LABORATORY BIOSAFETY MANUAL
FOURTH EDITION
AND
ASSOCIATED MONOGRAPHS

OUTBREAK PREPAREDNESS AND RESILIENCE

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Outbreak preparedness and resilience

(Laboratory biosafety manual, fourth edition and associated monographs)

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Glossary of terms

Biological agent: A microorganism, virus, biological toxin, particle or otherwise infectious material, either naturally occurring or genetically modified, which may have the potential to cause infection, allergy, toxicity or otherwise create a hazard to humans, animals, or plants.

Biosafety: Containment principles, technologies and practices that are implemented to prevent unintentional exposure to biological agents or their inadvertent release.

Biosecurity: Principles, technologies and practices that are implemented for the protection, control and accountability of biological materials and/or the equipment, skills and data related to their handling. Biosecurity aims to prevent their unauthorized access, loss, theft, misuse, diversion or release.

Communicability: Capability of a biological agent to be transmitted from one person or animal to another, either through direct or indirect transmission. This is often related to/represented by an epidemiological measurement called the basic reproduction number (R_0) which is an average number of secondary infections generated by a single infected individual in a fully susceptible population.

Containment: The combination of physical design parameters and operational practices that protect personnel, the immediate work environment and the community from exposure to biological agents. The term "biocontainment" is also used in this context.

Decontamination: Reduction of viable biological agents or other hazardous materials on a surface or object(s) to a pre-defined level by chemical and/or physical means.

Disinfectants: Agents capable of reducing the number of viable biological agents on surfaces or in liquid waste. These will have varying effectiveness depending on the properties of the chemical, its concentration, shelf life and contact time with the biological agent.

Disinfection: A process to eliminate viable biological agents from items or surfaces for further safe handling or use.

Exposure: An event during which an individual comes in contact with, or is in close proximity to, biological agents with the potential for infection to occur. Routes of exposure can include inhalation, ingestion, percutaneous injury and absorption and are usually dependent upon the characteristics of the biological agent. However, some infection routes are specific to the laboratory environment and are not commonly seen in the general community.

Hazard: An object or situation that has the potential to cause adverse effects when an organism, system or (sub)population is exposed to it. In the case of laboratory biosafety, the hazard is defined as biological agents which have the potential to cause adverse effects to personnel and/or humans, animals, and the wider community and environment. A hazard does not become a "risk" until the likelihood and consequences of that hazard causing harm are taken into account.

Inactivation: Removal of the activity of biological agents by destroying or inhibiting reproductive or enzyme activity.

Incident: An occurrence that has the potential to, or results in, the exposure of laboratory personnel to biological agents and/or their release into the environment that may or may not lead to actual harm.

Infectious dose: The amount of biological agent required to cause an infection in the host, measured in number of organisms. Often defined as the ID_{50}, the dose that will cause infection in 50% of those exposed.

Infectious substances: The term applies to any material, solid or liquid which contains biological agents capable of causing infection in either humans, animals or both. Infectious substances can include patient specimens, biological cultures, medical or clinical wastes and/or biological products such as vaccines.

Overpack: Several packages combined to form one unit and sent to the same destination by a single shipper.

Pathogen: A biological agent capable of causing disease in humans, animals or plants.

Personal protective equipment (PPE): Equipment and/or clothing worn by personnel to provide a barrier against biological agents, thereby minimizing the likelihood of exposure. PPE includes, but is not limited to, laboratory coats, gowns, full-body suits, gloves, protective footwear, safety glasses, safety goggles, masks and respirators.

Primary containment device: A contained workspace designed to provide protection to its operator, the laboratory environment and/or the work materials for activities where there is an aerosol hazard. Protection is achieved by segregation of the work from the main area of the laboratory and/or through the use of controlled, directional airflow mechanisms. Primary containment devices include biological safety cabinets (BSCs), isolators, local exhaust ventilators and ventilated working spaces.

Prophylaxis: Treatment given to prevent infection or to mitigate the severity of the disease if infection were to occur. It can be delivered before possible exposure or after exposure before the onset of infection.

Risk: A combination of the likelihood of an incident and the severity of the harm (consequences) if that incident were to occur.

Risk assessment: A systematic process of gathering information and evaluating the likelihood and consequences of exposure to or release of workplace hazard(s) and determining the appropriate risk control measures to reduce the risk to an acceptable risk.

Transmission: The transfer of biological agent(s) from objects to living things, or between living things, either directly or indirectly via aerosols, droplets, body fluids, vectors, food/water or other contaminated objects.

Validation: Systematic and documented confirmation that the specified requirements are adequate to ensure the intended outcome or results. For example, in order to prove a material is decontaminated, laboratory personnel must validate the robustness of the decontamination method by measurement of the remaining biological agents against the detection limit by chemical, physical or biological indicators.

Zoonotic disease (zoonosis): Infectious disease that is naturally transmitted from animals to humans and vice versa.

Executive summary

A major factor in effectively controlling an outbreak of infectious disease is to have access to rapid and reliable laboratory diagnostic results. The need to provide diagnostic results quickly in an outbreak situation increases the workload for existing laboratories, and/or requires deployment of laboratory facilities and competent personnel to an outbreak zone, and brings extra challenges including maintaining or establishing good biosafety practices. This monograph is written for laboratory managers and others involved in establishing and running safe outbreak laboratories for public health threats ranging from localized infectious disease outbreaks in remote areas to worldwide emergencies such as the SARS-CoV-2 (COVID-19) pandemic. The monograph aims to guide personnel on operational procedures based on lessons learnt from responses to previous outbreaks, including the West African Ebola virus outbreak of 2014–2016.

The information in this monograph on outbreak preparedness and resilience is designed to accompany and support the fourth edition of the WHO *Laboratory biosafety manual* (core document) and other associated monographs. The manual and the monographs adopt a risk- and evidence-based approach to biosafety rather than a prescriptive approach in order to ensure that laboratory facilities, safety equipment and work practices are locally relevant, proportionate to needs and sustainable. Emphasis is placed on the importance of a "safety culture" that incorporates risk assessment, good microbiological practice and procedure and standard operating procedures, relevant introductory, refresher and mentoring training of personnel, and prompt reporting of incidents and accidents followed by appropriate investigation and corrective actions.

The other associated monographs provide detailed information and help implement systems and strategies on the following specialized topics: risk assessment, laboratory design and maintenance, biological safety cabinets and other primary containment devices, personal protective equipment, decontamination and waste management, and biosafety programme management.

The emphasis in this monograph is the application of the risk- and evidence-based approach to the planning, preparedness and operation of the outbreak laboratory. The purpose of the risk assessment process described is to evaluate the laboratory activities selected for the biological agent(s) and the expertise and resources available in order to guide the laboratory design and workflow. The laboratory containment strategy selected will require relevant personal protective equipment and operational practices to protect laboratory personnel within the laboratory and prevent inadvertent release of biological agents from the laboratory. This can be difficult where resources are limited, and pragmatic solutions for specimen transport and decontamination of waste may be required. Working in an outbreak laboratory can bring extra challenges to the laboratory personnel so guidance on training, support, occupational health and responses to emergency situations is also provided.

SECTION 1

INTRODUCTION

Biosafety and biosecurity are central to the protection of human health from hazardous biological agents because these disciplines enable a safe targeted response to disease to be conducted based on scientific evidence in order to limit the spread and consequences of infectious diseases. This is of particular importance in an outbreak, which can occur without any warning, and can affect the health of whole populations as well as their social well-being and economic security. Risks associated with highly infectious diseases emphasize the need for effective measures to prevent, detect, respond to and learn from outbreaks.

Ensuring that potentially infectious specimens can be safely taken, transported, inactivated, processed and securely stored in adequately equipped facilities by well trained competent laboratory personnel are all elements of biosafety and biosecurity.

Since 2003, many outbreaks have been caused by human pathogenic viruses (Ebola virus, Zika virus, SARS-CoV-1, MERS-CoV, chikungunya virus, yellow fever virus, SARS-CoV-2) and bacteria (*Vibrio cholerae, Bacillus anthracis*) when either a new pathogen emerged in a population, or an existing pathogen emerged in a new population, or the number of cases of a known pathogen swiftly rises above the normal range. These outbreaks bring challenges to the responding laboratories, whether they are already operational in the region or specifically established to respond to the outbreak. These challenges include providing sufficient diagnostic capacity, and rapidly training and deploying the workforce needed.

Using lessons learnt from responding to previous outbreaks, including the West African Ebola virus outbreak of 2014–2016 and the early phase of the SARS CoV-2 outbreak, this monograph aims to guide laboratory managers and others involved in setting up outbreak laboratories in how to rapidly and effectively respond to the demands placed on them by the outbreak and establish safe ways of working.

The information in this monograph on outbreak preparedness and resilience is designed to accompany and support the fourth edition of the WHO *Laboratory biosafety manual (1)* (core document) and other associated monographs. The manual and the monographs adopt a risk- and evidence-based approach to biosafety rather than a prescriptive approach in order to ensure that laboratory facilities, safety equipment and work practices are locally relevant, proportionate to needs and sustainable.

The other associated monographs provide detailed information and help implement systems and strategies on the following specialized topics: risk assessment *(2)*, laboratory design and maintenance *(3)*, biological safety cabinets and other primary containment devices *(4)*, personal protective equipment *(5)*, decontamination and waste management *(6)*, and biosafety programme management *(7)*.

1.1 Stages of an outbreak

An outbreak has several stages. These can vary in severity and progression depending on the type of pathogen causing the outbreak, the effectiveness of early warning systems, the preparedness and response time, and cultural and security factors. The stages of an outbreak include:

- pre-outbreak,
- individual cases and small clusters of disease,
- widespread disease,
- outbreak control, and
- post-outbreak.

The amount and type of resources required by laboratories will change throughout the course of an outbreak.

1.1.1 Pre-outbreak

This is the period when no cases of disease are reported in humans. However, ongoing surveillance systems should be in place at the local, country and international level to monitor signs of potential outbreaks. At the laboratory level, research for improved detection methods, pathogenicity models, transmission routes and communicability of emerging pathogens should continue alongside identification/manufacture of potential prophylactic and post-disease onset treatments. It is important to mobilize sufficient resources for maintenance of laboratory equipment and infrastructure and for refresher training for laboratory personnel to maintain their expertise.

1.1.2 Individual cases and small clusters of disease

The onset of an outbreak starts with individual cases and leads to small clusters of people contracting a disease. Surveillance systems should detect these cases and alert the appropriate authorities to enable suitable and timely preparation to respond to a potential outbreak that may require extra supplies and resources. At this stage, the number of specimens received by laboratories for diagnostic analysis is likely to be low.

Steps taken at this stage include:

- identifying the causative pathogen,
- determining the type of diagnostic test(s) required to establish whether a patient is infected with the causative pathogen of the outbreak or another agent that causes similar symptoms,
- establishing the logistics of transporting specimens and supplies,
- ensuring availability of supplies, and
- establishing the logistics of processing a high influx of specimens in a timely way (surge capacity).

It is important to be aware that an increase in the number of cases of a particular disease above the normal level can sometimes go unnoticed for some time, and that symptoms of many diseases can begin with non-specific fever symptoms. Detection and identification of outbreaks can be challenging, especially when background endemic diseases such as malaria or influenza are prevalent.

If an outbreak of a highly infectious disease is suspected, this should be reported to the appropriate national and international authorities as stated by the International Health Regulations *(13)*. If the affected health care facility, for example, hospital, has its own laboratory, this should be notified so that appropriate biosafety and biosecurity measures can be taken, such as secure storage of specimens, disinfection, contact logging of laboratory personnel and possibly the interruption or discontinuation of routine work.

1.1.3 Widespread disease

At this stage, the disease may spread to other communities, regions or countries. The number of specimens received by laboratories for diagnostic analysis is likely to be very high at this stage. As a result, laboratory resources and supplies can become exhausted. The laboratory management must, however, ensure sustained availability of supplies and equipment. Prioritization of testing may be required, for example, tests for patients and health care workers prioritized over the general population.

1.1.4 Outbreak control

The government, frontline health care workers and health officials need to work together to limit the spread of the disease and put in place preventive measures. Often, additional knowledge can be gained about the pathogen's characteristics, its pathogenicity and transmissibility which can help control the spread of disease and aid research and future preparedness. The number of specimens received by laboratories for diagnostic analysis is likely to remain high, but the proportion of positive specimens will decrease as an outbreak is brought under control.

1.1.5 Post-outbreak

New cases of disease become less frequent until none are found. At this stage, vigilance is very important to ensure risk control measures remain in place to prevent further cases and minimise the risks of a second wave in the outbreak occurring. The number of specimens received by laboratories for diagnostic analysis is likely to be high, but will decrease gradually until the outbreak is declared over. An outbreak is normally declared over when two incubation periods of the disease have passed with no infections being detected. Once the outbreak is declared over, surveillance still needs to continue in order to detect any re-emergence of the disease. Lessons learnt from the outbreak should be recorded and used for future planning and preparedness.

1.2 Preparedness

The key to prevention and containment of outbreaks is preparedness. This includes early-warning surveillance, and local, national and international cooperation to ensure rapid and appropriate responses. The national capacity for handling hazardous biological agents should be regularly assessed and appropriate levels of support and resources to help with outbreak response should be made available and secured. Procedures should be in place for reliable and rapid communication between laboratories, hospitals, non-governmental organizations, international and government organizations and the wider public, including processes for information management such as recording and communicating patient data securely.

SECTION 2

RISK ASSESSMENT

Risk assessment is essential to ensure the safety of personnel working in laboratories. It allows the risks of working with hazards to be evaluated and used to determine and implement a set of risk control measures to reduce those risks to an acceptable risk. In the context of biosafety, risk is a combination of the likelihood of exposure to a biological agent (the hazard) and the consequences of that exposure (severity of infection and subsequent transmission potential). The steps to follow in a risk assessment are shown in Figure 2.1. The steps of the risk assessment framework (Figure 2.1) are described in detail in the *Laboratory biosafety manual*, fourth edition (section 2) and templates can found be in *Monograph: risk assessment (2)*. These steps are the same for outbreak preparedness and response.

Figure 2.1 Steps in the risk assessment framework

It is important to note that an additional risk assessment would be required if personnel are to be deployed into an outbreak area. This would assess risks to laboratory personnel outside of the laboratory since they would be living in an outbreak area and could be exposed to the causative agent, and other pathogens, by interaction with potentially infected people or through the environment or animal vectors.

2.1 Gather information

The first step of a risk assessment is to gather information about the biological agent and the range of tests that can be performed. The causative pathogen of an outbreak may be known and well characterized, but it may also be an emerging pathogen or a novel agent (pathogen X), in which case there may be limited or no information about its pathological characteristics or transmission.

Outbreaks which cause the most threat to human populations are those which have serious consequences of exposure, a high likelihood of (fast) spread in the population, and no or limited treatment options and prevention measures. This means that an outbreak is a threat not only to the local population but also to regional and potentially international populations.

Key considerations when gathering information for a risk assessment for an outbreak response include:

- the type of biological agent and its pathogenic characteristics, if known,
- the route of transmission (through the air, body fluids, a vector, or direct contact with infected individuals or an item they have contaminated).
- the type and number of procedures to be carried out on specimens received by the laboratory,
- the type of laboratory facilities and equipment available,
- human factors, for example, number and level of competence of the laboratory personnel,
- other factors that might affect laboratory operations, for example, legal, cultural and socioeconomic factors, public perception, location and accessibility, logistic difficulties, and security, and
- susceptibility of the biological agent to inactivation and disinfection procedures.

Where emerging or novel pathogens are the cause of an outbreak, other data might be requested to help risk assessment including medical information on patients, epidemiological data, suspected route(s) of transmission and geographical origins.

A range of tests may be available for diagnostic or research purposes including culture, detection of pathogen nucleic acid by amplification or sequencing, serology and blood biochemical assays to support patient treatment. Information about each test needs to be gathered to assess which methods are appropriate and can be performed safely. If a choice of diagnostic tests is available, it is advisable to select the method with the lower risk.

2.2 Evaluate the risk

Once information has been gathered, the laboratory risks can be evaluated to enable the development of a risk mitigation strategy. Key points to consider when evaluating the risks include:

- how exposure to the biological agent could occur,
- how the biological agent could be released from the laboratory,
- the likelihood of exposure or release occurring, and
- the consequences of exposure or release.

This information should be assessed to identify the overall initial risk of the laboratory activities (that is the risk before risk control measures have been implemented), and to determine the acceptable risk.

It is important to note that no work is risk free; a certain risk will always exist with any procedure. Therefore, a balance is required between carrying out the work and ensuring that personnel and the community are as safe as practicably possible. In outbreak situations, the risk to personnel could be higher compared with normal day-to-day work as there will be a higher frequency of positive specimens and the work environment may be more stressful. Therefore, better primary engineering and procedural risk control measures may need to be in place to protect the personnel than are found in a routine laboratory.

The acceptable risk for an organization or laboratory is the residual risk after the risk control measures have been put in place. Determining the acceptable risk allows a benchmark to be set against which initial risk can be reduced through the implementation of appropriate risk control measures. If the initial risk is higher than the acceptable risk, risk control measures will be needed to reduce and control those risks. Outbreak situations will almost certainly require many risk control measures to bring the risk of infection to laboratory personnel to an acceptable risk.

Characteristics of the pathogen that could influence the likelihood of an exposure occurring are: route of transmission, infectious dose, concentration of the biological agent, its stability in the environment and its sensitivity to disinfectants.

The factors that can influence the consequences of an exposure are: severity of the disease, transmissibility of the disease, incubation period (a long incubation period increases the potential of travellers to spread the disease in their home countries), prevalence of asymptomatic carriers and zoonotic potential.

The overall risk is increased by ill-advised laboratory activities such as: handling of leaking or badly packed specimens, insufficient disinfection and/or inactivation of specimens and waste, use of sharps when performing work with potentially infectious specimens, and laboratory personnel not following protocols.

These activities must be addressed in the risk assessment process and communicated effectively to laboratory personnel so they recognize the danger posed by these situation/practices and respond appropriately to protect themselves and others.

2.3 Develop a risk control strategy

The risk control strategy for outbreak laboratories should be based on the evaluated risk. The strategy should include risk control measures proven to be effective and practical in other standard and outbreak laboratories or strategies adapted from those. The choice of risk control measures will always depend on the resources available to support the risk control strategy for laboratory activities but deviation from standard practices must be carefully considered and justification given. When developing a risk control strategy, the following need to be determined:

- what resources are available for risk control measures,
- what are the most appropriate risk control strategies for the available resources,
- whether enough resources are available to put in place and maintain the risk control measures, and
- whether the proposed risk control strategies are effective, sustainable for the course of the outbreak and achievable in the local context.

Once the risk assessment has been completed and the required risk control measures defined, a gap analysis should be done to see what risk control measures are already in place and what further resources are needed to bring the risks to an acceptable risk. Risk control measures could include: primary containment devices, personal protective equipment (PPE), disinfectants, devices or chemicals for the inactivation of the biological agent, special standard operating procedures (SOPs) and good microbiological practice and procedure (GMPP), special specimen packaging, and training of personnel and other workers on laboratory activities. A combination of risk control measures is normally required to reduce risks to acceptable risks and to prevent incidents. More information and examples about GMPP can be found in the fourth edition of the WHO *Laboratory biosafety manual* subsection 3.1.

The risk control measures need to be sustainable throughout the outbreak response. Depending on the length of the outbreak, equipment will need to be maintained or replaced. It is likely the equipment will be detrimentally affected by the work more quickly than in a standard laboratory as it may be used for extended hours in less than optimal conditions. In addition, spare parts and engineers may not be locally available and so ensuring the availability of spare equipment at the beginning of the outbreak to replace faulty equipment will enable the risk control measures to be sustained over longer periods of time with minimal delay in service. If there are changes in activities, equipment, personnel or facilities, then protocols should be re-evaluated to determine if any adaptations are required to ensure safe working conditions.

2.4 Select and implement risk control measures

After information on the biological agent has been obtained, the risks of the laboratory activities evaluated and a risk control strategy developed, the risk control measures need to be selected and implemented. Before starting any work, the following conditions should be met.

- Any national or international regulations that have prescribed risk control measures have been identified and implemented.
- All risk control measures needed to carry out the work have been included in the budget, purchased and are available and sustainable.
- Available risk control measures are sufficiently effective or multiple risk control measures are used in combination to enhance effectiveness.
- Selected risk control measures align with the risk control strategy.
- The residual risk identified after risk control measures have been implemented is acceptable.
- Additional resources are available if required for the implementation of further risk control measures.
- Approval to conduct the work has been granted from the relevant authorities (local and/or international depending on the nature of the outbreak).
- The relevant personnel have been informed of the risk control strategies.
- Operational procedures are in place and personnel involved in the work have been appropriately trained.

The availability of high-quality reagents, laboratory consumables, disinfectants, equipment, telecommunication services and electrical power supply must be ensured, as must logistic considerations such as the reliability of the supply chain. Resources need to be selected that work reliably under the climate conditions in the outbreak area. Reagents or consumables that do not need a cold chain or cooling are preferred.

Any new equipment and/or laboratory facility must be properly installed, operated and maintained by trained and competent personnel. Reliable service and maintenance of the equipment must also be available, including spare parts, supplies and technical expertise. This expertise may not be available locally so laboratory personnel may need extra training to service equipment. Laboratory protocols and documentation should detail the monitoring and inspection of equipment carried out by laboratory personnel to ensure it is functioning correctly and a "buddy system" can be implemented where safety-critical steps are observed by a colleague.

A practical assessment should be conducted before the laboratory is operational to ensure that the selected risk control measures are feasible in the outbreak context. This assessment may include:

- test runs and exercises with mock specimens to demonstrate that the risk control measures are practical and compatible with the diagnostic workflow,
- test runs of equipment and facilities with performance checks, for example, ventilation, autoclaving equipment and electricity supply, and
- exercise challenges with simulated incidents, for example, hazardous spills, contamination-tracing indicators and power cuts.

Once all the risk control measures have been put in place, the residual risk then needs to be assessed and compared with the predefined acceptable risk. The approval to conduct work should be granted by an authority responsible for the diagnostic laboratory. If an international response to an outbreak in an affected country or countries is required, then the appropriate national authority should have a role in approving the laboratory, which may include review of diagnostic strategies and methodologies, review of test assay performance data and applied biosafety measures based on current scientific knowledge and evidence, as well as quality assessment of imported medical laboratory reagents and equipment.

All personnel involved in or at risk of being affected by the laboratory activities must be informed of the risk and risk control strategies. This people may include:

- anyone having access to the laboratory facilities,
- personnel directly working with specimens,
- personnel transporting the specimens,
- laboratory personnel working in the same or nearby laboratory rooms,
- cleaning personnel and liaison officers, and
- executive personnel and deputies coordinating and with responsibly for the laboratory activities.

Training of personnel is a key element during an outbreak response and essential for biosafety. All personnel should have relevant laboratory experience and skills before starting work. Laboratory personnel who have not been deployed before should receive appropriate and comprehensive training outside the outbreak laboratory with specialized trainers before deployment, including on the risk control strategies. More about training can be found in section 4 of this monograph on personnel competence and training.

2.5 Review risks and risk control measures

Risks are likely to change more often in outbreak situations than during routine diagnostic work. This is because knowledge of the biological agent is gathered throughout the course of the outbreak, the number of specimens to be tested changes, the types of test change, different laboratories and/or equipment are used, and incidents occur or feedback is received that indicate that improvements can be made. Therefore, to maintain biosafety in the laboratory, risks and risk control measures must be reviewed frequently to evaluate if the risk control measures are still sufficient and effective.

Assessments will need to be made regularly during the outbreak response to determine whether some risk control measures are put at risk by equipment failure or lack of supplies. In this case, suitable alternatives, which might need a new risk assessment, may be required; in the worst case, laboratory operations may have to be suspended. On the other hand, improved technologies may be available that decrease the risks in the laboratory.

Examples of possible changes during an outbreak could include:

- additional laboratory activities such as new tests need to be performed with new devices and new SOPs,
- SOPs of established procedures change,
- new personnel come to work in the laboratory who need to be trained before starting work,
- the laboratory is moved to another site or expanded to include additional sites, and
- working hours are extended.

New information on the biological agent or new developments might also influence laboratory activities. The development of a vaccine could mean a lower consequence of exposure for personnel when vaccinated, or a new or newly discovered route of transmission could mean that different risk control measures need to be considered in the laboratory. In such cases, the risk assessment must be reviewed to determine the effect of these changes and to decide if existing risk control measures are adequate or if additional risk control measures are needed.

Sometimes, an unexpected event can occur which requires an immediate dynamic risk assessment, such as an equipment breakdown resulting in a spillage hazard or a breach in the biological safety containment. Each situation will need to be assessed separately, sometimes rapidly, for safety of personnel, containment of any biological risk and continuity of laboratory activities.

SECTION 3

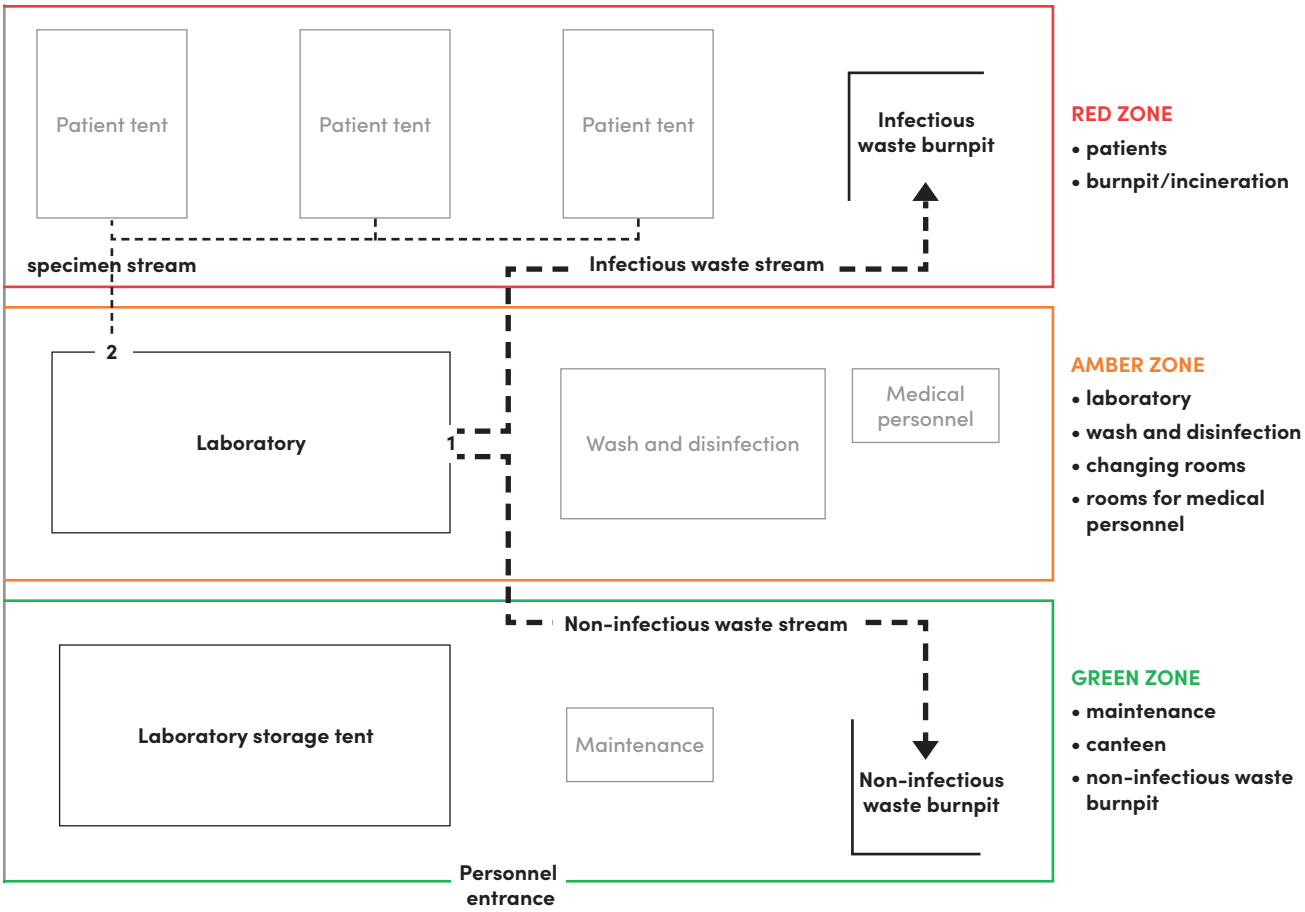
FACILITY DESIGN

Ideally, an outbreak laboratory is situated on a secure site where infrastructure such as power, water, effluent treatment, autoclaves and incinerators are located. It is also beneficial if the laboratory is also close to hospitals or treatment facilities so specimens can be delivered easily and communication with the medical teams is efficient.

A standard outbreak treatment centre is arranged to have a “green zone” (clean area), an "amber zone" and a “red zone” (where patients are treated and the infectious waste management system is located). If the laboratory is located within this type of facility it should be situated in the amber zone between the red and the green zones so the laboratory personnel can access the facilities in the green area, but the laboratory can connect to the red zone through a window for easy transfer of specimens (Figure 3.1).

3.1 Mobile laboratories

Mobile laboratories enable a quick diagnostic response. They are especially useful at the beginning of an outbreak as they have the potential to be quickly relocated with minimal external support. Two main models for mobile laboratories exist. In the first model, the laboratory equipment and consumables are boxed, transported and unpacked in a tent or simple building. In the second, the laboratory is built into a shipping container or lorry that can be driven to the outbreak. Mobile laboratories are equipped and validated in advance to perform diagnostic testing of different biological agents and are designed to operate as independently as possible. Ideally, these mobile laboratories will have reliable power and water supplies but often they can be run from generators or in the short term from vehicle batteries.



1 Laboratory entrance **2** Window for specimen reception

Figure 3.1 Example of a laboratory in the "amber zone" in an Ebola virus disease treatment centre between the "red zone" and the "green zone"

3.2 Outbreak laboratories in buildings

A simple building can be used as an outbreak response laboratory. This can have advantages over mobile laboratories because more space is usually available for equipment, the building will have water and power supplies, equipment can be more easily changed if needed than equipment in a container or lorry laboratory, and the building is more resilient to bad weather and more secure than a tent. Often, it will be necessary to work in established local laboratories which presents unique challenges as acceptable risks may be different than detailed in risk assessments. A risk assessment of working in that specific laboratory must be completed prior to work which will have to consider the whole laboratory and activities within, not just the outbreak response agent and activity.

3.3. Outbreak laboratory infrastructure

Whether an existing building or a mobile alternative is used, the local geographic and meteorological conditions must be considered, such as earthquakes, landslides, extreme temperatures and floods.

In most cases, the infrastructure on the laboratory site is limited and therefore organization of the laboratory work is challenging. Reliable electrical power and water supplies are essential for the laboratory to function and, an effluent system, autoclave and an advanced incinerator instead of a burn pit are preferred features of a laboratory site. If these preferred features are not available, then risks must be reduced using the most robust procedures possible before commissioning a laboratory. Examples of how these risks can be reduced include fitting an uninterruptable power supply (a back-up battery) to critical electrical equipment to allow safe completion of work where the power supply can fail.

The physical security of the laboratory facility and personnel must be ensured. Fences around the buildings, tents and stocks together with access risk control measures may be necessary depending on local security assessments, so that unauthorized people, including patients, cannot gain access to the laboratory facilities, which could put themselves and laboratory personnel at risk.

3.4 Laboratory integration as part of the outbreak response

Outbreak laboratories should develop a close working relationship with the local health care workers, clinicians, nongovernmental organizations and government organizations involved, public health officials and possibly also the local security forces. Regular meetings should be held and biosafety, biosecurity, infection control and hygiene should be brought to everyone's attention as the top priority in order to safeguard those working on the outbreak from health care- and laboratory-associated infections.

During an outbreak, the numbers of specimens a laboratory receives can vary considerably. At times, the number of specimens received may exceed the capacity of the laboratories to test specimens and provide results. The distribution of specimens between the outbreak laboratories needs to be managed to balance the number of specimens sent to the laboratory with the laboratory's capacity and response time. During periods of high work load, the opening times of the laboratory can be extended. In this case, it is better for the laboratory personnel to work in shifts rather than individuals working longer hours. There may also be times when the laboratory needs to temporarily extend working hours in order to provide a more urgently needed result that directly affects immediate patient treatment, such as the delivery of a baby to a potentially infected woman. Personnel should have adequate compensatory rest periods scheduled to reduce risks resulting from fatigue when working in the laboratory.

3.5 Laboratory equipment

Equipment that is used to protect the laboratory personnel from the pathogen is called primary containment; this can include screw-capped tubes, biological safety cabinets (BSCs), glove boxes and flexible-film isolators. Facilities and processes need to be in place to ensure that people and the environment outside of the laboratory are also protected.

The choice of a primary containment device depends on the risk assessment and on what is available locally or can be transported to the area. Flexible-film isolators with two high-efficiency particulate air (HEPA) filters on the extract air and pass boxes provided effective containment during the outbreak of Ebola virus disease in West Africa. This is because these devices offer effective containment, can accommodate the equipment required, are moveable and do not need a hard-ducted connection to exhaust air.

Simple strategies using primary containment that rely on engineering technology, such as an isolator, rather than human skills to provide protection are preferred because increased number of specimens and extended working days can lead to a higher error rate.

It is important to check that all the equipment selected for the work is compatible. Examples of factors to consider are that centrifuges do not disturb protective airflows, tubes fit into racks that allow labels to be read and tube lids can be removed while the tube is in the rack to minimize spilling the primary specimen.

SECTION 4

PERSONNEL COMPETENCE AND TRAINING

Laboratory risk control measures can be compromised by human error. Therefore, experienced, competent, well-trained and safety-conscious laboratory personnel are essential to lower the potential risk of infection to personnel and to produce accurate results safely. These personnel must be well informed of the biological and chemical hazards and the risk control measures in place to reduce the risks of working with those hazards. This is of particular importance during an outbreak response where the number of specimens received for diagnostic testing can be very high and the laboratory personnel deployed for the work may not have the support they are used to in their home laboratory, which may lead to a more stressful working environment and therefore a possible increase in errors.

4.1 Recruitment, training and assessment

A team of competent laboratory personnel that can be rapidly deployed to the outbreak laboratory is essential to provide a good first laboratory response during the initial stage of an outbreak. This team will need to be supplemented with more laboratory personnel if the outbreak is not controlled in the early phase.

It is unlikely that most of the laboratory personnel will have had experience working with all the equipment, techniques and types of pathogen involved in the outbreak. Before laboratory personnel are deployed, they should be given training in a safe environment outside of the outbreak zone. Mock specimens should be used so any mistakes the personnel make during training will not result in them being exposed to the pathogens. Even laboratory personnel who are experienced with the outbreak pathogen can have difficulties during training. This is because the risk control measures with regard to infrastructure, protocols and equipment in the outbreak laboratory may differ from what they are used to.

The training programme should include information, discussion and practice so that the laboratory personnel acquire sufficient biosafety and quality knowledge, skills and experience to allow them to be deployed to the outbreak laboratory. The biosafety curriculum should include information about:

- the pathogen causing the outbreak and the context of the outbreak,
- risk assessment for the work,
- psychological resilience and awareness of the situation being entered,

- technical training on the equipment,
- documentation on the operational principles of the laboratory with information on the interactions with the wider outbreak response,
- overview of the specimen workflow,
- PPE for each stage of specimen processing,
- methods to be used for detection of the biological agent,
- scenario-training for incident and accident response and emergency plans,
- update and revision of the methods, and
- maintenance and repair of the equipment.

Recreating realistic outbreak laboratory environments and situations during training will give the prospective volunteers an impression about their conditions of work once deployed. The laboratory personnel can then make a more informed decision on whether they still want to volunteer. It also allows the trainers to see if the volunteer laboratory personnel have the required understanding, attention to detail and team work that will enable them to make a positive contribution to the laboratory response.

Before deployment, the new personnel to the laboratory should have occupational health screening to ensure that they are offered appropriate vaccines and are sufficiently physically and mentally resilient. More information can be found under subsection 9.2 on occupational health.

Personnel joining the outbreak laboratory will need orientation training and support when they first start work in the laboratory to adjust to the new working environment. The immediate period after arrival is inherently highly stressful and measures to ease the transition into working in the laboratory should be considered carefully. An induction plan is highly recommended to ensure all personnel receive all relevant information on their deployment, especially as situations are fluid during outbreak responses and may differ from those outlined in the information received during training. Personnel should have the choice to leave the outbreak laboratory and return home if they do not adapt well or find it too stressful.

4.2 Considerations for deployment

There are different roles for laboratory personnel which include the laboratory leader, technical experts, IT experts, equipment experts and general laboratory personnel. The laboratory leader is usually a full-time post and the responsibilities of the laboratory leader should be made clear when they are appointed. Laboratory leaders will have to explain the work of their laboratories to local communities, work closely with other disciplines dealing with the outbreak, and work with more autonomy than they would normally be delegated. They will take overall responsibility for the biosafety and biosecurity in the laboratory and the welfare of the team and will rarely have time to work at the laboratory bench themselves.

The number of additional laboratory personnel that will need training in order to be deployed will depend on the number of hours the laboratory needs to be open. This depends on the time period over which the specimens are received, the number of specimens to be processed and the rate at which specimens can be processed. Often, there is a rate-limiting step in the diagnostic procedure; for example, for diagnosis of viral haemorrhagic fever, the rate-limiting step is the rate at which the pathogens can be inactivated in a BSC or flexible-film isolator. The size of the cabinet and centrifuge, together with the number of BSCs, may limit the number of specimens that can be processed at one time. The laboratory may need to stay open for longer hours which will require multiple shifts of laboratory personnel and will therefore increase the number of personnel needing training.

The length of time personnel should be deployed outside their home base or country needs to be decided and may range from several days to several weeks depending on the distance from their home and local conditions (for example, working hours, health, security, weather) and role (for example, laboratory personnel, team leader, logistician). Length of deployments, team size, team overlap, hand-over procedures and rotation frequency should be organized to benefit team members' safety, security and wellbeing and to achieve the best possible speed and quality of the diagnostic laboratory service in the outbreak. Rested, returning, competent team members wishing to redeploy are an extremely valuable asset with their knowledge, familiarity with the routine and experience of running outbreak diagnostic activities.

The training programme should also include measures to be taken to avoid infection risks outside of the laboratory. For example, no-touch policies, enhanced hand hygiene, social distancing and cough etiquette may be practised depending on community routes of transmission of the disease.

Having local personnel who can be placed within the laboratory team for a longer time helps sustain the response and build trust with the local community. However, the risks need to be assessed and managed because, in the initial stages of the outbreak, the team of trained laboratory personnel deployed from outside the area may not have the resources to provide training for local workers. In addition, laboratory personnel living in their community while the outbreak is at its peak may inadvertently compromise the laboratory response if they are at a higher risk of exposure to the pathogen and there is no provision for isolation when outside of work. As well as the no-touch policies, additional measures to prevent infections in the outbreak team can be implemented such as: separation of laboratory personnel from the local community where possible, installation of improvised hand-washing taps and buckets in public areas and implementation of special rules for behaviour such as hand disinfection after touching money. However, once the outbreak laboratory is established, this risk could be managed by daily health screening for all personnel supplemented with additional PPE to protect laboratory personnel if social distancing cannot be maintained with in the laboratory.

4.3 Selection and support of the laboratory team

Selection of workers for an outbreak laboratory is not only dependent on their technical ability. They also need to be good team players, have good mental health and resilience, and to be able to work flexibly and have good communication skills.

The laboratory personnel need to be able to work effectively for the duration of their deployment. This is helped by having safe accommodation, adequate food and water supplies, reasonable working hours, and being able to discuss and receive support for any mental or physical health concerns. Laboratory personnel should be given advice on how to stay healthy in a stressful environment, for example, by staying hydrated and nourished, and taking opportunities to exercise and communicate with family members. The team needs to care for each other, but the leader needs to have mechanisms to send individuals home if he/she finds that these people are not able to do the work or are not suited to it. The team leader must have the facility to secure suitable health care for team members, which could include evacuation of personnel if there is a health threat (due to an accident or exposure) or a security problem such as civil unrest.

Robust and reliable reach-back communications to the support team of the organization for consultation should be established to support all deployed personnel, including the team leader. Communication channels with fall-back options should be maintained and tested regularly and a system of reporting (for example, daily situation report) should be established.

Records should be kept for all deployed personnel of their competence and resilience to facilitate decisions about subsequent redeployment.

SECTION 5

PERSONAL PROTECTIVE EQUIPMENT

Risk control measures such as the use of robust primary containment devices which reduce splash and aerosol risks are the best method of pathogen control as they contain and therefore prevent contamination of the whole laboratory environment. Residual hazards after engineering controls have been implemented need to be assessed and PPE should be used as the last line of defence to supplement the other protection measures. The PPE used for each task needs to be determined by risk assessment taking into account the routes of infection for the pathogens being tested for, other pathogens that may be present in the specimens and other hazards such as chemicals.

Standard laboratory PPE when handling disinfectants or infectious specimens include a laboratory coat or gown, gloves of sufficient length to cover the cuffs of the coat/gown and eye protection when splash hazards are present in the laboratory. A range of PPE sizes must be available so that every user has PPE that fits to maintain the dexterity and vision of the user as much as practically possible. Additional PPE such as aprons and face visors, rather than laboratory goggles, can be used when more protection may be needed from splashes if larger volumes of disinfectants are used.

Temperature control within the laboratory may not be in place if the laboratory structure is basic. A pragmatic approach will need to be taken if temperatures are so high that wearing certain PPE results in an increased risk of heat stress and dehydration in laboratory personnel. This must be mitigated by, for example, limiting the time spent performing activities wearing the PPE or changes in practice which consider the risk versus the benefit of wearing particular PPE. Sweat can degrade PPE performance by forming liquid bridges where contamination may penetrate the protective barrier such as the filter in a face mask. The discomfort of wet and sweaty PPE may adversely affect the performance of the person wearing the PPE and lead him/her to inadvertently touch his/her skin resulting in contamination.

Different performance and application standards, and consequent compliance and approval systems are in place internationally for the design, manufacturing and application of PPE and only approved items meeting the applicable standards (for example, EN standards, Kitemarked) should be used. New batches of PPE must be thoroughly checked on arrival and generally all PPE should be thoroughly checked before use.

It is likely that a combination of disposable PPE (gloves and aprons) and reusable PPE (footwear, laboratory coats, visors) will be used. It is important to define how each piece of PPE will be made safe after use, either by disposal and incineration or disinfection and cleaning. Before reusing, it is important to check that the PPE is still protective.

SECTION 6

LABORATORY WORKFLOW

Depending on the pathogen causing the outbreak, the capacity of the laboratory can include culture, microscopy, serology or molecular techniques. Sometimes, the diagnostic service is accompanied by research activities, especially when the outbreak is protracted, or the pathogen is not well known or is rapidly changing. Such research in an outbreak laboratory often focuses on adaptation and evaluation of diagnostic tests, nucleic acid sequencing to aid epidemiologists and public health personnel, analysing immune responses in patients, and follow up of survivors (for example, for late sequelae or pathogen excretion). Research with already inactivated specimens and/or isolated nucleic acids has lower biosafety and biosecurity risks than working with specimens that have not been inactivated. Culture and other techniques that result in an increase in the biological agent for research activities need a new risk assessment.

For diagnostic work in already established laboratories, the protocols and equipment for detection of the biological agent causing the outbreak will have already been defined. The laboratory's capacity can be expanded by buying extra equipment if required. If laboratories already have existing work ongoing, then the outbreak response work may need to be separated from the routine work. For example, the outbreak work could be done at a different time, in dedicated rooms (especially when additional risk control measures are necessary) and/or with personnel responsible only for outbreak specimens. An advantage of using an existing laboratory already processing the agent is that a core of trained of personnel, who are experienced and familiar with the equipment and the laboratory, will be available.

In Figure 6.1, an example of the workflow of an outbreak laboratory using glove boxes and a hot room laboratory (potentially contaminated laboratory) is shown. In the hot room laboratory model the laboratory personnel are protected by stringent use of PPE and, although work on the pathogen is conducted within the BSC, the whole laboratory is considered contaminated. In the glove box laboratory, the specimens are inactivated within the glove box/flexible-film isolator and the strict procedural risk control measures for cabinet protocols, packaging of specimens for storage and packaging of waste mean that the rest of the laboratory is considered uncontaminated.

A decision needs to be taken on which system of working is going to be adopted. In the outbreak context, the hot room laboratory means that more specimens can be processed in a shorter period of time as the workflow is not as constrained by the size and capacity of the BSC. In addition, the level of confidence needed for pathogen inactivation is lower as the whole laboratory is treated as contaminated. However, in the hot laboratory model the critical safety aspects of the laboratory are dependent on a reliable power supply and provision of clean water for decontamination. While the limited capacity of the glove box can restrict the number of specimens processed in a day, the "lab within a lab" concept means that the work remains safe in the event of a power failure and there is a solid barrier between the personnel and the pathogen, so reducing the infection risk through splashes and spills. As long as sufficient data can be provided on the confidence of the pathogen inactivation, the requirement for PPE and respiratory protective equipment is less and the safety of laboratory personnel is not as dependant on strict procedures for putting on and removing PPE.

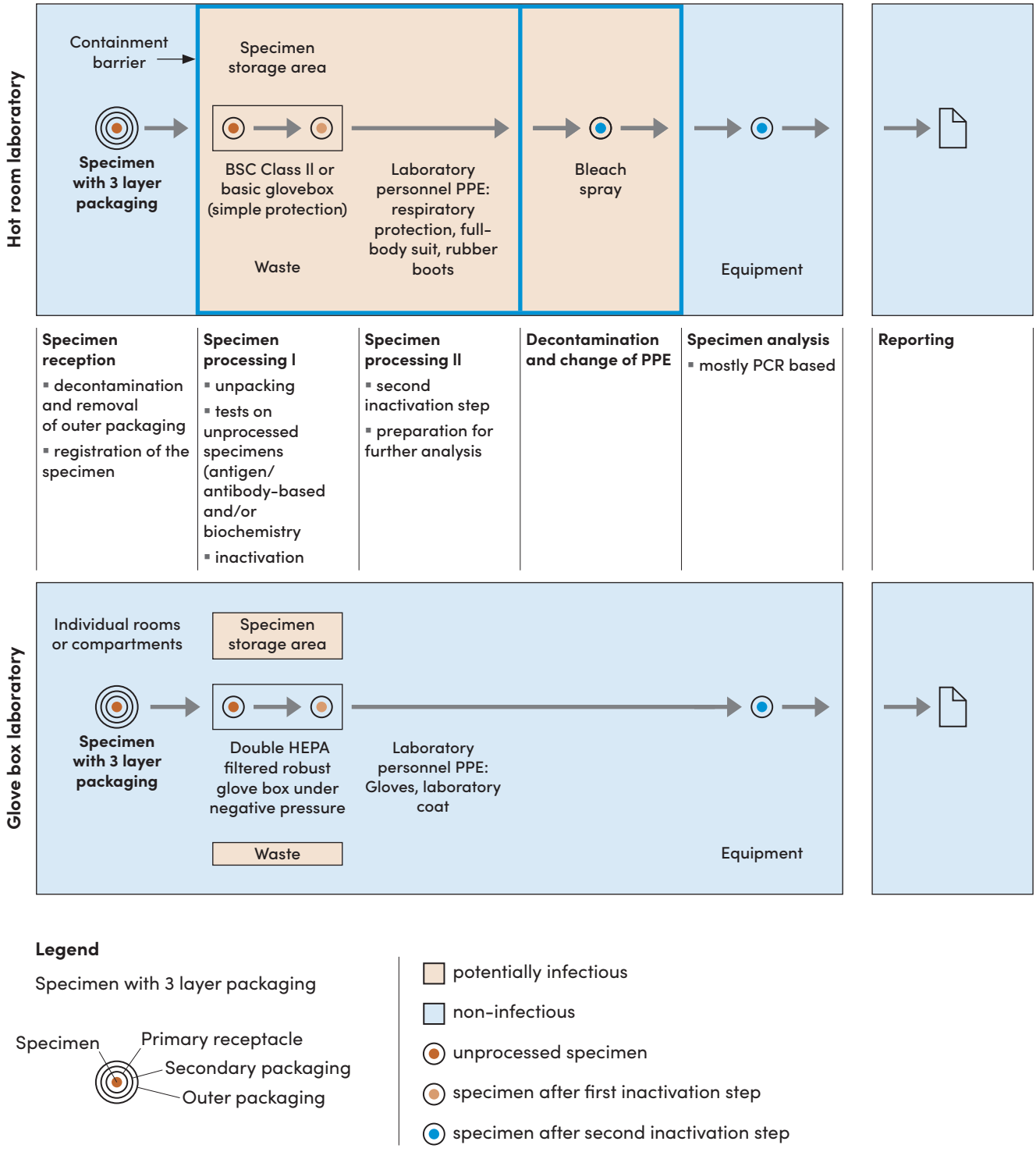


Figure 6.1 Workflow of an outbreak diagnostic laboratory in a hot room laboratory and a glove box laboratory (BSC: biological safety cabinet; HEPA: high-efficiency particulate air; PCR: polymerase chain reaction; PPE: personal protective equipment)

6.1 Specimen reception and patient data management

6.1.1 Specimen reception

Every laboratory should prepare a plan which includes the type of specimens they will receive and how the specimens should be packaged. This plan should be communicated to health care workers and clinicians who will potentially send patient specimens to the laboratory. The specimen reception desk/area of a laboratory is the physical interface between the uncontrolled outside environment and the biosafety regulated and controlled laboratory. The specimen reception desk/area can also act as a physical barrier to guard the entrance of the laboratory from entry of unauthorized people.

Important features at the specimen reception area are outlined below.

- It should be stocked with all the equipment and PPE necessary for the safe reception, evaluation and sorting of specimen shipments to the laboratory.
- It should have PPE that are appropriate for the hazards expected and for hazards from improperly packaged specimens, spilled contents and potentially corrosive disinfectants.
- It should have fresh and approved disinfectants.
- It should have a process to contain any items recognized as hazardous because they are inadequately packaged or leaking; this could include a BSC or a sealable box.
- It should have adequate lighting.

Laboratory personnel at specimen reception must carefully inspect containers, specimens and accompanying documentation (for example, analysis request forms and physicians' letters, chain of custody forms) to ensure the packaging is safe, the specimens are intact and the labelling is accurate with regard to the documents provided. They can then assess any substandard or irregular specimen packaging to determine whether they should be accepted into the laboratory, need more care and should be treated separately, or need immediate decontamination. Care should be taken not to erase any labelling/inscriptions/markings on the containers with the specimens during any routine disinfection processes.

Wearing adequate PPE, laboratory personnel at the specimen reception desk will open the outer packaging of the shipment (for example, third packaging layer). Secondary packaging may be decontaminated by wiping it down with or submerging it in disinfectant solution so that no contamination on the surface of the packaging is carried into the laboratory. In the case of an outbreak of a highly contagious and pathogenic agent, secondary packaging should be submerged in the disinfectant. If made of liquid-resistant material, analysis request forms may be disinfected as well. Otherwise, procedures should be used to make handling of potentially contaminated request forms safe by carefully wiping with disinfectant solution or the information should be transferred (for example, by photographing it) so that no further physical contact is needed.

The specimens should be registered (for example, assigned a unique laboratory ID number) and sorted for further processing in the laboratory diagnostic workflow pathway and the corresponding patient information entered into the data management system.

The laboratory should provide feedback to the frontline health care workers about biosafety in general and the quality of the packaging of specimen shipments delivered to the laboratory. Frontline personnel at health care facilities may lack the same level of biosafety training as laboratory personnel and the first packaging of patient specimens at the health care facilities may not comply with applicable biosafety rules and regulations for the transport of hazardous materials. Specimens might be inadequately packaged because of the pressure of packaging many specimens during an infectious disease outbreak or because of the lack of suitable packaging materials. Feedback can be given through a short meeting, demonstration session or training session, and by decontaminating and reusing packaging, providing written and illustrated packaging guidance documentation or leaflets. The need to provide all requested information on the specimen receptacles and the analysis request forms, and to use the appropriate packaging materials correctly should be explained to the frontline health care workers. The laboratory may decide to stop further specimen processing if specimen deliveries are hazardous or inadequately packaged. Clear rules to support the decision to reject specimens should be defined, communicated to frontline health care workers and applied. Criteria for stopping the processing of specimens include the following:

- the (bio-)risk in processing a leaking, broken or otherwise hazardous specimen shipment is higher than acceptable,
- the specimen is technically unsuitable for testing, either due to degradation or other pre-analytical considerations (for example, type, amount, transport media), and
- the specimen receptacles and/or the request sheets lack essential information so that an accurate assignment of the laboratory result to the correct patient would not be possible.

When a specimen shipment is rejected, the laboratory should immediately contact the facility that sent it for clarification and correction in the interest of the patients waiting for their laboratory results and to maintain a safe and collaborative working relationships between the laboratory personnel and health care workers. The laboratory should ensure safe disposal of rejected specimens.

6.1.2 Specimen and patient data management in the laboratory

A laboratory data management system should be in place so that patient specimens can be registered, laboratory results assigned to the correct patients and diagnoses communicated to the correct people (for example, clinicians). The laboratory data management system can be a computer or paper-based system. The complexity of the system will depend mostly on the scope of the laboratory service provided (variety and quantity) and the reporting mechanism. The outbreak laboratory may need to establish a new data management system onsite, preferably in close collaboration with the health care facility (for example, hospital or emergency treatment centre) that it serves. The most important role of these systems is to ensure the relaying of correct diagnostic test results to the requesting physician or treatment centre. For the laboratory itself, any errors resulting from data management will require a thorough investigation to find the cause of the mistake. Any retesting that needs to be done as a result of errors can lead to delays and additional costs and may in extreme cases exhaust diagnostic reagents where logistics are challenging and supplies limited.

The laboratory should inform health care workers and clinicians how to label specimen containers and complete forms to be compatible with the laboratory data management system. However, it is more likely that a data management system will need to be tailored to the specimen request forms which will often originate from the local health ministry. The minimum details supplied on patient specimen receptacles should be the patient's first and last name, date of birth (or age if date of birth not available), and hospital identification (ID) number when available. Additional information on the specimen receptacle could include time and date of specimen collection and the initials of the person who collected the specimen.

The specimens must be triple packaged and any accompanying papers (for example, test request forms, physician letters) should be placed between the second and third layers of packaging. A test request form must be provided for each specimen and should include, in addition to the information on the specimen: clinical data, contact information to enable reporting of results and the tests required.

Table 6.1 Suggested information to include in a laboratory patient data set and where it should be recorded

SPECIMEN COLLECTION RECEPTACLE	TEST REQUEST FORM	LABORATORY DATA RECORD (BOOK OR COMPUTERIZED)
▪ First and surname of patient ▪ Date of birth/age ▪ Patient ID number ▪ Time and date of specimen collection ▪ Initials of person collecting the specimen ▪ Unique laboratory ID number (assigned by the laboratory)	▪ First and surname of patient ▪ Date of birth/age ▪ Patient address ▪ Patient ID number ▪ Time and date of specimen collection ▪ Specimen type and source ▪ Unique laboratory ID number ▪ Clinical data ▪ Contact information of responsible person requesting the test ▪ Tests requested ▪ Additional requests, for example urgent test ▪ Test results and diagnosis can be noted here as well	▪ First and surname of patient ▪ Date of birth/age ▪ Patient ID number ▪ Time and date of specimen collection ▪ Unique laboratory ID number ▪ Date specimen was received by the laboratory ▪ Tests requested ▪ Test results ▪ Computerized systems can store scans of documents, for example, request forms

At the laboratory specimen reception, a unique laboratory ID number should be assigned to each patient specimen and the corresponding test request form. Every patient specimen arriving at the laboratory should be registered in a laboratory log book together with essential information (see Table 6.1) and the laboratory ID number. In addition, the test results and time the specimens were received and test results issued should be recorded in order to monitor the turnaround time. All other information, for example, information for quality/safety/operational purposes such as incubation or inactivation times, records of which personnel performed which test elements, will either be recorded in the computer system or in paper records.

Information governance

The laboratory must protect the privacy of patient data. Patient data including test results and diagnosis may only be communicated to authorized persons or entities (for example, hospital clinicians). The outbreak laboratory, particularly laboratories from foreign countries, should seek advice and clarification about local and national data protection and privacy rules. The laboratory should refuse to comply with requests for data that seem to be unauthorized. During infectious disease outbreaks and epidemics, situation report tables often need to be collated for epidemiological and reporting purposes.

The laboratory should make sure that these data are only transmitted to authorized bodies and that the data are kept anonymous. Access to and use of identifiable data of patients must be justified and done with care. Patient computer data should be backed up regularly and paper records should be securely locked away. The use of free source email accounts for transmission of patient information must be avoided if possible to restrict unauthorized access.

6.2 Specimen inactivation

Strict compliance with inactivation and disinfection protocols is essential to protect laboratory personnel and the environment. Specimens will need to be unpacked, aliquoted and prepared for analysis inside a BSC or equivalent. If the primary containment device is a Class III BSC or flexible film isolator, then this device should be considered potentially contaminated, but the wider laboratory can be regarded as uncontaminated (except for specimen storage and waste removal). If open-fronted BSC (Class I or II) are used or basic glove boxes without HEPA filtration, then the whole laboratory area should be considered potentially contaminated (hot room laboratory). In this case, more PPE and disinfection will be needed but the workflow will be potentially quicker.

The PPE to be used will be specified in the risk assessment and depends on the level of potential contamination within the wider laboratory. In the first example, using a Class III BSC, the PPE could be, for example, a laboratory gown, (double) nitrile gloves with long cuffs and eye protection. In the second example with an open-fronted BSC, a respiratory protective device and a complete change of clothing may be required. Personnel should put on the PPE before entering the laboratory and should remove it on exit under a strict protocol and risk control measures to prevent them from becoming contaminated.

The risk control measures in the risk assessment may state that patient specimens must be unpacked within the BSC and then processed. Often, this processing will include centrifugation. This can take place in sealed centrifugation buckets outside of the cabinet for large volumes, or within the cabinet for small volumes. A robust small centrifuge with a sealed rotor is preferred for use inside the cabinet.

Depending on the detection technique, a defined volume of the specimen is transferred to a new tube and inactivated. The remaining specimen can be kept in the laboratory if analysis needs to be repeated and to store the pathogen. The specimens or aliquots of the specimens must be inactivated by validated inactivation procedures before they are opened outside of the primary containment device for further processing. The inactivation procedures should be reviewed regularly and adjusted according to new scientific evidence. If heat treatment is used, then the temperature should be verified using a duplicate tube containing a thermometer. The outside of the tube with the inactivated specimen should be thoroughly disinfected before it is brought out of the containment device.

6.3 Selection of the diagnostic method

From early in the outbreak, careful consideration must be given to the choice of diagnostic assays that can be used, taking account of diagnostic sensitivity and specificity, specimen processing time, biosafety and usability.

This decision may be made by individual laboratories or a central decision by the government. Harmonization of testing strategies across all laboratories should be considered during the selection process.

Without compromising biosafety, outbreak laboratories need to establish strategies to deal with the possibility of high numbers of incoming patient specimens. These numbers may challenge the capacity of the laboratory to run tests in a given period of time because of the limited equipment, reagent assay kits and personnel available. Adequate amounts of laboratory consumables, reagents and PPE should be kept in stock, and supply chains should be planned in collaboration with manufacturers, suppliers and transport providers.

Accuracy of testing is of course important but is never 100%; selection of the most appropriate diagnostic method may require a trade-off between sensitivity and specificity but must also consider more practical considerations such as supply sustainability, ease of use, practicality and reproducibility. A false positive test result may lead to patients unnecessarily entering a treatment facility where they face a high risk of becoming infected. A false negative test result will expose the patient's family and community to the risk of infection. The laboratory, clinicians, health care workers and the competent authority should develop a diagnostic algorithm that will provide the best possible clinical sensitivity, specificity and safety for the affected patients, and the community and families affected by the outbreak. This algorithm should include case definitions based on scientific evidence, expert opinion, practicability under the given circumstances and public health.

The choice of diagnostic methods and assays should also be guided by biosafety in the outbreak laboratory. In the course of the risk assessment, diagnostic tests should be assessed for hazards in their workflow. Measures should be taken to contain these hazards or valid alternative methods should be sought and applied if these provide equally accurate results. Obviously, the handling of specimens and substances (for example, blood or other body fluids) suspected of containing or known to contain infectious pathogens is the main hazard in the laboratory. Therefore, steps in the workflow where vials need to be opened and liquids transferred between receptacles (for example, by pipetting) should be kept to a minimum whatever containment strategy is used.

Tests should avoid procedures where aerosol formation or spillage are a significant risk. Reducing the amount of specimen material or specimen volume needed, decreases the risk present. Centrifuging infectious materials is a high-risk process because of the potential for aerosol formation, centrifuge breakdown and leakage. Centrifugation should therefore only be done in biosafety containment environments (for example, glove box or hot room with PPE or using a centrifuge with a sealable airtight rotor). Alternative methods that avoid centrifugation are recommended, for example, separation of blood treated with ethylenediaminetetraacetic acid (EDTA) by gravity sedimentation over time.

Diagnostic tests that involve validated inactivation procedures early in the workflow are preferred so that manipulation of viable pathogens is kept to a minimum. Inactivation processes for serology include heat or chemical treatment of the specimens. If valid inactivation methods cannot be used in an essential diagnostic test, then the entire procedure must be conducted under appropriate containment conditions. The easier a test is to perform, the safer the point-of-care or laboratory work will be. Test procedures with as few steps as possible are likely to be safer to use in the laboratory because they reduce the number of opportunities for errors and accidents, especially where resources are limited, climatic conditions are challenging (for example, tropical heat) and during outbreaks when high workloads are common.

Other factors that are not directly related to biosafety but influence the choice of diagnostic method and test selection in outbreaks and epidemics of infectious diseases include:

- results from independent and ideally multicentre validation of the diagnostic test, for example, accuracy (sensitivity, specificity),
- results from laboratory verification in the outbreak diagnostic laboratory (for example, the test should be valid in conditions with limited resources),
- approval of the test by international or national bodies, for example, Food and Drug Administration of the United States of America or WHO,
- suitability of the test for the specific infection stage of the patient (for example, direct detection of the pathogen in viraemia and bacteraemia, or antibody detection in recovering patients),
- necessity to test for differential diagnoses (for example, malaria), and
- sustainability of supply.

6.3.1 Diagnostic specimens

The laboratory scientists and technicians should consult with the scientific community, national public health authorities, frontline health care workers and clinicians to decide on the types of patient specimen needed and diagnostic strategy to apply. Many pathogens, for example, viruses, are detectable at different times in different body fluids during the course of a patient's illness and this should be taken into consideration when taking specimens. Given the limited diagnostic capability of an outbreak laboratory and the biosafety measures needed, a diagnostic algorithm needs be established so that the disease in question can be ruled in or out with high reliability. This may require testing additional patient specimens obtained after specific time periods, for example, when viraemia might have developed in a patient with fever or at later times when seroconversion has taken place. Sometimes, a broad screening approach, for example, testing several different body fluids, may be appropriate.

The laboratory personnel should also advise health care workers on both suitable specimen receptacles to be used for the detection methods applied in the laboratory, and PPE and safe sharp practices. Some collection tubes may be entirely unsuitable for a particular laboratory method, for example, heparinized blood is unsuitable for PCR analysis because of inhibition effects, whereas urine is suitable for PCR for some infectious diseases but may be unsuitable for the detection of antibodies. Workflows for the different specimens need to be considered in the risk assessment.

Duplicate specimens may have to be taken and stored for confirmatory testing at a later time and possibly in another laboratory.

6.3.2 Direct pathogen detection

Several methods may be available to detect the biological agent causing the outbreak, such as PCR-based techniques, culture and serology. If detection is done using inactivated biological agents or isolated nucleic acids, then biosafety measures can be reduced after inactivation as the likelihood of a viable organism being present is lower. For detection using the live biological agent, full biosafety measures must be used during the detection step.

Nucleic acid amplification technologies including PCR usually have high sensitivity and specificity. The most commonly used specimen type for detection of viral pathogens, including highly pathogenic haemorrhagic fever viruses and other bloodborne pathogens, is EDTA plasma separated from EDTA blood drawn from patients by phlebotomy or throat/nasal swabs for respiratory diseases. Another advantage of a PCR-based test is the early inactivation of the specimen in the workflow which reduces the risk of exposure of laboratory personnel. Nevertheless, the reagent kit manual or other appropriate laboratory protocols should be consulted for suitable and validated specimen types during the risk assessment process.

Other direct pathogen detection methods are available for some pathogens and can be used in an outbreak, for example, bacterial culture of *Neisseria meningitidis* or *Vibrio cholerae*. Techniques such as virus or fungal culture, experimental animal inoculations, electron microscopy and antigen tests (for example, enzyme-linked immunosorbent assay (ELISA) and chromatographic assays) are unlikely to be used because either the equipment is not available in outbreak laboratories or they require larger biosafety containment facilities and more complex biosafety equipment.

6.3.3 Serology testing for infectious diseases

Testing for antibodies to the pathogens is sometimes necessary to identify the pathogen if it cannot be detected directly. For epidemiological purposes, screening of recovering patients and high-risk populations by antibody detection can give an indication of the incidence of the disease.

The most commonly used specimen type for laboratory analysis of antibodies is serum. Some serology tests may also use other body fluids such as saliva or cerebrospinal fluid; the manufacturer's manual should be consulted for valid options. Serology tests should be used under appropriate biosafety conditions according to the risk assessment. Users of antibody tests should select the appropriate validated pathogen inactivation method for the patient specimens used in the test. Pathogens could be inactivated by the action of specimen dilution buffers contained in the kit or a heat step. Local procedures or the manufacturer's information should include guidance on pathogen inactivation. Another biosafety strategy may be to first clear specimens by PCR testing for priority pathogens and then test for antibodies by serology. Risk assessments may indicate that laboratories with core requirements as described in the *Laboratory biosafety manual* may be suitable for testing serum from healthy afebrile donors for disease monitoring purposes.

6.3.4 Point-of-care testing

Conventional laboratory analysis of patient specimens for infectious pathogens by nucleic acid amplification technology/PCR, serology methods or culture techniques have to be performed in dedicated laboratories using specialized analysers, with complex biocontainment equipment. These techniques must be carried out by trained and experienced laboratory personnel. The processing time to obtain results can vary from about four hours in the case of nucleic acid amplification technology/PCR and serology to several days for culture techniques. Furthermore, the transport of patient specimens from the patient to the laboratory – sometimes over long distances – can further prolong the time until the clinicians get the results. Long turnaround times can mean that patients have to spend a long time in health care facilities waiting for their laboratory results and clinical decision, which results in longer than necessary exposure to infection risks.

Point-of-care analysers and point-of-care tests can eliminate some of the disadvantages of more complex laboratory testing by avoiding time-consuming specimen transport or patient travel to the laboratory. Health care workers, already wearing appropriate PPE, can perform the tests on the ward.

Point-of-care testing for infectious pathogens uses technologies for nucleic acid amplification technology/PCR *(8)*, or bloodstream circulating antigen and antibody detection. These techniques have different formats ranging from cartridge type all-in-one PCR analysers to chromatographic lateral flow and dipstick devices for antigen or antibody detection. These tests and devices often only have one or very few specimen handling (pipetting) steps which can often be rapidly executed by health care workers in PPE. Performance characteristics of point-of-care tests and devices should be compared with the accepted gold standard test method in laboratories, and confirmatory retesting in reference laboratories may be necessary. With further technological progress, more point-of-care tests and devices with ever increasing sensitivity and specificity and performance characteristics will likely become available.

6.4 Decontamination and waste management

A policy must be in place for each laboratory which details how equipment, consumables and laboratory waste are decontaminated after use. The risk assessment needs to consider the pathogens present and the decontamination methods available to determine the best process to ensure that no infectious hazards are released from the laboratory, and that there is no residual contamination of equipment when the laboratory is decommissioned. The policy should describe when, where and how the following take place: decontamination of the laboratory and equipment, routine disinfection measures, and application of hygiene protocols for laboratory personnel.

The methods described must state the parameters, for example, contact times, concentrations and temperatures, required to achieve the validated reduction in viable pathogens to ensure the decontamination is effective in the circumstances.

6.4.1 Decontamination

Decontamination of laboratory surfaces and equipment relies on the application of liquid disinfectants. This is because it is rare for a rapidly deployed outbreak laboratory to be sealable for fumigation with a gaseous disinfectant and to have the necessary ventilation system to enable safe removal of toxic vapours.

Broad-acting disinfecting chlorine solutions are often available and effective. Care should be taken to use only fresh, active and clean preparations at adequate concentrations. Commercially available chlorine solutions can lose their disinfectant activity through degradation during long term storage (especially at warmer temperatures). Household preparations are not suitable for the laboratory as they are not sufficiently active and stable *(9)*; therefore, preparation of fresh chlorine solutions made by dissolving sodium dichloroisocyanurate tablets in water is recommended.

Disinfectants should be used according to the manufacturer's recommendations and they should be given the correct time to act. Care should be taken if flammable disinfectants are used because of the risk of fire and fumes. Disinfectants may cause corrosion, may also be hazardous to humans and may damage the environment. Therefore, adequate PPE should be worn, residual disinfectant should be removed from the equipment by wiping with a damp cloth, and care should be taken to avoid release of high concentrations of the disinfectant into the environment.

Liquid infectious waste must be decontaminated before it is released from the laboratory (for example, by autoclaving, chemical disinfection or incineration). Solid infectious laboratory waste should be treated within the laboratory by autoclaving, which is the preferred method. If a standard laboratory autoclave is not available, then use of small size bench top autoclaves to treat high-risk material should be considered. Treated waste must be securely packed within the laboratory and taken directly for incineration.

6.4.2 Waste management

All laboratories generate a range of waste materials and a safe method for inactivation and disposal of all types of waste from the laboratory needs to be planned before work starts. Laboratory waste must be segregated, treated and packaged so it leaves the laboratory in a safe condition for final disposal. All waste should be treated within the laboratory to make it non-infectious or should be processed close to the laboratory to avoid transporting high-risk infectious waste.

A range of methods can be used to inactivate pathogens (chemical disinfection, gaseous disinfection (fumigation), heating with steam (autoclaving), incineration and radiation). However, many of these methods will not be available in an outbreak laboratory. In most outbreak settings with limited resources, the methods available are disinfection, followed by incineration (in an onsite constructed incinerator) or burning (in a burn pit).

If an autoclave is available onsite, it can be used to make safe even high-risk pathogen waste. It is the preferred method provided the autoclave cycles are controlled and validated, and trained and experienced operators are available.

Most waste can also be treated with a broadly active disinfectant such as chlorine by either immersing items in the solutions or spraying surfaces with the disinfectant. Ideally, the disinfection process should be incorporated into the method protocol so that items are disinfected as soon as they are used, rather than accumulating a lot of waste for disinfection at the end. Liquid infectious waste has to be inactivated either by the addition of appropriate amounts of chemical disinfectant or by heat. Ideally, all infectious waste from the laboratory should be treated with two different methods, such as heat and chemical disinfection, before being released into the environment.

The use of sharps or potentially sharp items should be avoided in the laboratory. If used, they must be disposed of in rigid containers, such as sharps bins or plastic bottles, where disinfectants can be added for extra safety. The sharps containers should be incinerated at a high temperature in an incinerator or burn pit and the burnt remains should be buried so that they pose no hazard.

For general laboratory waste that has a low risk of contamination, the most appropriate method is incineration, preferably in an incinerator; when an incinerator is not available, a burn pit should be used. The waste must be properly and safely packaged for interim storage and transport to the incinerator. The waste should be secured in incineration sacks so it cannot contaminate the area on the way to the incinerator and stored securely so it cannot be moved by unauthorized personnel or disturbed by animals. The incineration process must be monitored to ensure that all the waste is burnt. If waste containing plastics and chlorine is burnt in simple incinerators, then the emissions are toxic. In this case, the incinerator requires an exclusion zone of 20 m preferably with a chimney stack 9 m above ground level and at least 3 m higher than neighbouring buildings. Incinerator operators need to keep a suitable distance from the incinerator and wear appropriate PPE to protect them from infectious and heat hazards.

If waste cannot be treated within the laboratory and then incinerated, but instead needs transporting to other facilities, then the waste containing highly pathogenic agents falls into the transport category UN2814 (infectious substance affecting humans) and should be triple packaged for storage and transport to the site of final disposal. Low-risk laboratory (medical) waste or waste containing Category B substances falls under transport category UN3291 (medical waste). The impact on the environment and the community from the final disposal of the waste must be considered (for example, disinfecting chemicals, exhaust fumes from burning) and every effort should be made to keep this to a minimum.

6.5 Specimen storage

Untreated patient specimens and extracted nucleic acids are usually stored in controlled cold conditions (refrigerator or sub –20 °C freezer respectively) in the outbreak laboratory. Untreated specimens should be regarded as potentially infectious. The stored specimens should be contained in more than one layer to protect laboratory personnel in the general laboratory. The refrigerators and freezers should have a continuous electric power supply to avoid freeze and thaw cycles, which can lower pathogen and antibody titres and degrade nucleic acids in the specimens. Specimen storage areas, freezers and refrigerators should be kept locked and supervised to protect against unauthorized access to biological substances, and access logbooks should be kept for documentation. Usually, the specimens are stored in the outbreak laboratory for a limited time and may be transferred to a maximum containment facility or destroyed.

6.6 Reporting

An office area for data entry, reporting, communication and organization of the work is usually required and needs to be separated from the rest of the laboratory. If there is a lack of available space, it is sometimes necessary to have equipment such as molecular detection systems in the office area. However, these systems are low hazard and low risk as they are closed systems and only used with inactivated specimens. Where such systems are located in the office area, dedicated PPE must be used for that area. The same PPE must not be worn in the segregated office area and main laboratory.

Validated test results should be reported as soon as possible to the treating physicians or hospital because early discrimination between infected and uninfected individuals is critical to stop the spread of the disease and benefits patient management. It is important to ensure there is an agreement with public health officials, international agencies and the ministry of health on reporting requirements (for example, frequency and minimum information) and procedures (for example, related to data protection and security).

SECTION 7

SPECIMEN TRANSFER AND TRANSPORT

Once patient specimens have been taken, they will have to be packaged and safely delivered to the diagnostic laboratory in appropriate transport conditions and in an acceptable time. Depending on the stage of an outbreak and the availability of testing laboratories, the specimens may need to be transported locally, for example, from the point of specimen collection to the nearest laboratory for initial analysis; this can be a short walking distance within the hospital compound or a longer distance by motorcycle, for example, from a remote village. However the specimens may need to travel to a regional or national reference centre for confirmatory testing; this may be a longer distance covered by road, airplane or boat. Especially at the beginning of an outbreak, before specialized laboratories have been established locally, the specimens may have to be sent for analysis to reference laboratories or even networks outside the country if tests are not available in the country; this usually happens by airplane.

Detailed guidance on the transport of infectious specimens can be found in the WHO document *Guidance on regulations for the transport of infectious substances 2019–2020 (10)* and any subsequent updates of this document. Health care workers and those involved in taking, packaging and transporting specimens must be trained on all procedures necessary for the safe execution of all tasks and for compliance with national and international regulations (the ICAO's *Technical instructions for the safe transport of dangerous goods by air (11)*).

Some essential parts of the WHO guidance document are highlighted below. For a full understanding of the subject, the document itself should be consulted.

The transport of infectious substances requires good coordination, cooperation, communication and planning between the parties involved to ensure the safety and security of the goods conveyed and their timely arrival so that the specimens remain in a suitable condition for medical analysis and other processing. These parties are the shipper, the carrier and the receiver. All parties have their obligations to fulfil: the shipper researches the need for any permits, prepares documents and makes advance arrangements with the carrier and receiver; the carrier supports the shipper with documents and confirms the routing; and the receiver obtains the necessary import authorization, arranges for the timely collection of the goods and acknowledges receipt on arrival.

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Permission and clarification should be sought from the competent authority about improvised emergency transport of infectious specimens. National regulations exist in some countries that allow the transport of Category A and Category B (see specimen classifications in subsection 7.1) specimens by road in "non-certified" vehicles (for example, fire engines, police vehicles or ambulances) in case of emergency, providing that due care is taken of biosafety, biosecurity, and packaging and labelling of the transported goods. Very remote places can sometimes only be reached by poor roads or even narrow paths where specimens sometimes have to be conveyed by motorbike or helicopter. Care must be taken to conduct these deliveries as safely as possible with proper preplanning of travel routes, communication, equipment and condition of the vehicles, qualification and welfare of the drivers and emergency/contingency actions. If possible, these deliveries should be made in a convoy of at least two vehicles for back-up purposes if there is a risk of becoming stranded in a remote area.

7.1 Specimen classification

Infectious substances are classified in Division 6.2 of the dangerous goods regulations *(12)* and are assigned a shipping name or and/or a unique four-digit United Nations (UN) number (UN2814, UN2900, UN3291 or UN3373) according to their hazard classification and their composition. Biological substances are divided into three categories: A, B and exempt human or animal specimens. Each category has its own packaging requirements and required training for the shipper.

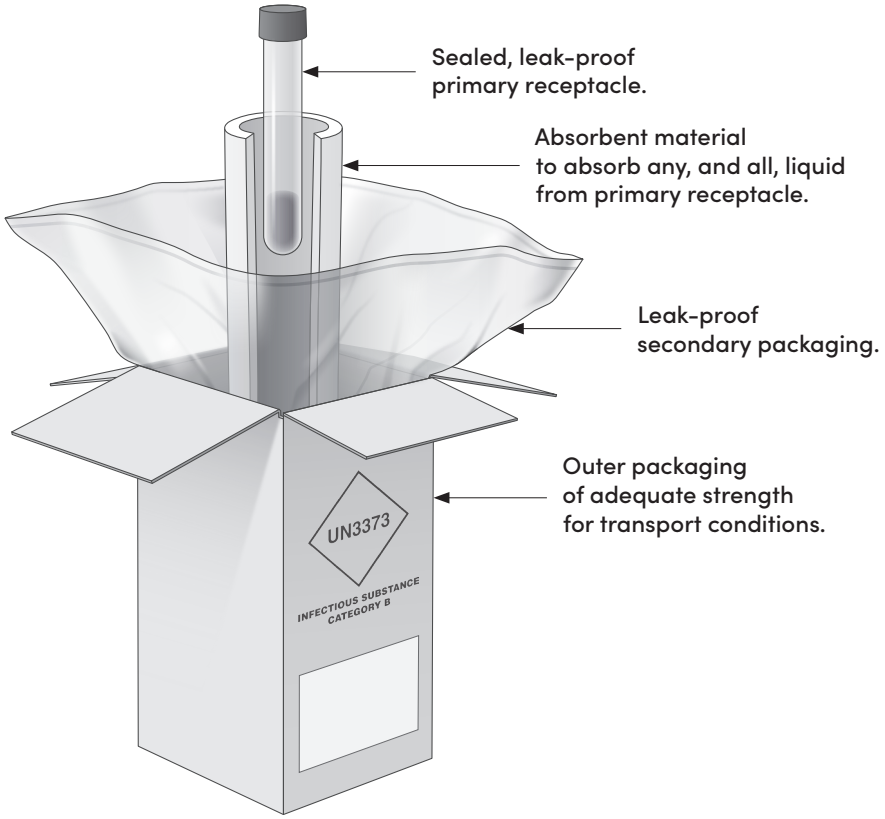

Figure 7.1 Triple packaging for patient specimen transportation

Category A: These are infectious substances transported in a form that, when exposure occurs, is capable of causing permanent disability or life-threatening or fatal disease in otherwise healthy humans or animals. These are assigned the numbers UN2814 for infectious substances that affect both humans and animals and UN2900 for infectious substances that only affect animals.

Category B: These are infectious substances that do not meet the criteria for inclusion in Category A. These are assigned the number UN3373.

Exemptions: These are substance derived from humans or animals (for example, clinical specimens) for which there is a minimal likelihood that infectious biological agents are present or are substances where pathogens have been neutralized or inactivated so they no longer pose a health threat. These are not subject to dangerous goods regulations, unless they meet the criteria for inclusion in another class.

Specimens collected from patients (or animals) in a suspected or confirmed infectious disease outbreak caused by an epidemic-prone and highly pathogenic agent for humans (or animals) in many cases qualify for inclusion into Category A and must therefore be marked with the UN numbers UN2814 or UN2900 *(10)*.

7.2 Specimen packaging

Patient specimens must be packaged so that any infectious contamination or spillage, which could put anyone at risk, is avoided. Packaging should conform to national (for example, for in-country surface transport) and international *(11)* guidelines and regulations, using suitable and approved materials. Specimen shipments must also be labelled so that they can be handled safely and hazards can be identified. The basic packaging principle that should be applied to all patient specimen transports (Category A, Category B and Exemptions) is the triple packaging method (Figure 7.1) *(14)*.

The patient specimen is collected in a leak-proof receptacle, which, in an outbreak situation, may be placed into an additional supplementary primary receptacle for added safety and ease of decontamination. The primary receptacle is placed into a leak-proof secondary packaging together with a sufficient amount of absorbent material to contain the contents of the specimen receptacle in case of leakage.

The specimen receptacle and secondary packaging should be wiped down with disinfectant. The secondary packaging is placed into a third outer packaging for mechanical protection. The labelling and markings are applied to the outer packaging. Preferably, the primary and the supplementary primary receptacles should be made of transparent materials which allow the identification of the contents from the outside without unpacking. Laboratory analysis request forms and physician letters should be put in an envelope and then placed between the third and secondary packaging. The specimen shipments should be accompanied by content lists so that laboratory personnel know what the contents are without having to open the secondary packaging. An overview of the packaging requirements and procedures for the three categories of biological substances is given in Table A1.1 in Annex 1.

As part of epidemic and outbreak preparedness, appropriate packaging materials for the transport of infectious substances should be kept ready in sufficient quantities for use by frontline health care workers and clinicians, as well as primary receiving laboratories and public health institutions. Frequently, however, initial and suspected cases in an infectious disease outbreak emerge in remote places where sampling and dedicated packing materials may not be available or where available packing materials quickly become used up. In this case, alternative strategies for taking specimens and packaging of infectious specimens will have to be established.

Frontline health care workers and clinicians should consult the laboratory and transport provider on the safest and best possible improvised alternatives. However, the basic principle of triple packaging should always be applied and due care taken.

In an outbreak situation where standard packaging is not available, specimen packaging for transport may be improvised using heavy-duty watertight plastic bags (for example, freezer bags for food, zipper bags or waste bags), empty plastic bottles, 50 mL plastic laboratory screw-cap tubes, or any watertight plastic containers as supplementary primary receptacles and secondary packaging. Care should be taken to ensure that unpacking of improvised packaging would not pose additional hazards or complications (for example, tearing of gloves due to the excessive use of adhesive tape). Paper towels, tissue paper or clean rags can be used as absorbent material placed between primary and secondary packaging, if needed. For third layer outer packaging, a container of sufficient strength and size should be used. Insulated camping boxes, heavy-duty cardboard boxes, buckets with lids that can close tightly can be used and marked appropriately. The smallest overall external dimensions of the outer packaging should be at least 10 x 10 cm. Sharp or pointed items, such as scalpels or needles, which would pose a hazard to laboratory personnel, must never be included in specimen shipments. Care should be taken to destroy any inappropriate materials to prevent further use.

7.3 Specimen transport conditions

The specimen transport conditions and the duration of transport may influence the quality of the specimen and affect the laboratory analysis. Best possible conditions and speed should be planned for. Laboratories doing the diagnostic testing should be consulted on suitable transport temperature, correct specimen type(s), appropriate specimen container and any other pre-analytical requirements. Unsuitable temperature during transport and longer transport duration may lead to degradation of the pathogen in the specimens and consequently any testing will have a lower diagnostic sensitivity. Ambient pressure changes during airplane transport may lead to leakage of liquid specimens from inappropriate containers. Once the specimens have arrived at the laboratory, they should be analysed without further delay and processed for storage at the correct temperature (for example, long-term storage at -20 °C or -70 °C).

In the absence of more specific information about transport conditions, the following guidance can be considered. In many cases, specimen types for diagnostic testing of many different infectious pathogens can be kept at room temperature (between 18 °C and 22 °C) for up to 24 hours and can be kept at 4 °C for up to 72 hours and possibly longer. Specimens should initially not be frozen as freeze and thaw cycles can lead to haemolysis of whole blood specimens and can lower pathogen titres in the specimens. In tropical climates, icepacks can be added to the shipments between the secondary and third packaging layers. Temperature monitoring within the package during transport can be done by electronic logging devices to provide evidence of suitable transport conditions.

SECTION 8

ACCIDENT AND INCIDENT RESPONSE

Outbreak laboratories need to have an emergency response to cover all potential incidents and accidents, such as:

- incidents with biological risks to the environment and surrounding community,
- incidents with biological risks to laboratory personnel,
- fire,
- chemical spills and release, as well as hazardous substance recovery,
- biosecurity breaches and incidents,
- personnel accidents, illness and injury, and
- security threats and incidents.

The emergency response should also include cooperation with and support from partners onsite, international organizations, UN organizations, and national and local entities (for example, hospitals, ambulance service, fire service, police and public health agencies). All health care workers, clinicians, and transport and laboratory personnel need training on awareness of emergencies and how to respond appropriately to them. The means to call for help must be available and emergency telephone numbers must be kept up to date and accessible to all personnel.

With international deployments, organizations should pre-plan emergency evacuation of personnel in case of injury, illness, security threats and (suspected) illness due to the outbreak pathogen.

In the case of spill accidents involving infectious substances, the first priority is to reduce exposure to the pathogens to those at risk. This may require leaving the accident site, safe removal of contaminated PPE, and cordoning off the area. In the case of human exposure or contamination, immediate decontamination should be started; often dilution of the pathogen followed by washing with soap and water is sufficient unless non-corrosive antiseptics are available. Medical advice and follow up must always be sought after (suspected) human exposure.

The affected laboratory area should be secured until the decontamination strategy has been decided. During the clean-up procedure, appropriate protective clothing must be worn including face protection and respiratory protection if infectious aerosols could be present. Disinfectants, absorbent material, waste bags and other items should be collected before re-entering the contaminated area.

The spill should be covered with absorbent material (for example, paper towels, rags, scrubs or laboratory coat) to absorb any liquid. Then, an appropriate disinfectant should be poured over the absorbent material in a circular pattern starting from the outside margin of the spill area and working towards the centre. After 30 minutes, the material can be cleared away and double wrapped in incineration bags. A dustpan or similar can be used to scoop up the material in case any sharp objects such as broken glass or other sharps are involved. Finally, the area should be disinfected again and cleaned up.

More information about emergency situations are given under section 9 human factors and occupational health.

All incidents must be reported according to laboratory, local and/or national regulations, investigations should take place to identify the root causes and risk assessments and procedures re-evaluated if necessary. Re-training may be needed to improve practices.

SECTION 9

HUMAN FACTORS AND OCCUPATIONAL HEALTH

9.1 Human factors

The interaction of laboratory personnel with their environment, their behaviour, their performance and the consequences of their actions are part of human factors. Individuals and organizations should always refer to their own occupational health care providers for locally accepted practice and advice. Nevertheless, a brief overview of essential points related to the safety of workers in infectious disease outbreaks is given here to raise awareness about issues that could have adverse effects on laboratory personnel in outbreaks and epidemics *(13)*.

It is likely that most deployed laboratory personnel responding to an infectious disease outbreak will face many new and uncertain situations and pressures that they will not have encountered in their normal laboratory work. Despite training before deployment or individual experience from previous deployments, various stressors, if not properly managed, may adversely affect the performance of personnel. This may in turn lead to errors, which may be especially important if working in an outbreak situation. Stressors include the following:

- psychological pressure because of the high lethality of the outbreak disease/pathogen and unfamiliarity with transmission risks and risk mitigation measures in the laboratory,
- exposure to human suffering, rapid deterioration of patients and even death,
- absence from home, family and social support with possibly limited opportunity to regularly contact home,
- psychological effects of chemoprophylaxis (for example, against malaria) and travel-related illness,
- constricted work environment and working with an unfamiliar team for an extended period of time with little room for privacy,
- longer working hours, higher workload and physically demanding work (for example, having to wear heavy PPE) with risks of heat stress, and
- security threats, including conflicts with the local population and lack of support for and acceptance of outbreak control measures in the population.

Apart from the short-term consequences on worker performance, prolonged exposure to stressors may lead to negative, sometimes pathological, reactions in individual team members. Reactions may be physiological (for example, increased heart rate), emotional (for example, depressed mood), cognitive (for example, narrowing of perception), and behavioural (for example, increased alcohol consumption, absenteeism).

Team members themselves, colleagues, friends and family members back home should be aware of the risk of traumatic consequences, be vigilant about possible symptoms and seek help and advice early. Personnel who are stressed may attempt to hide personal difficulties for fear of letting the team down or being sent home early (even when this is in their own interest), so it is important that signs of stress are actively looked for, particularly by team leaders and senior personnel.

9.2 Occupational health

Health care workers including laboratory personnel are usually monitored and cared for by occupational health services according to national regulations. This may include the following to prevent disease and accidents:

- provision of an ergonomic and safe work environment with organizational and engineering provisions (for example, safety plans and reliable equipment),
- provision of measures to safeguard the health and well-being of personnel including scheduled working hours and adequate rest, and
- provision of protective measures (for example, PPE), preventive measures (for example, prophylaxis such as vaccinations) and regular health checks (for example, of blood pressure, temperature, checking skin integrity on the hands).

In an outbreak or epidemic situation, personnel, are likely to be exposed to higher levels of stress and more challenges than usual. This will make the work in the laboratory riskier. Residence in the area or region of an outbreak may pose its own hazards because of undetected disease cases in the community.

Therefore, heightened personnel safety, security and occupational health measures in an outbreak should be carefully planned and implemented to keep laboratory personnel safe, healthy and productive, and safeguard the home-based family and wider community. These include:

- comprehensive safety, security and medical preparation and emergency response,
- careful medical preparations,
- health monitoring and provision of care for personnel working in the outbreak laboratory,
- medical prophylaxis,
- medical emergency contingency planning, including response to a suspected exposure to the outbreak pathogen or disease symptoms in team members,

- a reach-back advice line/occupational health advice capability for all personnel where feasible,
- evacuation plan for common medical emergencies and accidents, including provision of suitable medical care in the home country,
- adequate insurance, and
- medical debriefing after the mission and possibly monitoring procedures.

Personnel must always have the opportunity to discuss their personal concerns with an appropriate person in their organization, a friend or other trusted person of choice.

9.2.1 Before deployment in an outbreak area

Medical preparation of personnel before deployment should be carefully planned taking into account the region where they are deployed to, climate, available help onsite and in the country, the outbreak pathogen and other pathogens endemic in the area. As much as possible, fevers in health care and laboratory personnel should be avoided during laboratory deployment and in home-based laboratories during epidemics. Delayed access to or non-availability of post-exposure medications may put the health laboratory personnel at risk and drain already scarce resources in the country. Activities that should be performed before deployment include the following.

- Carry out health checks for fitness to travel before deployment (for example, according to national regulations) and possibly medical clearance according to deploying employer or organization.
- Consider psychological fitness assessments.
- Check and update required routine vaccinations and possibly evaluate level of protection (for example, hepatitis B antibody levels).
- Manage pre-existing medical conditions and medication requirements in personnel.
- Provide travel vaccinations for the region (for example, against yellow fever, rabies, typhoid fever, meningitis, hepatitis A, Japanese encephalitis, tick-borne encephalitis and cholera) and seasonal vaccinations (for example, influenza).
- If a vaccine against the outbreak pathogen is available, provide vaccination and plan a response in case of exposure to or illness from the outbreak pathogen.
- Provide chemoprophylaxis (for example, against malaria).
- Provide stand-by medications and post-exposure medications (for example, against malaria, HIV, rabies or snake antivenom).

- Provide travel medication that may be life-saving in case of delayed availability of advanced medical help (for example, antimalaria drugs and antibiotics).
- Provide both personal and facility first-aid kits including eyewash devices.
- Provide PPE, personal disinfectant supplies and vector control equipment (for example, mosquito nets).
- Plan for emergency aid, evacuation and medical care (for medical and trauma reasons as well as infectious disease).
- Give detailed briefing to personnel and provide written advice and contact details for seeking help and advice.
- Depending on the outbreak pathogen and other infectious disease health threats during laboratory work, consider storing a baseline blood specimen from all laboratory personnel before each deployment to help provide the best care for them if they become ill.

Some chronic medical conditions prohibit laboratory work and deployments in an outbreak or epidemic situation. Personnel who cannot be deployed because of these reasons should be reassured and given a full explanation.

9.2.2 During outbreaks

Laboratory personnel during an epidemic or deployed personnel to the site of an outbreak should be monitored for health and well-being and should always stay vigilant to hazards and threats. New/emerging information on safety and health threats (for example, research findings related to the outbreak pathogen) in an epidemic should be freely communicated inside and between organizations and agencies. Issues that should be considered for and by personnel during an epidemic and deployment to an outbreak are outlined below.

- Personnel should always stay vigilant and adopt a dynamic risk assessment attitude.
- Personnel should practice adequate (hand) hygiene procedures both while working in the laboratory and outside the laboratory. A laboratory hygiene plan should be drafted and displayed and organizations must provide sufficient supplies of PPE and disinfectants to their personnel.
- Personnel should report even minor illness and injuries early to their team leader or agreed medical focal point.
- Personnel should practice recommended infection prevention behaviour inside and outside the laboratory, including social distancing measures, according to the known or suspected transmission routes of the pathogen(s) concerned (for example, avoiding handshakes, never touching one's face).

- As much as possible, comfortable working conditions should be provided (for example, climate-controlled laboratory, ergonomic furniture) and personnel should be aware of environment-induced stresses and strains (for example, heat stress).

- Personnel should care for their own well-being by keeping well hydrated, well-nourished and have sufficient rest. Organizational guidelines for appropriate behaviour should be established before deployment.

- Personnel should be aware of their own physical and psychological well-being as well as their colleagues. Team members may adopt the "buddy" system by which team members are paired up to specifically look out for the welfare of each other.

- Personnel should adhere to prescribed prophylaxis regimes (for example, malaria prophylaxis) and should monitor colleagues for compliance and adverse reactions.

- Personnel must comply with monitoring protocols that may become necessary (for example, daily body temperature readings).

- Clear chains of communication should be in place for the management of medical, trauma or infectious disease emergencies. Personnel should notify an appropriate person about any incident, for example, suspected exposure to, or illness from, the outbreak pathogen. Protocols to deal with the incident should be in place, including arrangements for diagnostic testing and (early) safe evacuation of the affected person.

- Laboratories, particularly when deployed in close proximity to hospitals or emergency treatment centres, should protect the laboratory entrance from unauthorized entry of patients with the disease. Local personnel working in the laboratory should be strictly monitored for symptoms as well.

9.2.3. Follow-up after deployment

The return of personnel to their homes after deployment should be carefully planned and should take occupational health into account. The well-being and health of the returning laboratory personnel and their family, friends and wider community must be considered. The International Health Regulations (2005) *(13)* may influence the conditions under which personnel are able to return to their home countries, and local or national authorities and employers may have regulations for infection control. Personnel and their deploying organizations should consider the following issues related to their return and plan accordingly.

- International and transcontinental commercial airline flights may be cancelled or reduced in frequency, and medical checks before boarding may be applied.
- Requirements for the grouping, monitoring and quarantine of returning personnel according to their exposure risk to the outbreak pathogen and risk of infecting others may be introduced by home countries and organizations. Returning personnel must comply with these requirements and codes of behaviour (for example, body temperature monitoring, social distancing, daily reporting) for the required period of time.
- For a period of time (to be defined individually, for example, longest known incubation period), returning personnel may be required to avoid any activities and medical interventions (for example, vaccinations and dental care) that might lead to diagnostic uncertainty should they develop a fever. In the observation period, personnel should avoid travelling anywhere where prompt isolation, testing and treatment in case of illness would not be possible.
- Returning personnel should be provided with details of an appropriate person to contact if medical problems related to the outbreak deployment arise and with clear instructions for easy access to care.
- Important and imminently life-threatening differential diagnosis (for example, malaria or sepsis) must not be missed and left untreated in returning personnel with a fever if infection by the outbreak pathogen is suspected and needs laboratory testing.
- Personnel should undergo a routine occupational health check after the mission, if necessary.
- Personnel should continue to take prophylactic medication (for example, malaria prophylaxis) for as long as prescribed.
- Personnel should be aware that they may be excluded from blood donation for a period of time.
- Depending on the pathophysiology of the outbreak pathogen and other endemic diseases, clinically unapparent disease may occur. Exclusion testing (for example, by serology, also using the baseline blood specimen) could be an option to exclude late transmission of the pathogen.

SECTION 10

LABORATORY BIOSECURITY

The secure storage of specimens containing highly virulent biological agents is of prime importance, both during an outbreak and once it has been declared over, to prevent loss, intentional release, theft, misuse and proliferation of biological agents.

The patient specimens and the associated information gathered during an outbreak are a highly valuable resource for further research. Such research could be related to developing improved diagnostic assays, determining genetic variability in the outbreak, undertaking epidemiological studies to understand transmission routes, and developing therapeutics and vaccines. Continued safe and secure storage is necessary, particularly once an outbreak has been declared over. These specimens must be controlled to allow fair and equitable access by relevant researchers conducting legitimate research, while at the same time preventing access by parties with questionable agendas. It is preferable that specimens stay in the country of origin or, if this is not possible, that national authorities retain ownership of the specimens and can influence decisions about future access, storage, inactivation and/or destruction. Risk assessments relating to storage should be carried out and reviewed regularly. As with laboratory facilities during an outbreak, storage facilities should be secure and located where security can be guaranteed, even if this requires that specimens are shipped to alternative storage sites. Specimen storage facilities will require adequate funding to ensure continued security and power supplies, and to prevent degradation of either specimens or the surrounding security. A competent national focal point should oversee and coordinate decision-making on the use of these specimens for scientific research purposes in national or international collaborative projects.

Specimens should be aliquoted where possible when first received and stored safely (preferably in duplicate) to ensure the material stays intact. Access to the laboratory and specimens within the storage facility must be limited to authorized personnel. Freezers used to store the specimens need to be maintained, kept in secure rooms and connected to a reliable power supply with a back-up generator available. Inventories

must be made of all the specimens and these should also be stored securely.

In addition to ensuring long-term specimen security and integrity, consideration should be given to assuring laboratory managers' control of laboratory security and biosecurity. Many of the issues related to biosecurity have been covered in previous sections in this monograph and include:

- selection and training of laboratory personnel,
- specific training of personnel on biosecurity issues,
- access to the facility site and the laboratory,
- access to laboratory computer systems and the data management system,
- data security, including back-ups,
- continued data protection,
- access to personnel and generic laboratory email accounts,
- inventories of specimens,
- ownership and control of specimens,
- adequate freezer space and power supply,
- retention of equipment temperature records, and
- waste management, ensuring that all clinical waste is adequately inactivated before disposal.

Protection measures for biosecurity are similar to those required for personnel protection (see subsection 3.3 on outbreak laboratory infrastructure).

See also the Nagoya Protocol on access to genetic resources and the fair and equitable sharing of benefits arising from their utilization *(14)*.

SECTION 11

DECLARING AN OUTBREAK OVER

Measures to contain the infectious disease outbreak or epidemic will lead to a decline in the number of new cases (incidence) of the disease and eventually to the end of the outbreak. A decline will also occur as the natural course of an infectious disease because, for example, the population has become mostly immune. This will likely be reflected by a decline in positive results found by the laboratory(ies). Depending on the case definition applied for the disease, the laboratory capacity will still be required to test many specimens as active surveillance measures will still be in place for a defined time, even after the last cases of the disease have appeared (for example, a surveillance period of two incubation times after the last diagnosed case). The nature of the outbreak will determine the point at which an outbreak can be declared over by the competent authority. Recovering patients, although asymptomatic, can sometimes excrete pathogens for prolonged periods through different body fluids and be a source of infection, which may even lead to delayed sporadic cases of the disease. The health care system and the diagnostic laboratories need to adjust their biosafety procedures to this situation and appropriate advice must be given to the affected patients or even the whole population to prevent infections and their consequences (for example, as in the case of Zika virus infection, Ebola virus infection and SARS-CoV-2).

11.1 Communication

The competent and coordinating authority will collect feedback from laboratories and epidemiology surveillance systems on the number of disease cases. Decisions will need to be made and communicated on the necessary continued laboratory diagnostic capacity. All agencies involved in the outbreak response, the wider population and the international community should be notified once the outbreak is declared over. Public health agencies including laboratories should plan for sporadic suspected cases or a re-emergence of the epidemic.

11.2 Lessons learnt

During and after an outbreak or epidemic, debriefing sessions should take place. These sessions provide an opportunity to identify strengths and weaknesses in the outbreak response both within and between organizations, and provide information to improve the management of outbreaks in the future. Laboratories should evaluate what worked well and what did not. Topics for discussion may be:

- laboratory set up, infrastructure and workflows,
- availability of reagents,
- biosafety containment equipment,
- PPE,
- occupational health and safety,
- workload and working hours, and
- communication and coordination in the laboratory and between laboratories and health care personnel.

The laboratory's diagnostic response during the outbreak and lessons learnt should be documented in written reports which could be published in peer-reviewed journals so that the wider community can benefit if another outbreak occurs.

11.3 Maintained heightened surveillance

Heightened surveillance will need to continue for a period of time in case new cases and outbreaks re-emerge. Countries or subregions should keep some diagnostic capacity available. Ideally, they should have a network of laboratories and a plan for which laboratory should be sent the specimens if suspected cases arise. Health care workers should be advised to look out for biological threats and hazards and indications that infections are increasing. Laboratory and public health surveillance focal points should stay active, visible and approachable so that a response to re-emerging epidemics can be started without delay.

11.4 Laboratory decommissioning

Treatment centres and hospitals must be informed well in advance about termination of laboratory services. Alternative diagnostic testing laboratories and transport of specimens to these laboratories should be planned in case testing of sporadic suspected cases is needed.

Stationary laboratories that have provided diagnostic surge capacity during the outbreak will reduce these activities and readjust to their usual routine diagnostic work. Biosafety containment equipment before decommissioning or servicing will need to be decontaminated or destroyed by incineration so that personnel are not put at risk from residual contamination.

Laboratories that were specifically set up for the outbreak response will either be dismantled and, after appropriate decontamination, their accommodation will be handed back to the owner of the property. Alternatively, the laboratory may be handed over to local health care or public health providers for further use. Laboratory equipment will probably be sent back to the home laboratories, checked and repacked for the next outbreak deployment.

Depending on the number of specimens received by the laboratory and the policy on custody of patient specimens, the laboratories will probably have accumulated many vials with leftover patient specimens of different kinds. These specimens should be stored according to national regulations and decisions should be taken on the best storage conditions (for example, temperature). For biosafety reasons, the specimens should be kept in the appropriate biosafety containment environment and preferably triple packaged (for example, specimen tubes arranged in boxes – biosafety pouch – storage container). For biosecurity reasons, storage facilities should be kept locked and access should be restricted and documented. Specimens must not be removed without the appropriate approval; if specimens are removed, they must be tracked. An inventory of specimens should be kept which documents type, identification and volumes. Stocks should be checked at regular intervals.

The leftover specimens may be used for operational research during or after an infectious disease outbreak or epidemic. Such research can contribute to the containment of the emergency or future incidents. The specimens should be safeguarded and the decision to discard patient specimens should be made only after consulting relevant authorities and research institutes.

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Further information

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ANNEX PACKAGING REQUIREMENTS

Table A1.1: Packaging requirements for the different categories of substances

	INFECTIOUS SUBSTANCE CATEGORY A	INFECTIOUS SUBSTANCE CATEGORY B	EXEMPT SPECIMENS
	It is the responsibility of the shipper to ensure the correct classification, packaging, labelling and documentation for all infectious substances being transported.		
UN number	UN2814 and UN2900	UN3373	None
Proper shipping name	Infectious substance affecting humans/ infectious substance affecting animals	Biological substance Category B	Exempt human specimen/ exempt animal specimen
Labelling	Diamond label stating "Infectious substance" and "In case of damage or leakage immediately notify a Public Health Authority" Minimum label size: 100 x 100 mm Orientation label showing the right way up for air transport if primary receptacle exceeds 50 mL	Diamond label bearing: UN3373, and next to it "Biological substance Category B" Minimum label size: 50 x 50 mm	
Marking	Shipper's name and address Emergency contact telephone number Receiver's name and address	For air: shipper's name and address For air: telephone number of the person responsible for shipment Receiver's name, address	

Table A1.1: Packaging requirements for the different categories of substances (continued)

	INFECTIOUS SUBSTANCE CATEGORY A	INFECTIOUS SUBSTANCE CATEGORY B	EXEMPT SPECIMENS
UN number	UN2814 and UN2900	UN3373	None
Documentation	For air: shipper's Dangerous Goods Declaration Packaging list/proforma invoice Any import/export permits/ declarations if required (Air-) Waybill Itemized list of contents put between secondary and outer packaging The words "Suspected Category A infectious substance" in parenthesis should be shown on the transport documents if the biological agent is unknown	(Air-) Waybill Contact person given on air waybill Packaging list/proforma invoice Any import/export permits/ declarations if required	
	Additional labelling and markings must be used if other hazards exist, for example, dry ice or liquid nitrogen used for cooling, and may also be applied to describe temperature storage requirements and technical name of the refrigerant used.		
Training/qualification of packing person	Personnel must undergo training in accordance with modal agreements such as the test and verification of an individual's knowledge and competency for any person involved in dangerous goods transportation	Clear instructions on the use of the packaging must be given by manufacturer or distributor to the user/ shipper	

Table A1.1: Packaging requirements for the different categories of substances (continued)

	INFECTIOUS SUBSTANCE CATEGORY A	INFECTIOUS SUBSTANCE CATEGORY B	EXEMPT SPECIMENS
UN number	UN2814 and UN2900	UN3373	None
Packaging instructions	Triple packaging system according to packaging instruction P620 with outer packaging bearing the UN packaging symbol Primary or secondary receptacle must be able to withstand a pressure differential of 95 kPa and a temperature range of –40 °C to +55 °C (–40 °F to +130 °F)	Triple packaging system according to packaging instruction P650, testing documents are not required Capable of passing a drop test of 1.2 m height	Triple packaging system according to packaging instruction P650, testing documents are not required Capable of passing a drop test of 1.2 m height
	Ice, ice pads or dry ice, when used, should be placed outside the secondary receptacle or in the outer packaging or overpack. All packaging material must be able to withstand the temperatures (that is very low) generated by the cooling materials. The hazards posed by the evaporation of large quantities of dry ice must be considered. Dry ice must always be placed in a ventilated container. Hand carriage and transport in diplomatic pouches is strictly prohibited by international air carriers.		

Source: Guidance on regulations for the transport of infectious substances 2019–2020. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/bitstream/handle/10665/325884/WHO-WHE-CPI-2019.20-eng.pdf?ua=1, accessed 26 July 2019)


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