



Laboratory Processing of Specimens

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Introduction and Background

The laboratory processing of clinical specimens is an essential function for any hospital providing care for patients. Accordingly, laboratory administrators are required to have an operational laboratory that can provide not only accurate and reliable results but also an environment that is safe for the laboratory worker. Although low risk, any specimen has the potential to contain a pathogen that could cause a laboratory-acquired infection; thus whether supporting a small critical access hospital or a large acute care facility, the laboratory needs to be prepared to handle specimens with a potential to contain or known to contain a high-risk pathogen. These emerging high-risk pathogens (also defined as high-consequence pathogen [HCP] or risk group 4 [RG-4] pathogen) have the ability to cause serious or lethal human disease for which preventative or therapeutic interventions are not readily available.

The Ebola virus (EV) epidemic of 2014–2016 highlighted the need for medical facilities to enhance their capabilities to handle specimens that might contain a RG-4 pathogen [1]. In a recent survey of infectious diseases physicians, a question was asked as to where they think specimens with the potential to contain a RG-4 pathogen were tested. The results showed that <50% of these physicians surveyed had a clear understanding where this testing was performed. They suggested that laboratory testing was most likely performed off-site (38%) without describing where this might be or they were unsure where this testing was done (22%) [2]. In

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a follow-up to this survey, a compilation of comments from these physicians showed that the clinical laboratory generated the second highest level of comments after personal protective equipment (PPE), suggesting that many unknowns still existed on how the laboratory supported the care of patients infected with a HCP [3]. Another study also showed significant discrepancies in guidance documents for clinical laboratories from both professional and government sources which exacerbate the difficulty and confusion inherent in dealing with an emerging infectious disease [4].

Since the EV epidemic, the Centers for Disease Control and Prevention (CDC) in collaboration with individuals from medical facilities in the USA and those from resource-limited areas in Africa where patients with Ebola virus disease (EVD) were treated developed guidance materials for medical facilities for the management of patients with EVD. These documents included information for the laboratory such as generalized protocols for PPE usage [5], the safe handling and management of infectious waste [6], the managing and testing of clinical specimens [7], and the collection, transport, and submission of specimens [8]. Although these documents were developed with EV in mind, they were compiled as generalized to be useful for the handling of other high-risk pathogens. In addition, more specific protocols have also been developed for other emerging infectious diseases caused by such pathogens such as highly pathogenic influenza viruses [9] and Middle East Respiratory Syndrome (MERS) coronavirus [10]. These documents also provide templates for guidance as other new infectious diseases are identified.

Laboratories supporting small critical access hospitals or those supporting large acute care facilities therefore need to be prepared to handle specimens that might contain a RG-4 pathogen. This chapter provides simplified information on how to conduct a biological risk assessment, provide measures to mitigate risks, and perform pre-analytical, analytical, and post-analytical processing within a safe environment. In addition, advice is provided on how to expand testing as needed and to sustain readiness of the laboratory when the need for testing specimens that might contain a HCP occurs.

Safety: Risk Assessment and Mitigation

Given the ease of global travel, any facility, regardless of location, may face the need to identify and care for a patient with a dangerous or novel infectious disease. All laboratory workers therefore must be prepared to handle specimens from patients with highly hazardous communicable diseases that may be admitted to their institution [11]. The OSHA general duty clause requires that “employers furnish every employee a workplace that is free from recognized hazards that can cause or are likely to cause death or serious physical harm” [12]. Safety therefore is not a new concept for medical facilities, and procedures should be in place to allow for the safe handling and processing of specimens, no matter what the infectious source.

Recently, the CDC provided a framework for a tiered approach for US medical facilities to provide care for a person under investigation (PUI) for or a patient

Table 6.1 Laboratory resources needed to support the various roles of acute healthcare facilities to manage a patient under investigation for or infected with a high-consequence pathogen^{a,b}

Role	Facility needs
Frontline healthcare facilities ^c	Identify and isolate the person under investigation (PUI)
	Training in advanced techniques of PPE
	Training in specimen collection using advanced PPE
	Sufficient PPE to maintain PUI for up to 24 h
	Certified biosafety cabinet (or plastic shield barrier)
	Centrifuge with sealed rotors or safety cups
	Written procedures to safely perform in-house lab testing
	Specimen transport procedures (category A packaging)
Assessment hospitals ^d	Meet all processes for frontline healthcare facilities
	Have minimal laboratory testing capabilities ^e
	Appropriate staffing to operate laboratory 24/7
Treatment centers ^f	Meet all processes for frontline facilities and assessment hospitals
	Have essential laboratory testing capabilities ^g

^aPrepared from CDC Guidance documents [14–16]

^bAll facilities need to perform a biological risk assessment to identify and mitigate risks

^cRapidly identify and isolate patients with relevant exposure history and signs or symptoms, provide laboratory support for up to 24 h of care (to include transport of specimens for confirmation testing), and transport patient to assessment hospital or treatment center if needed

^dSafely receive and isolate patient, provide laboratory support for up to 5 days (including evaluation and management of alternative diagnoses), and transport patient to a treatment center as needed in consultation with public health officials

^eMinimal testing capabilities described in guidance documents [7, 11, 21]

^fSafely receives and provides medical care for a patient with a confirmed high-consequence pathogen to include laboratory support for the duration of the illness

^gEssential testing capabilities as provided by CDC guidance [7]

infected with EVD [13]. Although this was initially developed with EV in mind, the approach is now being developed around the assessment of any patient with a possible HCP. This tiered approach encompasses designating acute healthcare facilities as either frontline healthcare facilities [14], assessment hospitals [15], or treatment centers [16]. Table 6.1 describes some of the laboratory resources needed to support the various roles in this tiered approach for healthcare facilities.

One major goal of any laboratory to support these various roles for healthcare facilities is to minimize risk to laboratory personnel when handling clinical specimens. To do this, a biological risk assessment is first performed to determine the potential for exposure from sprays, splashes, or aerosols generated during laboratory activities. Although a qualitative assessment is a subjective process that involves professional judgment, the assessment is performed based on the potential of what can happen with assumptions made in the process [7]. The first part of the assessment is to identify the hazards (i.e., activities) that can cause exposure, prioritize the risks, and mitigate the identified risks using engineering controls, administrative controls (work practices), and the use of appropriate personal protective equipment (PPE). Although the utilization of appropriate PPE with training in proper donning

and doffing is a critical step for worker safety, the use of a certified biological safety cabinet for primary containment when handling or manipulating patient specimens is also recommended for the laboratory [5, 7, 17]. In addition, laboratory equipment that is used to process specimens should have closed tube processing (i.e., sealed rotor or safety cups for centrifugation), and if open tube processing occurs, the equipment should be manipulated within a biosafety cabinet. The ultimate goal for safety is to protect the laboratorians and environment from contamination while ensuring that an optimal level of care is provided to the patient [18].

Laboratory Testing

Pre-analytical Processes

The pre-analytical processes include the initial screening by triage staff of a PUI, the activation of protocols to isolate the patient during the assessment, the collection of specimens for screening, the transport of specimens to the laboratory, and the activation of a dedicated laboratory if needed. The decision to screen a patient is made in consultation with the relevant local and state health departments with advice as needed from the CDC. Once a decision has been made that laboratory testing is necessary, in-house developed procedures are followed concerning the collection of the specimens in the isolation room (hot zone) as well as the proper procedures to package and transport specimens to the appropriate laboratory for testing [19]. Table 6.2 provides a supply checklist for facilities to safely collect specimens that could possibly contain a HCP.

Prior to the collection of specimens, procedures should be developed to identify best method of collection (line draw, vacutainer, syringe, avoiding butterfly), as well as to identify those who have experience in specimen collection and have been routinely trained in advanced PPE techniques (nurse, laboratorian, phlebotomist, or other medical staff). When collecting a specimen, a partner system is suggested as a means to monitor for a safety breach and to provide a “second pair of hands” to help in the collection and initial processing of the specimens for transport. A recommended step-by-step partner method for specimen collection in the isolation area is provided in Table 6.3.

The initial screening process might include a limited number of specimens such as whole blood (to collect for plasma or serum) or specimens from other body sites such as a respiratory specimens or blood for culture. All facilities should have protocols developed and procedures drilled and exercised on an annual basis to safely collect specimens to evaluate a PUI for a HCP. For instance, guidelines are available to help facilities create appropriate processes to safely collect blood samples as needed [20]. Each step in the collection process should be evaluated by experts in infection control in an effort to limit exposure. This process requires multiple glove changes during the collection, multiple disinfection steps, and triple packaging of specimens within the patient isolation area. In addition, all facilities should have a plan in place to manage other potentially serious medical issues that may develop

Table 6.2 Supply checklist for the collection of specimens from a person under investigation for an infection with a high-consequence pathogen^{a-c}

Area	Supplies needed ^d
Isolation (hot zone)	Proper advanced PPE
	Appropriate specimen collection devices
	Appropriate disinfection wipes
	Medical waste container
	Preprinted patient labels with at least 2 identifiers
	Blue or black ink pen ^e
	Small sealable biohazard bags with absorbent material
	Large sealable biohazard bags
Packaging (clean zone)	Insulated category A box system (UN certified) ^f
	Insulated triple packaged system ^g
	Chain of custody paper work ^g
	Appropriate refrigerant
	Appropriate disinfection wipes

^aPrior permission is required from the local or state public health department to test for a high-risk pathogen

^bState public health officials should determine the best method to transport specimens to the jurisdictional public health laboratory for confirmation testing

^cFor the collection and transport, follow CDC or public health developed procedures

^dCheck supplies for expiration dates

^eUsed to label specimen collection containers with collector’s initials and date/time of collection. Use ink that will not smear when disinfected

^fIf transported by a commercial courier, follow Department of Transportation guidelines for packaging and labeling of these Category A infectious substances

^gFor in-house and local transfer of specimens. Chain of custody may be required for transport from public health laboratory to the CDC

while the PUI is in isolation and awaiting results of confirmation testing. Specific tests might include a complete blood cell count, electrolyte analysis, or specific direct tests for other infectious diseases caused by such pathogens as the influenza viruses, group A *Streptococcus*, and malaria protozoans. For those laboratories that support facilities where these patients might be sent for treatment, a list of essential tests have been described with additional supplemental tests that might be considered (Table 6.4) [7, 21]. Each medical facility needs to define which tests will be available following consultation among the appropriate medical staff and the laboratory administration.

When developing protocols to assess a PUI, facilities should carefully plan what supplies will be needed and the best placement for these supplies so they are readily available when needed. Storage of PPE and specimen collection kits placed near

Table 6.3 Recommended partner method for specimen collection in the isolation area (hot zone)^{a,b}

Step 1. Preposition supplies on a clean adjacent table/tray ^c
Step 2. Prepare patient according to specimen collection type(s)
Step 3. Collect specimen(s) following standard procedures and next place on disinfectant wipe open on table/tray
Step 4. Remove top glove, hand sanitize with new disinfectant wipe, and replace top glove
Step 5. Using a new disinfectant wipe, pick up the specimen collection container
Step 6. Wipe each container thoroughly with a new disinfectant wipe to remove any visible blood/specimen
Step 7. Lay specimen containers on a new disinfectant wipe and allow to air-dry
Step 8. Discard disinfectant wipes into the waste container
Step 9. Remove top glove, hand sanitize with a new disinfectant wipe, and replace top glove
Step 10. Pick up the collected specimen using a new disinfectant wipe, and place preprinted label on the container
Step 11. With the help of the partner, place the specimen collection container into a small biohazard bag (secondary container has absorbent material as appropriate)
Step 12. Wipe the outside of the small bag with a new disinfection wipe from bottom to top
Step 13. Carefully fold small bag to expel air and seal
Step 14. With the partners help, place the small biohazard bag(s) containing the collected specimen(s) into a larger biohazard bag (third layer)
Step 15. Repeat steps 10–14 for each specimen collected. All specimens can be placed into one large biohazard bag as space allows
Step 16. Once the specimens are in the large biohazard bag, carefully expel the air and seal
Step 17. With the help of the partner, wipe the outside of the large biohazard bag with a new disinfection wipe
Step 18. The partner not holding the large bag removes top glove, hand sanitizes with a disinfection wipe, and handed the larger bag while holding with a new disinfection wipe
Step 19. Carefully hand the triple packaged specimen(s) to a third person stationed within the clean zone
Step 20. Additional packaging will be done in the clean zone, dependent on where the specimen is to be transported for testing

^aFollowing approval, only predesignated staff trained and exercised in the proper PPE and collection procedures will collect specimens

^bRead out loud the step-by-step checklist when performing the collection process, and observe for any breach in safety

^cSupplies to include disinfection wipes, specimen collection containers, waste container, pre-printed patient labels, ink pen, and small/large biohazard bags

patient isolation areas should not contain supplies with short expiration dates, such as vacutainer tubes or disinfectant wipes. Instead, facilities should consider having supplies made available from the hospital current inventory for immediate availability.

Once a decision has been made to collect specimens and the appropriate specimens have been collected, the next step is to prepare the specimen for transport. Following the transport of the collected specimen(s) to the clean zone, additional packaging will need to be considered prior to transporting the specimen to the laboratory. The level of packaging will be determined by where the specimen is to be

Table 6.4 Other supplemental tests to consider depending on type of illness and travel history

Test	Method ^{a,b}	Disease
Antimicrobial susceptibility	Manual/automated	Bacterial
Blood culture	Manual/automated	VHF/Resp
Blood type	Manual (agglutination)	VHF
Influenza subtyping ^c	Molecular test ^d	Resp
Group A <i>Streptococcus</i>	Manual	Resp
Malaria	Manual/immunological	VHF
MERS	Molecular test ^d	Resp
Respiratory panels	Molecular test	Resp
Troponin	POC test	VHF
Urine	Dipstick manual	VHF
Emerging pathogen ^e	Varies	Varies

Abbreviations: *VHF* unspecified viral hemorrhagic fevers, *Resp* known/unknown respiratory pathogens, *POC* point-of-care, *MERS* Middle East Respiratory Syndrome

^aThe safety risks involved in using an automated or molecular test system need to be considered

^bSome of these assays involve the use of kits that can be manipulated within a biosafety cabinet.

^cIncludes avian influenza viruses H5 and H7 depending on travel history

^dTesting for avian influenza and MERS coronavirus is generally performed at the jurisdictional public health laboratory

^eRare emerging pathogen detection frequency will require screening to be performed at the CDC using research methods for detection

transported, whether to an adjacent in-unit laboratory, to another on-site laboratory, or to an off-site laboratory (local public health laboratory or federal laboratory). Specimens transported outside of the patient isolation area and through any public area must be triple packaged before transport. These specimens are considered “suspected Category A infectious substances” and therefore must be transported in accordance with OSHA (29 CFR 1910.1030) and DOT (49CFR Part 171–78) guidelines. For safety reasons, this holds true for transport of these high-risk specimens even within the confines of the hospital environment.

Triple packaging consists of a primary receptacle with secondary and outer packaging included. The specimen container used to collect the specimen from the patient is considered the primary receptacle (plastic recommended) and therefore must be sealable and leak-proof. Screw-capped tubes must be secured by adhesive tape and paraffin tape or have a manufactured locking closure. If collecting multiple primary receptacles, each should be placed into separate secondary containers (small biohazard bag). For liquid infectious substances, absorbent material sufficient to absorb all fluids in case of breakage should also be included inside each of the secondary containers. One larger, sealable biohazard bag is then be used as the third layer of packaging.

Triple-packaged specimens that are processed without additional testing within the patient containment unit laboratory can be handed directly to the laboratorian without any further packaging, while those transported outside the patient isolation area are to be packaged following guidance for Category A infectious substance packaging. In addition, a buddy system for specimen transport should be considered

with the appropriate security as needed when transporting specimens outside of the patient care area. A log or chain-of-custody form should also be considered for specimen tracking.

Any specimens collected from a PUI that are to be transported outside the facility to the public health laboratory or from the public health laboratory to the CDC should be shipped in UN specification packaging. The shipper must be trained and certified in Division 6.2 packaging (every 2 years) and is legally responsible for complying with all federal regulations for shipment of a Category A infectious substance. Commercial couriers must also meet requirements of the DOT (49CFR part 171–178) to include maintaining sufficient liability and documentation for each shipment. It is important to understand that commercial couriers have restrictions and variations on which Category A infectious substance shipments will be accepted for transport. Most commercial couriers will accept Category A packages that contain a specimen from a PUI for confirmation testing; however, once a patient has been identified as having a known HCP (by culture or by a molecular or serological assay), most commercial couriers will no longer accept these specimens for transport. To address issues for transport off-site using a commercial courier, facilities need to be advised of the complexity in shipping and have plans to address questions that may arise. In lieu of using a commercial courier, federal designation of a public health emergency also allows for law enforcement agents or other designated state or federal officials to transport specimens which have been triple packaged as Category A shipments without the shipper's declaration documentation or specialized training generally required of the transporter.

Facilities also need to be conscious of the regulations pertaining to the handling and shipping of specimens that might contain a select agent pathogen [22]. Current federal law states that specimens obtained from a patient infected with a select agent which are generated during the delivery of patient care are not considered regulated under the select agent regulations if not cultured; thus there are no requirements to document the transfer or destruction of these specimens [23]. However, these specimens are subject to the select agent regulations after acute care of the patient concludes. Further discussion of this issue can be found in the post-analytical section of this chapter describing the storage of excess clinical materials as well.

During the pre-analytical process, there may also be a need for frontline, as well as assessment facilities, to process specimens in-house prior to transfer. These steps might include centrifugation for the collection of plasma or serum, the preparation of a fixed smear for malarial testing, or the extraction of nucleic acid material [24]. A risk assessment should be performed to define where and how these processes can be safely implemented.

Analytical Processes

The analytical processes include those activities involved with the actual testing of the specimens. Having available the appropriate methods and equipment to conduct the laboratory testing are essential parts of this process. Included in this testing process

are equipment management plans such as documentation of the original test validation, a continuous validation process during testing, and ongoing calibration criteria as pertaining to reagent testing and validation. As a part of this, all clinical laboratories should have methods in place to provide a sufficient validated laboratory test menu to ensure that the care of the patient is not compromised. Laboratorians also need to be mindful that reference laboratory testing may not be available to handle specimens from these patients and alternative methods for testing need to be considered. Selecting the appropriate methods for testing might also include a combination of manual kit assays such as testing for malaria, pregnancy, or influenza; automated core testing assays such as those for electrolytes, liver function, and coagulation; and to point-of-care (POC) testing devices for multiple activities to include the evaluation for blood gases. The availability of resources and the risk assessment processes will help to determine which of these methods can be utilized safely in the laboratory and what alternative methods are available to provide patient care as needed.

Alternatively, testing for microbial pathogens other than the HCP will generally require kit-based methods. Automated instrument processing such as blood cultures, single-plex and multiplex assays using molecular methods, and identification/susceptibility testing methods need to be evaluated for the biohazard risks. In many instances, manual-based methods can be incorporated to perform the needed test to alleviate the need for processing on an automated instrument where close-tubed testing might not be available. In addition, if lab testing cannot be performed safely, empiric therapies may be considered by the medical care team.

All testing methods require the laboratory to have a quality management plan available to meet Clinical Laboratory Improvement Amendments (CLIA) regulations. These include performing quality control and proficiency testing and documentation that personnel have relevant laboratory education and experience qualification to perform the tests. A process for validation of new methods prior to implementation as well as processes for continued validation of accuracy, precision, and reliability to meet regulatory standards also needs to be considered. Furthermore, instruments will also require an ongoing maintenance plan as required by the manufacturer.

Finally, the ability to have access to validated POC instruments at the site of patient care to perform clinical chemistry and hematological assays, which can be manipulated in a safe environment by competent individuals, is important to meet patient management needs. Numerous POC instruments have been developed that could provide this support (Table 6.5). It is important however to ensure that these instruments are used as approved by the Food and Drug Administration (FDA). For instance, some POC devices that are used to test samples from critically ill patients may be considered off-label use (i.e., glucose meters), requiring that the laboratory establish performance specific for accuracy, sensitivity, specificity, reportable range of test results, reference intervals, and other performance characteristics as required. It is also important to ensure that a quality management program for each instrument be developed to meet all applicable federal and state regulations as well as the standards of the laboratory's accrediting agency and the device manufacturer's instructions. The regulatory standards may differ substantially depending on

Table 6.5 Point-of-care and compact analyzers used to provide laboratory testing in the care of patients known or under investigation for an infection caused by a high-consequence pathogen^{a-c}

	Test	CLIA	
Instrument	Type	Waived	Measured parameters ^c
Hemochron Jr.® Signature Elite	APTT cuvette	No	APTT
Hemochron Jr.® Signature Elite	PT cuvette	No	PT/INR
Piccolo® Xpress ^f	Liver plus disc	Yes ^h	ALB, ALP, ALT, AMY, AST,GGT, TBIL, TP
Piccolo® Xpress ^f	MetLAC 12 disc	No	ALB, BUN, Ca ⁺⁺ , Cl ⁻ CRE, GLU, K ⁺ , Na ⁺ , PHOS, tCO ₂ , LAC, Mg ⁺⁺
Piccolo® Xpress ^f	MetLYTE plus CRP disc	No	BUN, CK, Cl ⁻ , CRE, GLU, K ⁺ , Na ⁺ , tCO ₂ , CRP
i-STAT® System ^f	CHEM 8+ cartridge	Yes ⁱ	Na ⁺ , K ⁺ , Cl ⁻ , AG, iCa ⁺⁺ , GLU, BUN, CRE, HCT
i-STAT® System ⁱ	G3+ cartridge	No	pH, pCO ₂ , pO ₂
Sysmex pocH-100i	pochH-100 ⁱ pack	No	CBC with three-part differential (WBC, RBC, PLT), HGB, HCT
epoc™ blood analysis system	BGEM test card	No	pH, pCO ₂ , pO ₂ , Na ⁺ , K ⁺ , Ca ⁺⁺ , GLU, LAC, HCT

Abbreviations: *APTT* activated partial thromboplastin, *PT/INR* prothrombin time with international normalized ratio, *ALB* albumin, *ALP* alkaline phosphatase, *ALT* alanine aminotransferase, *AMY* amylase, *AST* aspartate aminotransferase, *GGT* gamma glutamyl transferase, *TBIL* total bilirubin, *TP* total protein, *BUN* blood urea nitrogen, *Ca⁺* calcium, *Cl⁻* chloride, *CRE* creatinine, *GLU* glucose, *K⁺* potassium, *Na⁺* sodium, *PHOS* phosphorus, *LAC* lactate, *Mg⁺* magnesium, *CK* creatine kinase, *HCT* hematocrit, *HGB* hemoglobin, *CRE* C-reactive protein, *AG* anion gap, *pCO₂* partial pressure of carbon dioxide, *pO₂* partial pressure of oxygen, *CBC* complete blood cell count, *WBC* white blood cell, *RBC* red blood cell, *PLT* platelet, *CLIA* Clinical Laboratory Improvement Amendments

^aControls are run at least daily or more frequently if specified in the manufacturer's instructions when patient testing is performed

^bA program is available to ensure that each person performing non-waived and waived testing maintains a satisfactory level of competence

^cAn appropriate proficiency testing or alternative assessment program has been established for each assay

^dQuality control and verification testing are required with each new lot received and if instrument or reagent performance is questioned

^eDoes not include calculated values

^fThese point-of-care instruments have multiple panels/cartridges that can be considered for testing

^gThis instrument performs a "self-check" every time the machine is activated and a test is performed

^hFor testing on whole blood only

ⁱFor testing on venous samples only

whether a CLIA-waived or non-waived assay is chosen. Frequency of external quality control testing can range from a per reagent lot verification to every 8 h dependent upon the FDA test complexity level, the manufacturers' recommendations, and any applicable accreditation standards. In some cases, external quality control frequency may be reduced by performing a thorough risk assessment of the device and

assay and developing an individualized quality control plan (IQCP). Facilities will also need to determine where POC testing is performed (at the bedside, in-unit laboratory, or in-hospital laboratory) and who will perform the testing. Individuals who will be operating the instruments must meet the competency standards as required for each assay. Another advantage of these instruments is the small size and the ability to perform testing within a biosafety cabinet as primary containment for safety. With the proper use of a biosafety cabinet, the potential for exposure to aerosolized highly infectious materials from these POC instruments can be reduced.

Other compact analyzers technically were not developed for POC testing, but are small enough in size to be useful for in-unit or dedicated small lab space testing. The compact size does allow for the placement of these instruments within a biosafety cabinet when testing highly infectious materials. Some instruments use a disc spinning (centrifugation) to perform microfluidic operations and therefore could result in the potential of aerosolization during the testing process [25]. These instruments are not CLIA-waived for all assays, and the testing of patient samples must be validated on-site before they can be used for testing.

Post-analytical Processes

The post-analytical processes include results reporting, reflex testing, waste management, environmental decontamination, storage of excess clinical materials, and an appropriate occupational health plan to monitor employees for potential exposures. The reporting of results becomes complicated when specimens are submitted to multiple laboratories, especially when the reporting involves multiple laboratory information systems (LIS) while maintaining compliance with the Health Insurance Portability and Accountability Act (HIPAA) regulations. Laboratories need to have procedures in place to deal with how the information will be transferred and build in the available LIS test fields to evaluate the reporting processes that will be used. The results reported will also impact what reflex testing might be needed to provide additional information for the care of the patient with the ability to have a rapid turnaround time. This additional testing may require help from not only the jurisdictional public health laboratory but also the submission of specimens to other federal laboratories such as the CDC.

Protocols also need to be developed on how to handle laboratory waste, to include processes for decontamination of specimens and procedures to archive excess clinical materials for follow-up testing (which may be required following experimental drug treatments) or for research in the evaluation of new diseases. Numerous processes have been described for the decontamination of waste that might contain Ebola virus [6, 26, 27]. The Division of Select Agents and Toxins (DSAT) has recently described protocols for the inactivation of select agents [23]. Included is guidance on how to determine non-viability. Although viability testing is no longer considered the standard in all instances, specimen samples that are retained and subsequently identified to contain a select agent pathogen must meet

the standards for inactivation that shows the materials contains no viable pathogen before being retained in a laboratory not approved for the select agent involved.

An additional issue to consider is the decontamination of laboratory equipment after testing samples that may contain a RG-4 pathogen. Manufacturers have provided methods that might be considered, but these range from minimal processing using bleach wipes to incineration of the instrument after utilization [28]. Although studies have shown that 10% bleach at a minimal contact time of 5 minutes is highly effective to inactivate EV and most likely other high-risk pathogens, an internal risk assessment and consultation with manufacturers needs to be considered as protocols are defined to monitor equipment used under these circumstances [29].

Finally, employers whose workers may be at risk of a laboratory-acquired infection are required to have a comprehensive occupational safety and health program to not only anticipate work-related risks but also to describe strategies for protection against these risks [30]. This program needs to be facility specific and includes processes designed so that the healthcare worker will not be subjected to unreasonable burdens such as quarantine in the absence of symptoms. Overall, specifics of working with known or unknown RG-4 pathogens need to be considered on a case-by-case basis.

Sustainability

The Ebola epidemic has engaged laboratory administrators to not only examine their existing capabilities but also to determine laboratory sustainability to respond to an event that may or may not occur in the future. Although frontline hospitals should have programs in place to isolate and assess a PUI for a HCP, the real risk for the diversion of significant funds to be ready for a rare event is for those facilities that will be responsible to provide expanded laboratory support to screen and care for these patients, i.e., assessment hospitals and treatment centers. In addition to an essential list of laboratory tests that will be available to provide care for the HCP patient, the laboratory also needs to define what equipment/supplies are necessary to provide these required tests. The validation of new test protocols and the ability to sustain readiness while adhering to the regulatory requirements to offer testing are costly. These costs include having available and competent staff to support the specialized laboratory testing for an in-unit laboratory, but also the costs for maintenance of accreditation for specialized equipment, equipment depreciation and service contracts, and inventory to keep an adequate supply of reagents available for patient testing (Table 6.6). These are added costs that are necessary to preserve a quality management program that will meet the regulatory requirements of a certified laboratory. Although some governmental support may be available for medical facilities to sustain the capability to provide treatment for patients with HCPs, financial commitment from the facility will also be required. Time will tell how much of an obligation will be necessary for these medical facilities to be in a ready state to care for these patients.

Table 6.6 Major costs to maintain readiness of a laboratory to support the care of a patient infected with a high-consequence pathogen

Cost category	Needs
Training	Personnel have appropriate education and experience
	Regular in-service training on each instrument to maintain competency
	Donning and doffing of PPE
	Working within the containment laboratory
	Competent staffing to operate laboratory 24/7
Accreditation	Packaging and shipping of Category A substances
	All POC tests meet standards for accreditation
	Proficiency testing program participation
	Record maintenance required for accreditation
	Temperature monitoring of equipment and reagent storage
	Patient reporting system
Equipment	Test documentation for adverse events
	Meet all regulatory standards/manufacturers recommendations
	Ongoing equipment assessment
	Service contracts and depreciation
Inventory control	Preventative maintenance program
	Inventory control checklist template
	Adequate storage conditions for reagents
	Monitor shelf life of consumables
	Adequate supplies to provide care upon activation of the laboratory
	Specimen collection devices adequate supply

Abbreviations: *PPE* personal protective equipment, *POC* point-of-care

Conclusions

Laboratorians understand that work in any laboratory, whether classified as high containment or not, is not without risks and that their employer is required to have available the equipment, facilities, and access to specialized training to mitigate these risks. Laboratorians also acknowledge that technology is constantly changing and that adaptation to these changes is necessary. The balance of safety and providing quality results for patient care continues to be a delicate balance for the laboratory. Two future areas that may impact the laboratory overall, but are clearly needed for the high containment labs, include access to specimen collection devices that have the capacity to inactivate pathogens but still allow for the specimen to be acceptable for testing and the development of automated instruments by manufacturers that provide work flow efficiencies that includes close system testing along with specimen tracking. The development of specimen collection devices containing chemicals that can render a pathogen inactive while still stabilizing the specimen for testing has only recently been commercially developed for HIV testing [31, 32]. Additional work needs to be done in this area to expand the commercial

availability of these types of collection devices for other applications. Making specimens noninfectious will also enhance the ability to transport and provide the means for in-house, long-term storage of these specimens to evaluate experimental drug applications and for potential future research activities without the regulations of the select agent program. With the development of safer equipment by manufacturers, the ability to test specimens with minimal handling will also reduce exposure opportunities in the laboratory. These and other ongoing changes will help hospitals enhance safety while providing optimal care for patients with infections caused by HCPs.

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