers (cloth or surgical mask) even when individuals are not handling hazardous biological materials in a laboratory environment for pandemic protection rather than protection of self from the work hazard; and
  - rearranging the laboratory set up to accommodate physical distancing (e.g., 6 feet or 2 m) and population density per institutional guidance.

At the PPE level:

- Selecting PPE according to the hazard assessment and equipment selection process conducted by the employer/supervisor;
- availability of quality PPE due to the supply shortage. PPE must meet the country-specific manufacturing requirements and counterfeit materials must be avoided;
- providing medical clearance, fit testing, and training for correct use of respiratory protection such as N95 or powered air purifying respirator or controlled-air purifying respirator, or other PPE; and
- implementation of PPE reuse procedures based on risk assessment and verified safe practices.

The Drivers for Additional Risk Management Frameworks to Increase Laboratory Safety

In 1975, the historic Asilomar Conference suggested assigning a ''risk estimate'' to experiments involving emerging recombinant DNA technology to guide the safety precautions needed depending on the risk. The

Asilomar attendees noted that a high-level biocontainment approach should be used in situations wherein there were unknown/unpredicted risks, with a decrease in biocontainment requirements as novel agents and vectors become better studied and understood.[9]

In 2010, the World Health Organization published the *Responsible life sciences research for global health security: A guidance document*, which provided a framework to achieve a culture of ''scientific integrity and excellence, distinguished by openness, honesty, accountability and responsibility.''[10] The framework relies on three pillars: (1) research excellence to ensure quality in research, (2) ethics to foster responsible and good laboratory practices, and (3) biosafety and biosecurity to ensure that workers have a safe place to conduct research and accountability for hazardous biological materials.

This WHO framework also took into consideration lessons learned from emergence of novel microbes such as the viruses that caused the novel influenza A (H1N1) disease in 2009, infections of humans with avian influenza (H5N1) associated with close contact with infected live or dead birds, or H5N1-contaminated environments, in 2008, and the SARS in 2003. We can certainly add the novel SARS-CoV-2 to this list.

Patrick Lagadec in his 1993 book ''Preventing Chaos in a Crisis: Strategies for Prevention, Control, and Damage Limitation'' emphasizes that the response to a crisis cannot be developed unless the institution has prepared to adapt to an emergency/crisis[11]

> ''the ability to deal with a crisis situation is largely dependent on the structures that have been developed before chaos arrives. The event can in some ways be considered as an abrupt and brutal audit: at a moment's notice, everything that was left unprepared becomes a complex problem, and every weakness comes rushing to the forefront.''

Thus, an argument can be put forth whereby research and clinical laboratories that had implemented and invested in a robust biorisk management system such as the ISO 35001 standard, or its predecessor CWA 15793:2011, would be better positioned to take on the COVID-19 challenges due to the fact that the two broader pillars would be in place: (1) a biorisk management system to *identify, assess, control, and evaluate* the biosafety and biosecurity risks and (2) an iterative process for continuous improvement involving planning, implementing, monitoring, and taking action (PDCA model). In a time of emergency, laboratory systems that had integrated these components would prepare an organization to make the adjustments needed to respond to a surge in cases of known or unknown infectious diseases. The investment in management systems generally involves significant personnel and/or equipment/facilities capacity, resulting in a facility that would have ready-to-go trained personnel, equipment, and other resources to address a novel pandemic virus even when the full biological characteristics of the novel agent are unknown.

Existing Guidance for Risk Assessment and Handling COVID-19–Related Samples or SARS-CoV-2

The planning component of the ISO 35001 includes the goals and expectations when performing a risk assessment. For example, in a recent symposium, Dr. Reynolds Salerno, director of the CDC Division of Laboratory Systems, emphasized the importance of risk assessment as the ''foundation of every good biorisk management system.''[12] Specific guidance for conducting a biorisk assessment when handling samples suspected of containing SARS-CoV-2 is available through various organizations. For example, in February of 2020, Annex 2 of the WHO laboratory biosafety guidance for COVID-19 included a qualitative tool to assess biorisk according to the activity or procedure, a description of the risk control strategy and implementation of the risk control measures, and an assessment of residual risk, level of organizational tolerance, and final review by laboratorians.[13] Recently, the WHO also published a laboratory assessment tool for SARS-CoV-2 testing to assess the capacity of laboratories that have implemented or are implementing testing with an emphasis on strengths and weaknesses of the facility.[14]

Guidance for handling COVID-19–related samples also has been issued by multiple organizations across the globe; organizations or governments include the WHO,[15] the CDC,[16] the Government of Canada's biosafety advisory for SARS-CoV-2,[17] and the European Union Centre for Disease Prevention and Control.[18] The guidance for laboratory biosafety related to COVID-19 is updated by these organizations as scientific information becomes available and highlights the importance of periodic literature review to guide the need for updating the risk assessments. In the face of the COVID-19 pandemic, many countries have followed the WHO standards for risk management and laboratory safety and security. Alternatively, countries have adopted or adapted COVID-19–related international guidance. In conclusion, there are various models or templates available to conduct a biorisk assessment that should be revised as frequently as needed, using continuous improvement practices, to address changes in guidance, procedures, equipment, personnel, or facilities.

Biorisk Management Elements Applied to Laboratories Processing COVID-19 Samples

Two frameworks are presented here to provide considerations that may help the biorisk manager address the adaptation of the laboratory to high-paced work/production due to the demands of the COVID-19 pandemic. The first framework is the international standard ISO 35001 that

defines a process to *identify, assess, control, and monitor* biorisks. The ISO 35001 standard may be applied to the current challenges faced by laboratories worldwide, including public health laboratories, blood banks, research laboratories, veterinary laboratories, university laboratories processing COVID-19 samples or pharmaceutical laboratories processing COVID-19 samples, and various types of laboratories propagating SARS-CoV-2 or validating diagnostic assays.

A practical approach to applying the components of the ISO 35001 is presented in Table 1. This table includes key considerations and concrete examples that may enhance the biosafety and biosecurity practices in laboratories handling COVID-19–related samples or propagating SARS-CoV-2. These considerations may be applicable to those laboratories that were following a biorisk management plan before the pandemic. An in-depth review and analysis of the ISO 35001 components and implementation requirements would be needed for settings that are in the process of establishing a biorisk management system, and this is beyond the scope of this article.

A critical benefit of implementing ISO 35001 is that it provides a consistent and thorough framework for laboratories handling valuable biological materials across the globe that are looking to improve their performance through systematic quality and safety controls. In the context of the COVID-19 pandemic, another benefit of implementing the ISO 35001 is the standardization of terms and definitions that facilitate global communication. Various other documents have provided guidance for U.S.-based and international laboratories. Such guidance includes the good clinical laboratory practices (GCLPs) guidelines, for example, which is limited to clinical laboratories. Ezzelle et al. published in 2009 the guidelines for GCLP that apply to clinical laboratories involved in research (clinical trials) to ensure that *accurate, precise, and reproducible data* are generated for such studies.[18] These guidelines consolidated U.S. regulatory requirements (21 Code of Federal Regulations [CFR], vol. 1, Part 58, Good Laboratory Practice for Nonclinical Laboratory and 42 CFR, vol. 3, Part 493, Laboratory Requirements) and the industry best practices (ISO 15189: Medical laboratories, particular requirements for quality and competence), the College of American Pathologists' Laboratory General Checklist GEN.54300, and the British Association of Research Quality Assurance (BARQA, later named the Research Quality Association).[21]

The second framework is the high-reliability organization (HRO) model presented in the 2007 Weick and Sutcliffe publication on ''Managing the Unexpected.''[22] Health care providers operate in hazardous environments (e.g., hospital emergency room and intensive care units) where the consequences of errors are high (i.e., death, medical malpractice, erroneous drug administration, hospital-acquired infections, and occupational risks). HROs, such as the health care industry, air traffic controllers, or aircraft carriers, follow five core principles[23]:

(1) Preoccupation with failure (near misses or close calls are an opportunity to improve);
(2) reluctance to simplify (accepting that work is complex and has unknowns);
(3) sensitivity to operations (from top leadership to front-line workers);
(4) resilience (anticipate emergency situations); and
(5) deference to expertise (value expertise instead of seniority).

Christianson et al. provided applications of these principles in health care, specifically in the intensive care unit.[24] Table 2 provides additional considerations to apply the HRO principles to the current operations of COVID-19 laboratories. The HRO principles complement the core risk assessment from ISO 35001 by showcasing a culture of accountability from front-line workers to top management by means of setting clear expectations and behaviors. Overall, the components and subcomponents of ISO 35001 and the pillars of the HRO principles allow for setting up matrices for gap analyses, to determine whether a requirement has been implemented, partially implemented, or has not been addressed by the organization, with the ultimate goal of establishing a plan of action.

Quality Management, Biosafety, and Biosecurity

The American Society for Quality defines quality as ''fitness for use, conformance to requirements, and pursuit of excellence.''[25] In fact, other ISO standards such as the ISO 9000 family are devoted to providing overarching quality management principles that are described in ISO 35001.[26] Other industries, such as building construction, have assessed the relationship between quality and safety, two factors considered to be critical for project success. Wanberg et al. demonstrated that the Occupational Safety and Health Administration (OSHA) recordable injuries (unsafe conditions) correlated positively with rework (low quality of product), and similarly, that first aid rates positively correlated with the number of product defects.[27]

Recognizing that personnel competency had a direct impact on the quality of results, the CDC and the Association of Public Health Laboratories (APHL) partnered in 2010 to produce a set of competencies for laboratorians working in BSL-2, BSL-3, and BSL-4 facilities, also intended to be used by biosafety professionals in developing their programs.[28] These competencies were refined and then formally published in 2015 as ''Competency Guidelines for Public Health Laboratory Professionals,'' which outlined the *knowledge, skills, and abilities* not only for public health laboratorians but also applicable

Table 1. How can the ISO 35001 standard be applied to laboratories handling coronavirus disease 2019-related materials?

ISO 35001 components	*Considerations for COVID-19 laboratories*	*Examples of mitigation measures*
Organization	Coordinate procurement of appropriate PPE and disinfection supplies Provision of sufficient personnel and financial resources for biorisk management for normal operations as well as for emergency situations Support for the biorisk manager (i.e., biosafety officer or biosafety responsible person) Clearly defined responsibilities and competencies Development and communication of a comprehensive COVID-19 workplace plan, in compliance with latest local/state/national guidance Personnel policies support COVID-19 isolation and quarantine policies and remote work guidance	Explore methods to reuse/recycle masks, PAPR hoods and respirators, if necessary Recruit in house (campus, pharmacy) to produce appropriate disinfectant solutions, hand sanitizers if not commercially available Encourage remote work, when possible, identify additional surge laboratory space and staggered shifts to reduce laboratory density Hire additional personnel, recruit senior year medical/nursing/medical technology, graduate students to staff surge capacity, if available Hire additional clerical help to track and report sample results, inventory, etc. If necessary, provide funding for additional biorisk management staff to provide training, review policies, and SOPs, oversee disinfection of facilities, generate policies such as those for personnel reliability and a whistleblower policy, if not already in place Review leadership communication plan Capitalize on existing trained personnel for BSL-3 containment
Leadership	Guidance and support of the biorisk management committee (i.e., Institutional Biosafety Committee, Biosafety Committee, Research Health and Safety Committee) Demonstrate management commitment to a robust biosafety and biosecurity program Laboratory staff is represented on the biorisk management committee Facilitate availability of financial resources when infrastructure changes or engineering controls need to be made or acquired Identify and communicate emergency policies with all stakeholders (laboratorians, supervisors, environmental services, emergency response, and other interested parties) Facilitate determination and implementation of emergency policies Management commitment to regular safety/biosafety meetings to include laboratory and support staff Ensure that qualified personnel (i.e., biorisk management advisor) are available to review the risk assessment Leadership displays best practices for the workplace (wearing face covers, travel avoidance, and social distancing)	Encourage/fund additional biorisk management committee meetings to address increased activities (risk assessments, protocol reviews, SOP review, etc.). Appoint a senior laboratory staff member to the biorisk management committee Involve HVAC personnel in discussions of engineering control improvements (increasing air changes/hour, adding additional fresh air to ventilation system, changing filters in HVAC to higher MERV ratings, if possible) Increase communication and training for emergency response, firefighters, police, and security personnel Schedule monthly meetings to include laboratory and support staff, encourage participation Recruit other experts (primary investigators, infection control, quality personnel, and industrial hygienists) to help review risk assessments and SOPs Encourage all staff, including directors, managers, supervisors, and laboratory workers to comply with the stated COVID-19 protocols
Planning	Identify, assess, and control the risks of handling various types (swabs, blood, fluids, and sewage) and sources (human, animal, and autopsy) of COVID-19 samples Individual risk assessments must be completed for using novel diagnostic devices and methodologies Structured process for risk assessment to define mitigation measures Provide institutional guidance to users Determine national/international containment guidance (e.g., United States and Canada: BSL-2/ABSL-2, BSL-3/ABSL-3; WHO: core, heightened containment) based upon risk assessment Determine additional training and practices necessary to mitigate identified risks	Provide training on how to perform a risk assessment. Tools include the Association of Public Health Laboratories Risk Assessment Templates,[19] and the Canadian Pathogen Risk Assessment Template[20] Develop training and additional SOPs for any new engineering controls, equipment, and procedures Confirm completion of bloodborne pathogen training and hepatitis B vaccination for personnel handling human source materials (good practice)

(*continued*)

Table 1. (Continued)

ISO 35001 components	*Considerations for COVID-19 laboratories*	*Examples of mitigation measures*
Support	Knowledgeable and competent trainers Pathogen-specific reference document (i.e., Canadian Pathogen Safety Data Sheet) Training for emergency personnel, vendors Verification of technical competency Support for biorisk management consultants if expertise is not available in house Implement policies controlling personnel reliability	If not already in place, designate a senior laboratory staff member to serve as an official trainer, provide train-the-trainer training for this individual, document all SOP and on-the-job training in writing Determine (in writing) what constitutes ''competency'' before allowing trainees to handle pathogenic material Assemble fact sheet for the pathogen tailored to your institution. Resources include the Canadian Pathogen Safety Data Sheets, the CDC agent-specific summaries included in the *Biosafety in Microbiological and Biomedical Laboratories*, or other resources Develop and provide relevant training for visitors, vendors, emergency personnel, and custodial/environmental services Recruit experienced biorisk management consultant(s) if additional expertise is needed and cannot be recruited/trained in house
Operations	Standard operating procedures for specimen processing, inactivating, transferring, shipping, and donning and doffing of PPE Facility engineering controls (i.e., airflow check, biosafety cabinet certification, and eyewash station) Centrifuge with aerosol containment Inventory management systems to control access and movement of VBMs and other laboratory reagents based on the biosecurity assessment (i.e., log of samples transferred from high containment) Inventory of inactivated samples Validation of inactivation methods Emergency alert card Quality of reagents used	Purchase additional engineering control equipment, such as centrifuge safety cups and workspace dividers Coordinate for the certification of biosafety cabinets Provide portable handwash stations and eyewash bottles in surge or mobile laboratories Purchase commercially available or develop an in-house inventory system to track VBMs, inactivated samples, and other valuable laboratory reagents Recruit BSL-3 principle investigators to assist in inactivation studies, if necessary Generate a handbook of acceptable inactivation methods, based on in-house studies Work with engineers to evaluate the ventilation system and, if possible, increase the air exchange per hour
Performance evaluation	Document name and location of individuals trained Training evaluation feedback Safety performance included as part of employee evaluation Solicit feedback from laboratory and support staff for improvement (nonpunitive) Biorisk management committee update and feedback Internal and external audits, inspections, or certifications (i.e., self-inspections, laboratory inspections, American Biological Safety Association International Laboratory Accreditation Program, regulatory inspections) Whistleblower policy	Develop a robust training and evaluation program, if not already in place The training program should include feedback opportunities, written documentation of all training, and regular retraining or competency testing Increase communication with the biorisk management committee to include regular updates on laboratory operations, assessments, and review of SOPs and policies Encourage internal and external review of facilities and operations, including policies and SOPs. Encourage laboratory safety officers to perform reciprocal inspections.
Improvement	Reporting/follow-up/root cause analysis for incidents, near misses, accidents Management meetings include discussion of incidents/near misses/accidents Periodic SOP and training review/revision Periodic occupational health follow-up Mental health support	Implement a robust incident follow-up process that requires root cause analysis of all types of incidents and near misses Schedule time during management meetings to discuss safety incidents and near misses as well as inspection findings Schedule annual review of SOPs and policies or more often if procedures change Work with occupational health to develop a program to assess and respond to specific laboratory health concerns (immune suppression, pregnancy, infectious agents handled, vaccination, exposure incidents, stress, etc.). Include the occupational health professional to the biorisk management committee.

ABSL, Animal Biosafety Level; BSL, biosafety level; coronavirus disease 2019, COVID-19; HVAC, heating, ventilation, and air conditioning; PAPR, Powered Air Purifying Respirator; PPE, personal protective equipment; SOPs, standing operating procedures; CDC, U.S. Centers for Disease Control and Prevention; VBMs, valuable biological materials; WHO, World Health Organization.

Table 2. Application of high-reliability organization principles to laboratories handling coronavirus disease 2019-related materials

High-reliability organization principles	*Considerations for COVID-19 laboratories*
Preoccupation with failure	Conduct daily or weekly huddles with stakeholders to report on how things are going, deviation from procedures, etc. Nonpunitive reporting Accident/incident reporting Encourage near-miss reporting Encourage laboratorians to identify early signs of failure or near misses, e.g., using tubes with slight cracks not enough to cause a spill, gloves that rip easily when doffing, fogging of eye protection due to using a surgical mask
Reluctance to simplify	Clarify SOPs Clarify and specify details related to cleaning and disinfection procedures Ask the five ''W's'' (who, why, when, what, and where) when doing accident investigation to find the root cause Challenge long-held beliefs
Sensitivity to operations	Understand all processes and potential risks associated with the handling of samples (i.e., example, mixing with vortex, sonication, centrifugation, cell culture, cytometry, and concentration) Encourage laboratorians to visualize or enact their actions and decisions during an emergency, for example, during a biological spill Pay attention to PPE availability, different sizes needed for personnel, correct type of PPE (fluid-resistant gown, nitrile gloves, medical-grade surgical mask) Accommodate different schedules so that physical distancing is maintained as well as density of population in facility Use the virtual buddy system for individuals working alone by using technology such as text message notification when going into high containment Be mindful of personnel turnover or understaffing
Resilience	Work together as a team Communicate problems to supervisor Review emergency procedures and feasibility for a new facility when personnel are transferred to a surge laboratory Avoid unnecessary stress and physical fatigue Encourage time off, breaks, and mental and physical health support Review lessons learned from previous episodes or events
Deference to expertise	Promote basic knowledge and understanding about novel pathogens Include all stakeholders when completing risk assessments Involve other specialties (HVAC, infection control, and occupational health) Seek expert guidance and current information available, always verify the source of your information

to other work settings such as academic, public and private laboratories, and veterinary laboratories handling biological, chemical, or radioactive materials.[29] This document was also referenced by APHL's position statement on improving biosafety in U.S. laboratories and encouraging its use as a tool for conducting risk assessments and establishing milestones for training competency.[30]

Furthermore, Gumba et al. showed how the Kenya Medical Research Institute—Centre for Microbiology and Research (KEMRI-MR) implemented a quality management system based on the GCLP guidelines to support medical research. The take-home messages from this implementation include conducting a baseline assessment, mentorship, and collaboration with the sponsoring organization (in this case, Wellcome Trust Research Programme), training of personnel to write and follow standing operating procedures, and continuous monitoring to meet the GCLP milestones. The outcome of the implementation (exit assessment) showed a significant decrease in nonconformance items according to the GCLP criteria.[31]

In 2017, the U.S. Federal Experts Security Advisory Panel (FESAP) Working Group issued guiding principles to promote and strengthen a culture of biosafety and biosecurity in life science research as part of a quality management system, with the ultimate goal of protecting the health and safety of workers, the community, and the environment. This advisory panel was convened following incidents involving safety and security of biological select agents and toxins, also referred to as biological agents of security concern. The recommendation actions that emerged from the working group's deliberations include, among various principles, providing workers with

knowledge (information), skills (actual performing), and abilities (capacity to perform) to be competent in carrying out their assigned duties and responsibilities. Lastly, the recommendations provide definitions of quality management and of culture of biosafety, biosecurity, and responsible conduct that are useful to review when bringing together quality and biosafety/biosecurity in the context of improving workplace safety and the products or outcomes[32]:

- *Quality Management System: Coordinated activities (including policies, processes, and procedures) on all aspects of a laboratory operation (including organization, personnel, and equipment) to direct and control the quality of research and results that are accurate, reliable, and timely.*
- *Culture of Biosafety, Biosecurity, and Responsible Conduct: An assembly of beliefs, attitudes, and patterns of behavior of individuals and organizations that can support, complement, or enhance operating procedures, rules, and practices as well as professional standards and ethics designed to prevent the loss, theft, misuse, and diversion of biological agents, related materials, technology or equipment, and the unintentional or intentional exposure to (or release of) biological agents.*

In the context of the COVID-19 pandemic, a laboratory that has a robust quality management system in place, such as the ISO 35001, is prepared with methodology to address emergent infectious diseases because its personnel are aware of the knowledge, skills, and abilities required to deal with unknown threats and recognize where additional competencies are needed to perform optimally under such conditions. A culture of safety and biosafety allows for direct channels of communication with the different levels of leadership.

Summary

The SARS-CoV-2/COVID-19 pandemic has challenged the status quo in every walk of life. Life science laboratories (e.g., diagnostic, research, and pharmacological) that may work with human and animal samples are no exception. The emergency response plans that these entities needed to have in place have been challenged as well. There are various sources of guidance for laboratories, domestic and international, to ensure that these can respond to a demand for high-capacity processing and/or testing. It is expected that good laboratory practices are instilled in the early years of the laboratorian's education and training. Once at the workplace, following the ISO 35001 biorisk management principles emphasizes the use of a hierarchy of controls together with an iterative PDCA process to continuously improve work processes as technical knowledge evolves. Interactions between the leadership and the laboratorian confirm the commitment to promote both safety in the laboratory and the quality of the outputs. Similarly, the application of the HRO framework to life science laboratories will improve the culture of safety through open channels of communication not only with the leadership but also with all stakeholders.

Acknowledgments

The authors thank David Gillum, Karen Byers, Kalpana Rengarajan, and Barbara Owens for their comments and recommendations.

Author Disclosure Statement

No competing financial interests exist.

Funding Information

No funding was received for this article.

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