Sep-7-2023

A New Species of Trouble

Strengthening Capacity and Capability for the Identification, Attribution, and Consequence Management of Accidental and Deliberate Pathogen Releases in Africa

Pandemic Center at the Brown University School of Public Health

BROWN
Pandemic Center

A New Species of Trouble:
Strengthening Capacity and Capability for the Identification, Attribution, and Consequence Management of Accidental and Deliberate Pathogen Releases in Africa.

By

Peter Babigumira Ahabwe (Makerere University & the Public Health Operations Centre, Uganda)
Rym Benkhalifa (Institut Pasteur of Tunisia)
Nellie Bristol (Brown University)
Daniel Donachie (World Organisation for Animal Health)
Fanny Ewann (INTERPOL)
Wilmot James (Brown University)
Talkmore Maruta (Africa Society of Laboratory Medicine)
Chinwe Ochu (Nigeria Centre for Disease Control and Prevention)
Lawrence R. Stanberry (Columbia University)

Brown University Pandemic Center
in support of the
Signature Initiative to Mitigate Biological Threats in Africa, a partnership between the Global Partnership Against Materials and Weapons of Mass Destruction and the Africa CDC

Co-Authors

Peter Babigumira Ahabwe serves as the Border Health Technical Lead at the Infectious Diseases Institute within Makerere University's College of Health Sciences. He is also an Epidemic Intelligence Analyst at the Uganda Public Health Emergency Operations Centre in Kampala, where he is responsible for surveillance of Chemical, Biological, Radiological, and Nuclear events.

Daniel Donachie, BVMS MRCVS, is a Program Manager in Emergency Management working in the Preparedness and Resilience Department of the World Organisation for Animal Health (WOAH).

Rym Benkhalifa, PhD, is a Neurobiologist and research team leader in the Laboratory of Biomolecules, Venoms and Theranostic Applications and Biosafety-Biosecurity activities coordinator in Institut Pasteur of Tunis (Tunisia).

Nellie Bristol MPH is an independent global health analyst, researcher, writer, and editor working with Brown University's Pandemic Center. Through work with international bodies and academia and with the Center for Strategic and International Studies, she has developed expertise in pandemic preparedness and response, infectious disease control, biosafety and biosecurity, and global immunizations.

Fanny Ewann PhD is a Specialized officer in the Bioterrorism Prevention Unit under the CBRNE and Vulnerable Target Sub-directorate of the International Criminal Police Organization (INTERPOL), Lyon, France.

Wilmot James PhD is Professor of Practice in Health Services, Policy and Practice and Strategic Advisor to the Pandemic Center at Brown University's School of Public Health. He is the editor of *Vital Signs: Health Security in South Africa,* Johannesburg, Brenthurst Foundation, 2020. He is principal co-author of 'Building Global Vaccine Manufacturing Capacity: Spotlight on Africa' *Vaccine* 2023 June 19:41(27).

Talkmore Maruta PhD is Acting Director of Programs at the African Society for Laboratory Medicine.

Chinwe Lucia Ochu MBChB is the Director of Planning, Research, and Statistics at the Nigeria Centre for Disease Control and Prevention where she supervises policy and strategic planning, research and knowledge management, infection prevention and control, antimicrobial resistance, and risk communication and community engagement programs

Lawrence R. Stanberry MD PhD is Professor of Pediatrics at the Columbia University College of Physicians and Surgeons. An infectious disease specialist, he is the co-editor of *Vaccines for Biodefense and Emerging and Neglected Diseases,* London, Elsevier, 2009 and *Viral Infections of Humans Epidemiology and Control,* 6th Edition, New York, Springer, 2022-23.

Acknowledgments

Many thanks to Kiran Rodrigues (Brown University) for his research assistance and Andrea Uhlig and Bentley Holt for bringing the paper to production. Yenew Kebede (Africa CDC) provided extensive comments for which we are most grateful. The research and publication of this policy brief was supported and funded by the Brown University's School of Public Health's Pandemic Center.

Foreword

By Jennifer Nuzzo
Director: Brown University Pandemic Center at the School of Public Health

COVID-19 has provided direct evidence of unprepared societies' vulnerabilities to biological threats. To date more than 7 million people are known to have lost their lives–a figure that, given global weaknesses in surveillance, is considered to be a vast undercount. This level of mortality has in many countries contributed to historic declines in life expectancy. Millions of those who survived their infections are still struggling with post-acute sequelae of SARS-CoV-2 infection (PASC), or "long COVID". Perhaps the longest shadow cast by the pandemic is felt by children across the globe whose schooling was interrupted and now are experiencing pandemic-associated learning losses. As governments move on from the pandemic emergency, we should not forget how much we've lost during this crisis–a consequence of our lack of preparedness for biological threats.

In taking stock of COVID's tolls it is important for our preparedness for future biological emergencies, that we recognize other plausible disease scenarios that could cause even greater harm to our health, peace and prosperity than what we've seen to-date. The same biological progress that enables rapid development of life-saving medicines, vaccines and diagnostic tools can be misused to cause harm. A deliberate or accidental release of a deadly pathogen, such as a genetically engineered organism, could disarm our existing medical and public health defenses. The list of ways biological threats can up-end societies is long and growing.

Though we don't know when or what type of biological crisis will be the next to occur, we should not prepare only for the last crisis. We must contend with how we'd prevent or respond to a range of plausible scenarios. This report, A New Species of Trouble, offers a roadmap for preparing for some of the most challenging scenarios: accidental or deliberate release of a deadly biological agent. Written with expert input from those on the front-lines of protecting us from biological threats, this document considers the challenges of detection not only the events that have occurred to-date as well as biological threats of the future. Though this guide was written with a particular geography in mind (Africa), the guidance offered here will be relevant to a range of settings.

We may hope that future biological crises don't occur, but hope is not a strategy for being prepared. We must contend with our known vulnerabilities given past events. We must also prepare ourselves to be ready for plausible crises not yet seen.

Executive Summary

Determining the origin of disease outbreaks and developing effective protocols based on the specific cause is critical to controlling the spread of disease and protecting human, animal, and environmental health and welfare as well as economies and national security. Many African countries have policies to address naturally occurring outbreaks. However, African countries are by no means alone in lacking the tools to identify and manage incidents caused by accidental or deliberate pathogen release. Recent growth in laboratory systems and widespread access to innovative but potentially dangerous technologies is creating a new species of trouble requiring a re-evaluation of the threat landscape. This policy brief, focused on Africa, discusses established protocols and measures aimed at preventing and containing outbreaks. It then takes a broad approach by recommending policies related to assessment and handling of accidental and deliberate pathogen releases as an integral part of existing outbreak protocols. The proposals provide specific strategies for surveillance, rapid response, containment, investigation, and mitigation of these human-made outbreaks, emphasizing strong biosafety and biosecurity measures. They further emphasize the importance of training, capacity building, collaboration (including collaboration in developing diagnostics and medical countermeasures), and early warning mechanisms. To further support the guidelines, the authors recommend establishing national multidisciplinary outbreak assessment units and consequence-management systems, capacity building of relevant security and law enforcement personnel, and sustainable domestic financing. The authors recommend piloting the guidelines outlined in this policy brief. Adopting the proposed strategies and instituting needed support structures will improve countries outbreak assessment and response capabilities and thus mitigate the health and economic consequences of accidental or deliberate infectious disease outbreaks.

Introduction

Three types of outbreaks can threaten public health: naturally occurring and those caused by accidental or deliberate release of dangerous pathogens.[1] Natural outbreaks are those resulting from the transmission and spread of infectious diseases in the absence of human intervention or through human contact with wildlife. Accidental outbreaks are caused by laboratory mishaps, unintended pathogen releases linked to lawful or illicit activities, or human error in handling dangerous materials. Deliberate outbreaks involve intentional release or dissemination of pathogens to cause harm, instill fear, or disrupt societies. They also could be used for extortion or personal financial or commercial gain. Natural outbreaks have been part of the human condition since the beginning of recorded memory and there have been focused biological attacks throughout history. However, recent growth in laboratory systems and widespread access to innovative but potentially dangerous technologies is creating a new species of trouble requiring a re-evaluation of the threat landscape. African countries, as in many others in both the developing and developed world, have protocols for managing naturally occurring outbreaks, but fewer policy measures govern those arising from accidental or deliberate actions. This policy brief intends to motivate countries to develop policies to assess the cause of outbreaks with epidemic and pandemic potential. It then outlines specific necessary management actions if the outbreak was accidental or deliberate. We recommend that countries pass legislation to establish national multidisciplinary outbreak assessment units and consequence-management systems for accidental and deliberate events. This will serve as a multi-sectoral complement to the Africa CDC's *Biosafety and*

[1] The World Health Organization (WHO) groups various threats as follows: "Biological threats refer to the intentional or accidental release of biological agents, such as bacteria, viruses, toxins, or other biological substances that have the potential to cause illness, death, or ecological harm. These threats may be deliberate acts of bioterrorism or arise from naturally occurring outbreaks of infectious diseases."

Biosecurity Initiative's Model Legal Framework. As a first step, a pilot project in one or two countries should be undertaken as a proof-of-concept.

Outbreak Origins and Consequence Management Framework Rationale

Determining the origin of an outbreak helps to (1) identify the source, a crucial step for implementing effective control measures to prevent the further spread of the disease; (2) understand the epidemiology of the disease, including how it spreads and who is most at risk, and thus inform public health policies and interventions; (3) identify potential risk factors for the disease, such as exposure to contaminated food or water, which can inform prevention strategies; (4) as seen with the COVID-19 pandemic, alleviate public anxiety and fear by providing accurate information about the disease and its transmission; (5) if accidental, identify which threat and risk reduction measures to take to build resilience in biosecurity and biodefense systems; and (6) if deliberate, and if feasible, preserving the integrity of the crime scene and collecting evidence that can be used to prevent further attacks, to identify victims and a modus operandi for the pursuit and prosecution of offenders whether they are states, terrorists, and/or criminals.

As part of an effort to improve outbreak assessment and facilitate appropriate responses, in April 2019 the Africa Centres for Disease Control and Prevention (Africa CDC) launched the Biosafety and Biosecurity Initiative (BBI) to strengthen biosafety and biosecurity systems in African Union Member States and ensure compliance with World Health Organization International Health Regulations (IHR). To further the initiative, Africa CDC developed a strategic plan (2021-2025) that outlined a coordinated approach to strengthen biosafety and biosecurity capacities. The strategic plan's priority area no. 6 aims to enhance infrastructure, training, and capacity building for prevention, detection, and response to biological events by strengthening public health institutes. Africa CDC will establish a surveillance program for high-consequence agents and toxins to promote early detection and prevent severe public health consequences. While the agency has implemented surveillance frameworks and guidelines to support the plan, it needs policies to identify and manage accidental and deliberate pathogen releases. In its strategic plan for the BBI, Africa CDC documents highlight the need to strengthen national public health institutes and national reference laboratory networks in their capacity to prevent, detect and respond to accidental or deliberate biological events, working collaboratively by taking a One Health approach that involves plant and animal related entities and laboratories. This document fills knowledge gaps related to these human-induced releases and proposes policy options and implementation strategies to address them.

Background and Context

While governments have invested in infrastructure, research, and public health initiatives to enhance the capacity to respond to disease outbreaks, the risks associated with accidental and deliberate releases require special attention. Swift identification and response of accidental outbreaks are crucial to minimizing their impact on health and economies. Recognizing the importance of preventing accidental outbreaks, governments, especially those in the G7-G20, have invested in measures to reduce the threat, including laboratory biosecurity initiatives.

Deliberate outbreaks, including bioterrorism, pose unique challenges because of their clandestine nature and the need for collaboration between health authorities and law enforcement. Strong international cooperation and coordinated strategies are necessary to combat the intentional use of biological agents as weapons. Governments' ability to address deliberate outbreaks is in its early stages and should be accelerated, as detecting and effectively responding is essential for public safety and security.

Like other regions, Africa faces challenges in outbreak prevention and response; Africa CDC's BBI demonstrates heightened regional awareness of preparedness needs. COVID-19 reinforced the potentially catastrophic impact of highly contagious respiratory viruses, emphasizing the need for stringent safety protocols. Further, recent incidents in two Khartoum, Sudan, laboratories served as a reminder of the risks posed by inadequate security in labs, emphasizing the importance of preventive measures, especially in conflict zones.

Recognizing the potential consequences of different outbreak origins, particularly accidental and deliberate outbreaks, underscores the need for a comprehensive framework. Differentiating among natural, accidental, and deliberate outbreaks allows response strategies–including containment, investigation, accountability, and prevention—to be tailored to specific risks. The framework outlined in this brief would equip assessment teams with the expertise and tools to promptly identify the nature of an outbreak.

Protocols for Identification, Detection, and Management of Naturally Occurring Pathogens

African countries have developed a range of protocols, strategies, policies, and systems to address naturally occurring pathogens. They include:

1. Adoption of Integrated Disease Surveillance and Response (WHO AFRO, 1998) as a framework for early detection, reporting, and response to epidemic-prone diseases.
2. Creation of regional networks that facilitate cross-border communication and coordination in disease surveillance, such as the East African Integrated Disease Surveillance Network (EAC, 2000) and Antimicrobial Resistance Surveillance Network (Africa CDC AMRSNET) established by Africa CDC's five Regional Collaborating Centers (RCCs) in Egypt, Nigeria, Gabon, Zambia, and Kenya (Africa CDC, 2017).
3. National laboratory Systems (WHO Afro, 2010): Strengthening diagnostic capabilities and establishing reference laboratories, for example, through Regional Integrated Surveillance and Laboratory Networks (Africa CDC RISLNET).
4. Creation of the Africa CDC (African Union, 2017), which coordinates disease control and prevention efforts across the continent (Africa CDC, 2017).
5. Establishing a One Health program (Africa CDC, 2018) and coordination group (Africa CDC, 2022).
6. Creation of national public health institutes (Africa CDC, 2019) responsible for disease surveillance, outbreak investigation, and laboratory testing.
7. Collaborative approach addressing human, animal, and environmental health through the Framework for One Health Practice in National Public Health Institutes (Africa CDC, 2020).
8. Adoption of mobile technology (UNIPH, 2021) for real-time data collection, case reporting, and public health communication.

In addition, Africa CDC has developed guidance and policies based on World Health Organization (WHO), World Organisation for Animal Health (WOAH), and the UN Food and Agriculture Organization (FAO) documentation, including:

1. Framework for Development of National Public Health Institutes in Africa (Africa CDC, 2019).
2. Framework for Public Health Workforce Development, 2020-2025 (Africa CDC, 2020).
3. COVID-19 Guidance for Educational Settings (Africa CDC, 2020).
4. Africa CDC Guidance for Assessment, Monitoring, and Movement Restrictions of People at Risk for COVID-19 in Africa (Africa CDC, 2020).

5. Africa CDC Biosafety and Biosecurity Initiative 2021–2025 Strategic Plan (Africa CDC, 2021).
6. Africa CDC Advocacy and Communication Strategy for the Biosafety and Biosecurity Legal Framework (Africa CDC, 2021).
7. Africa CDC Handbook for Public Health Emergency Operations Center Operations and Management (Africa CDC, 2021).
8. The Regulatory and Certification Framework for Institutions Handling High-Risk Pathogens in the Africa Region (Africa CDC, 2022).
9. Africa CDC Guidance to Member States on Development of a National Biosafety and Biosecurity Strategy (Africa CDC, 2022).
10. Africa CDC Strategic Plan 2022-2026 (Africa CDC, 2023).
11. Africa CDC Event-Based Surveillance Revised Framework and Event-Based Surveillance Training Manual (Africa CDC, 2023).
12. African Union Health Information Exchange Guidelines and Standards (African Union, 2023).
13. African Union Health Information Exchange Guidelines and Standards (Africa CDC, 2023).

From these, we can infer the following:

Natural outbreaks are those resulting from the transmission and spread of infectious diseases in the absence of accidental or deliberate release. They can occur because of zoonotic infections, environmental changes, contamination of food, water, and environment, or the emergence of new pathogens or re-emergence of agents. Understanding the characteristics and patterns of natural outbreaks is crucial for effective response and consequence management. Implementing several measures is vital to effectively manage a crisis or outbreak's economic, social, and political consequences. Here are some examples:

1. Surveillance and early detection: Establishing a sophisticated surveillance system that monitors and detects potential threats and shares information (including rumor tracking, news monitoring and social media posts) among sectors. Implementing real-time data analysis tools to track disease patterns and detect unusual infection spikes can help identify outbreaks early on. Similarly, up-to-date vector mapping, and associated surveillance, can help anticipate the emergence or successful implantation of specific vector-borne diseases. Advanced algorithms and machine learning models are used to monitor and predict the spread of diseases like COVID-19. Laboratory capability to test for emerging infectious agents is critical for successful pandemic management.
2. Rapid response: Developing a well-coordinated and swift response mechanism. For example, establishing emergency response teams and protocols, including those for misinformation and disinformation management, that can be activated in advance of a potential threat or immediately after an outbreak can help contain and mitigate its impact. The Africa CDC Volunteers Health Corps (AvoHC), as an example, allows rapid deployment of experts from African Union Member States. These teams can include healthcare professionals, emergency services, and relevant government agencies collaborating to provide timely medical assistance, implement containment measures, and communicate vital information to the public.
3. Outbreak containment at source: Taking proactive measures to contain outbreaks at their source to prevent further spread. Examples include deploying resources to affected areas to isolate and treat infected individuals, implementing quarantine measures, and conducting thorough contact tracing. An example of this approach is the effective containment measures implemented during the 2022/2023 Ebola outbreak in Uganda, where efforts were made to isolate infected

individuals in Mubende District, provide proper medical care, and educate communities about preventive measures.

4. Recovery: Implementing strategies to ameliorate the consequences and facilitate recovery for long-term stability. Examples include economic stimulus packages to support affected industries and businesses, financial assistance to affected individuals and communities and implementing policies to restore essential services. An example of this can be seen in recovery efforts after natural disasters, where governments provide financial assistance, infrastructure rebuilding programs, and support for affected communities to aid their recovery (Ihekweazu, 2020). Recovery also should include after action reviews and lesson management to enhance future preparedness and response.

Finally, unintended sequelae can arise as a result of interventions such as loss of social interaction affecting mental health during the COVID-19 *Cordon sanitaire* measures (Staempfli, 2022). Special consideration should be given to the physical and emotional well-being of vulnerable populations, including women, who are more likely to be exposed to pathogens and suffer fatigue given their outsized role as caregivers.

By implementing these consequence management pathways, public health agencies and stakeholders can effectively respond to natural outbreaks, minimize their impact, and protect the health and well-being of populations (Madhav, 2017).

Multi-hazard consequence management strategies.

Implementing consequence management strategies in outbreak response efforts necessitates adaptability, flexibility, and a continuous learning approach, taking into account the unique characteristics of each outbreak. The following scenarios provide more context:

1. Epidemic Control: In the case of a highly contagious airborne disease outbreak, such as the influenza pandemic, consequence management strategies may focus on widespread vaccination campaigns, public health messaging to promote personal hygiene and preventive measures, and the establishment of temporary treatment facilities to handle the surge in patient numbers.

2. Biological Threat Response: In the event of a deliberate release of a biological agent, consequence management strategies would require additional coordinated effort among law enforcement, public health agencies, veterinary services (in the case of an animal or zoonotic pathogen) and emergency services. Strategies could include immediate evacuation and decontamination of affected areas, distribution of personal protective equipment and medical countermeasures, and thorough investigation to identify the source and prevent further harm.

3. Natural Disaster Recovery: Following a natural disaster like a hurricane or earthquake, consequence management strategies may involve the rapid deployment of search and rescue teams, provision of emergency shelter and supplies, restoration of critical infrastructure such as power and water systems, and–a requirement for all types of crises–psychological support services for affected individuals including all responders.

4. Cybersecurity Incident: In the case of a large-scale cyberattack compromising critical infrastructure systems, consequence management strategies may include isolating affected systems, conducting forensic investigations to determine the extent of the breach, implementing

backup systems to ensure continuity of operations, and enhancing cybersecurity measures to prevent future incidents.

By tailoring response planning and consequence management strategies to the specific characteristics of each outbreak or crisis, authorities can effectively respond to the situation, mitigate the impact and facilitate a successful recovery. This approach highlights the importance of adaptability, flexibility, and continuous learning in outbreak response efforts.

Protocols for Accidental Release of Pathogens

Introducing threat reduction measures can be crucial to mitigating outbreaks caused by the accidental release of pathogens. Accidental outbreaks occur because of laboratory accidents, unintended pathogen releases, human error in handling dangerous materials, or as a byproduct of illicit activities. These incidents have profound implications for public health and law enforcement demanding a systematic approach to manage their consequences effectively. Essential factors to consider include: characterizing and documenting laboratory accidents and unintended releases and possessing the necessary expertise and technologies for identification and confirmation. When unintended release is linked to illegal activities, further work with law enforcement is needed to understand modus operandi and illicit flows linked to disease spread. It also requires educating first line officers on biological risks and precaution measures to avoid further spread and/or exposure to the disease. Dealing with accidental outbreaks requires a comprehensive approach to effectively manage their consequences, prevent pathogen spread, conduct thorough investigations, establish accountability, and implement measures to prevent future incidents.

Effective threat-reduction measures should be implemented to mitigate the accidental release of pathogens. These measures include:

1. Robust biosafety and biosecurity protocols: Adhering to established guidelines and biosafety levels for handling pathogens.
2. Identification of country specific high priority pathogens and conducting risk assessments to check preparedness, response, and mitigation measures for each identified pathogen.
3. Adequate training and education: Comprehensive training for personnel, including law enforcement at risk of exposure, on biosafety measures and emergency response procedures.
4. Simulation exercises: To practice and test plans and procedures and validate training.
5. Robust facility design: Incorporating physical barriers, controlled access points, and proper air filtration and waste management systems.
6. Regular inspections and audits: Conduct routine assessments to identify and address safety vulnerabilities.
7. Incident reporting and investigation: Establishing a reporting system to identify and learn from accidents or protocol breaches.
8. Risk assessment and management: Evaluating potential hazards, assessing risks, and implementing mitigation strategies. Interagency risk assessment and management would be beneficial, including with law enforcement, if some criminal activities have the potential to accidentally spread or introduce disease into the country.
9. International standards and collaboration: Following recognized biosafety and biosecurity standards and collaborating with international partners.
10. Research into effective biosafety and biosecurity measures: There are significant gaps in the current scientific evidence base to support effective laboratory biological risk management, and

some biosafety measures commonly used for selected high consequence pathogens are not based on scientific evidence.

Implementing these measures can significantly reduce the risk of accidental releases, enhancing overall biosafety and biosecurity practices in laboratories and other facilities.

Critically, an accidental release could be the result of a staff member becoming accidentally exposed/infected and subsequently spreading the infection outside the facility. The following clinical measures are essential:

1. Staff members who develop any illness must be evaluated by a physician who is aware of pathogens being worked on in the facilities.
2. All staff members need to be vaccinated against pathogens for which there are available vaccines.

We propose adopting the following workflow chart by Pilch, Luster, and Lentzos to investigate the origins of a potential or suspected accidental release outbreak involving a laboratory or similar facility.

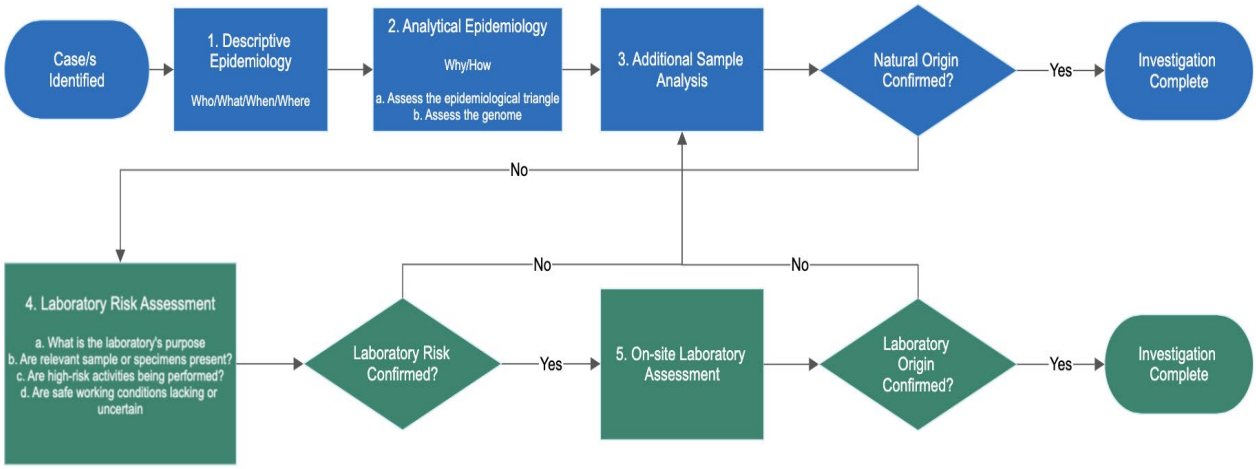


Figure 1. Proposed workflow for investigation of suspect accidental release from a laboratory (A Guide to Investigating Outbreak Origins: Nature versus the Laboratory Richard Pilch, Miles Pomper, Jill Luster, and Filippa Lentzos).

Accidental release occurring from incidents occurring during the transportation or disposal of infectious or contaminated material (including victims, corpses, and carcasses) and equipment should follow a similar strategy to determine the origin (e.g., gap in compliance, procedure, training, inadequacy of equipment or other resources) of the incident and remedy to it.

Protocols for Deliberate Release of Pathogens

Deliberate outbreaks involve intentionally releasing or disseminating pathogens to cause harm, instill fear, or disrupt societies. These outbreaks can result from biocrime, bioterrorism, or biowarfare. Biological warfare refers to using disease-causing agents as weapons, but it is prohibited under the Biological and Toxin Weapon Convention. On the other hand, bioterrorism involves the threats or intentional releases of viruses, bacteria, or other agents or toxins to cause illness or death in people, animals, or plants. It is driven by ideological, religious, or political beliefs and seeks to create casualties, instill fear, disrupt society, or cause economic losses. The success of bioterrorism lies in the level of societal disruption and panic it generates rather than the number of casualties. Even a few individuals becoming ill through a bioterrorism event can cause significant impact if it achieves the desired effect.

Biocrime, conversely, involves threatening to release or using a disease-causing biological agent or toxin to harm or kill an individual or a small group motivated by revenge or the pursuit of monetary gain through extortion or other means. Unlike bioterrorism, biocrime is driven by personal motives rather than political, ideological, religious, or other beliefs. While the likelihood of a successful bioterrorist attack is relatively low due to technical difficulties and constraints, the impact can still be significant, even with limited human casualties. Enhancing diagnostic, early warning surveillance, and therapeutic capabilities, training, and education can improve society's ability to combat infectious disease outbreaks and mitigate the effects of bioterrorist attacks.

As seen in the layout of the Aum Shinrikyo biological weapons facility below, biological weapons operations can go unnoticed in seemingly ordinary commercial or living spaces, unlike nuclear or chemical facilities.

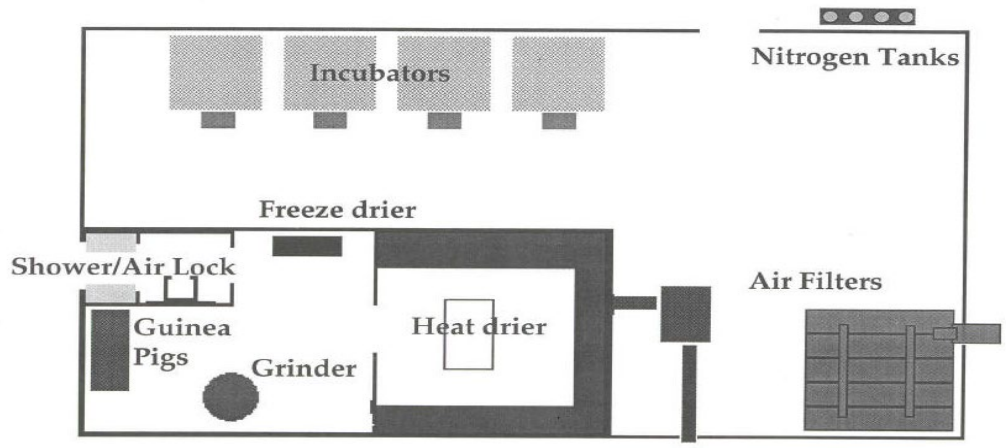


Figure 2. Layout of the Aum Shinrikyo biological weapons facility (*Responding to the Consequences of Chemical and Biological Terrorism*, 2006).

The timely detection and confirmation of deliberate outbreaks requires specialized expertise and advanced technologies within public health and law enforcement. Next-generation sequencing (NGS) technologies have revolutionized genomic investigations of pathogen outbreaks, allowing for unprecedented resolution and improved understanding of pathogen transmission dynamics. Other advanced pathology techniques, such as confocal microscopy, proteomics, and pyrosequencing, have also been used for detecting novel pathogens in a few specialized laboratories. In addition, web-based surveillance tools, infectious diseases modeling, and epidemic intelligence methods represent crucial components for timely outbreak detection and rapid risk assessment. Integrating these technologies and expertise can help in the early recognition of public health threats and the timely identification of causative pathogens.

The consequence management of deliberate pathogen-release outbreaks involves coordinated efforts to mitigate the event's impact, protect public health, and restore normalcy. It encompasses various strategies and actions aimed at minimizing casualties, treating affected individuals, containing the spread of the pathogen, and restoring societal functions.

Here are examples of consequence management measures for deliberate pathogen-release outbreaks:

1. Public health emergency response: Public health agencies and emergency management organizations activate response plans to rapidly mobilize resources, coordinate actions, and communicate critical information to the public. This includes establishing incident command systems, activating emergency operation centers, and deploying specialized teams to affected areas (Africa CDC, 2021).
2. Medical treatment and isolation: Efforts are made to provide immediate medical treatment to affected individuals and isolate them to prevent further transmission. Hospitals, clinics, and field medical facilities are set up to accommodate patients and provide appropriate care. Health workers follow strict infection prevention and control measures to protect themselves and others.
3. Contact tracing and quarantine: Contact tracing is conducted to identify individuals who may have been exposed to the pathogen. Those identified as contacts are quarantined or placed under active surveillance to monitor for symptoms. Advanced technologies such as mobile apps and digital surveillance systems can aid contact tracing efforts.
4. Mass vaccination or prophylaxis: Depending on the nature of the pathogen, mass vaccination or prophylactic measures may be implemented to prevent further infections. For example, mass vaccination campaigns may be conducted to protect susceptible populations, including health workers and first responders, in the case of a deliberate release of smallpox virus.
5. Risk communication and public awareness: Clear and timely communication is vital to inform the public about the situation, preventive measures, and available resources. Public health, animal health and agricultural agencies, government authorities, and media outlets collaborate to disseminate accurate joint information, address concerns, and promote appropriate behaviors to minimize the pathogen's spread. Misinformation and disinformation management will be critical to ensuring legitimate messaging is heard and correctly understood.
6. Decontamination and environmental remediation: Surge capacity is available to decontaminate affected areas and implement environmental remediation measures to eliminate residual contamination. This may involve thoroughly cleaning and disinfecting surfaces and vehicles, disposal of contaminated materials, including carcasses and other waste, and environmental monitoring to ensure safety.
7. Psychological and social support: Deliberate pathogen-release outbreaks can cause significant psychological distress among affected individuals and communities. Psychological support services, counseling, and mental health resources are available to help individuals cope with the event's emotional impact. Social support programs may also be implemented to address economic and social disruptions.
8. Investigation and law enforcement: Law enforcement agencies and specialized investigative teams collaborate to identify the source of the release and apprehend those responsible. Forensic investigations, surveillance data analysis, and intelligence analysis are conducted to aid in identifying, apprehending, and prosecuting individuals involved in the act of bioterrorism or biocrime.

These consequence management measures are coordinated and multidisciplinary, involving public health authorities, animal and agricultural experts, emergency responders, healthcare professionals, law enforcement agencies, government entities, and international partners. The goal is to minimize the impact of deliberate pathogen release outbreaks, protect public health, and restore normal functioning within affected communities.

Emerging Risks from New Technologies

While advancements in life sciences research have led to incredible breakthroughs, there are serious concerns about threats emerging from the intersection of artificial intelligence (AI) and synthetic biology. More than 300 experts, leaders, and public figures recently signed a *Statement on AI Risk* which stated: "Mitigating the risk of extinction from AI should be a global priority alongside other societal-scale risks such as pandemics and nuclear war."

In late May 2023, the Helena organization convened a group of senior leaders from industry, government, think tanks, and academia to discuss emerging threats related to AI. Their focus was on the governance and policy decisions required to remain safe and secure from biorisk while still benefiting from AI-enabled biology.

Their recommendations, delineated in a report produced in July 2023, all require swift action, meaningful engagement across all industries, sectors, and populations, and international cooperation: establish public-private AI task forces and subordinate technical working groups; safeguard the digital-to-physical frontier, starting with mandatory DNA synthesis screening; appropriately guardrail AI technology, including large language models (LLMs) and biological design tools (BDTs); refine policies concerning enhanced potential pandemic pathogen (ePPPs) and update and reinforce biorisk policies to mitigate against accidental and deliberate misuse; enhance biosecurity and biosafety norms to explicitly include AI-enabled biology and promote international organizations and practical tools to implement them; and resilience – invest in early warning and detection, response capacity, and accountability measures, and build biosafety and biosecurity into these approaches.

WOAH proposes the following algorithm for handling a suspicious biological event.

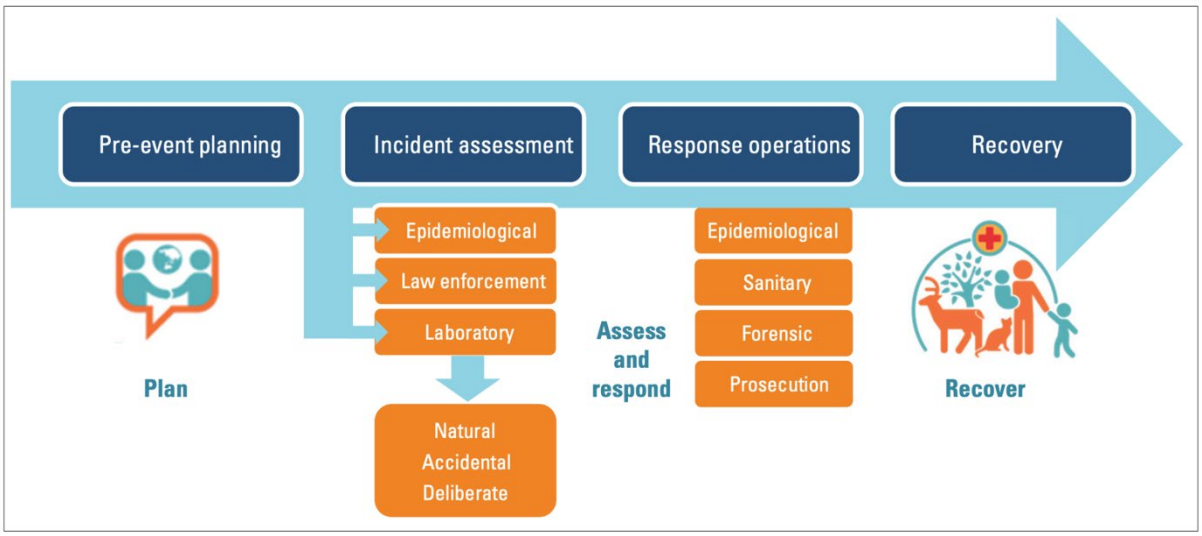


Figure 3. One health algorithm for handling a suspicious biological event (WOAH, 2021).

Planning (pre-event):

Public health authorities should engage in pre-planning activities to prepare for biothreat events effectively. This includes developing joint criminology-epidemiology protocols, training on them, and exercising built capabilities through simulation exercises. Other actions involve securing cooperation agreements among agencies to facilitate information sharing and capacity building, Conducting comprehensive assessments using tools like the World Organization for Animal Health Performance of Veterinary Services Pathway (PVS), the UN Food and Agriculture Organization Surveillance Evaluation Tool (SET), including its biothreat module, and Joint External Evaluations (JEE) helps identify gaps in capability and capacity related to biothreat events and target resources against priorities.

Contingency planning should address surge requirements, including laboratory needs that may not be available nationally. It is crucial to coordinate with intersectoral partners and stakeholders during pre-planning efforts.

In May of 2021, Chatham House issued a report on biosecurity and biosafety capacities and capabilities in Africa. The research identified as priority issues to improve progress in these areas: high-level political engagement and commitment; sustainability of both finances and resources; legislation and legal frameworks; multi-sectoral coordination and collaboration; training and workforce development; and non-proliferation, Biological and Toxin Weapons Convention implementation and universalization. The report concluded that many of these issues could benefit from larger scale, African-led, multi-partner initiatives. While there were, and are still, numerous challenges to compiling a list of all biosecurity initiatives in Africa, the report provided a high-level look at existing capabilities while highlighting pressing issues.

Incident Assessment:

Public health authorities, in collaboration with law enforcement, play a critical role in conducting joint assessments during biothreat events. These assessments aim to evaluate the credibility of potential intentional activities related to the event. Epidemiological and criminal indicators of suspicious activities that can guide the assessment process are identified and included in Standard Operating Procedures (SOPs). Similarly, triggers for the notification and coordination of specific actions with law enforcement should be clearly identified and included in response plans. Public health authorities should promptly notify the WHO, WOAH, and appropriate authorities (e.g., INTERPOL) when suspicion of an intentional event arises.

Response Operations:

1. Disease surveillance, indicators, and triggers: Routine disease surveillance systems are essential for providing baseline data on disease prevalence and identifying triggers or indicators of possible biothreats. Public health authorities should consider epidemiological and pathogen/toxin-related factors as possible triggers or indicators, understanding that further investigation may be warranted. Good communication between relevant authorities is essential to ensure rapid investigation by public health authorities.
2. Continuity of operations: Public health authorities should plan for continuity of operations, considering personnel, facilities, IT and communication capabilities, laboratory, mutual support, and focal points.
3. Information sharing: Secure communication channels should be established for sharing bio-threat information among law enforcement, veterinary authorities, public health, and other relevant entities. Protocols for information sharing and authority for releasing information should be established.
4. Logistics: Logistics planning should consider surge capacity requirements in field, laboratory, and epidemiological and countermeasure operations as well as support for the handling and examination of contaminated evidence.
5. Joint investigations: Investigations of suspicious biothreat events may require concurrent criminal and epidemiological work to identify the source, control the event, determine attribution, and support apprehension and prosecution of perpetrators. Consideration should be given to establishing joint investigative teams as part of preparedness planning and educating magistrates on the specificities of biological incident investigations. Biothreat investigations may require joint interviews between the public health and the security sector. Joint interviews can support the investigative process, and information must be collected and preserved for investigation and prosecution.

6. Safety and health: Enhanced personal protective equipment (PPE) and disinfection procedures should be implemented for personnel safety and to mitigate the agent's spread. Safety and health plans and SOPs should be developed to address the physical and psychological impact on responders and the general public.
7. Sample collection, preservation, and integrity: Public health authorities should prepare and plan for specialized sampling in biothreat events, ensuring chain of custody and sample integrity. Different strategies for collecting, submitting, and storing diagnostic specimens should be considered, and experts or relevant laboratories should be identified in advance. Developing a network of laboratories to ensure availability of the necessary techniques and expertise would be valuable.

Laboratory Operations – Analysis and Storage:

Public health authorities should know national and international laboratory capabilities in advance of an incident across veterinary, public health, and forensic disciplines. As an example, during the height of the COVID-19 pandemic, veterinary laboratories engaged in surveillance screening by testing human samples, demonstrating the value of One Health networks. Collaboration agreements should be in place with capable laboratories, ensuring surge capacity, chain of custody records, secure sample storage, and proper waste management. This is critical for non-traditional forensics analyses, such as microbial forensics, but also for the processing of contaminated traditional forensics evidence that cannot be decontaminated. Laboratories should adhere to international standards for quality assurance, biosecurity, biocontainment, and transporting dangerous goods.

Crisis Management Centre:

Coordination and management of biothreat events, whether suspicious or deliberate, require the activation of a crisis management team. Based on the circumstances, primary command and control of the incident may shift among veterinary services, public health, and law enforcement/security agencies. Public health authorities should plan for staffing their internal and joint operation centers and establish effective liaison officers for information sharing and operational planning across sectors.

Crisis Communications:

Public health authorities should develop joint communication strategies with law enforcement to ensure timely, accurate, and coordinated messages during biothreat events. Pre-scripted messages that address potential scenarios should be developed with relevant stakeholders. Effective communication channels, including traditional media, social media, and targeted notifications, should be utilized to reach different audiences. Pre-tested misinformation and disinformation management protocols should be employed.

Training and Education:

Training and education are essential components for enhancing the capabilities of public health authorities in mitigating biological threats. Training programs should encompass leadership, interagency coordination, forensic investigations, and laboratory-specific skills as well as being able to identify and respond to suspicious behavior or indicators of suspicious activities. The ability to provide training to veterinary students, private responders, law enforcement, security operatives, and other appropriate responders from other sectors is critical. Conducting multi-agency tabletop exercises and field-based drills can help assess competencies and interoperability and identify areas for improvement.

Lessons Learned and After-Action Report:

Following biothreat events, assessing the response and identifying potential lessons is crucial. Public health authorities should develop comprehensive after-action reports to document successes, challenges, and areas for improvement. These reports provide valuable insights to inform future operations and preparedness efforts for handling biothreat events effectively.

International Cooperation and Assistance:

In their discussion, Katz et al. delve into the relationship between the United Nations Secretary-General's Mechanism for Investigating of Alleged Use of Chemical and Biological Weapons (UNSG) and specific aspects of the Biological Weapons and Convention (BWC). They provide an in-depth analysis and explore ways to understand this interplay.

The authors examine the role of the UNSG General's Mechanism, which serves as a framework for investigating incidents involving biological and chemical agents, especially where state actors are suspected. This mechanism aims to facilitate gathering information, conducting objective assessments, and determining the facts surrounding such events.

Additionally, Katz et al. explored how the BWC, a treaty prohibiting the development, production, and stockpiling of biological weapons, intersects with the UN Secretary General's Mechanism. The authors discuss how these two entities can collaborate to enhance the prevention, detection, and response to potential deliberate biological events.

By expanding on these points, Katz et al. provide a comprehensive understanding of the relationship between the UN Secretary General's Mechanism and the Biological Weapons Convention, shedding light on their combined efforts to address deliberate biological threats and ensure global security.

Where there is no allegation of state actors' or military involvement, INTERPOL can provide support to its membership in the areas of prevention, preparedness, and response to biological incidents. INTERPOL's primary aim is to advance international police cooperation to prevent and fight crime.

This organization offers a range of technical and operational support to law enforcement authorities in member countries, such as targeted interagency training, expert investigative support, relevant data sharing capabilities and secure communications channels, that can be applied to the coordinated investigation of biological incidents.

With regards to operational response and investigative support, if required and in line with INTERPOL's mandate and Constitution, INTERPOL officers from the relevant units can be deployed as part of an Incident Response Team to assist member countries in the event of a terrorist attack or criminal investigation involving biological material.

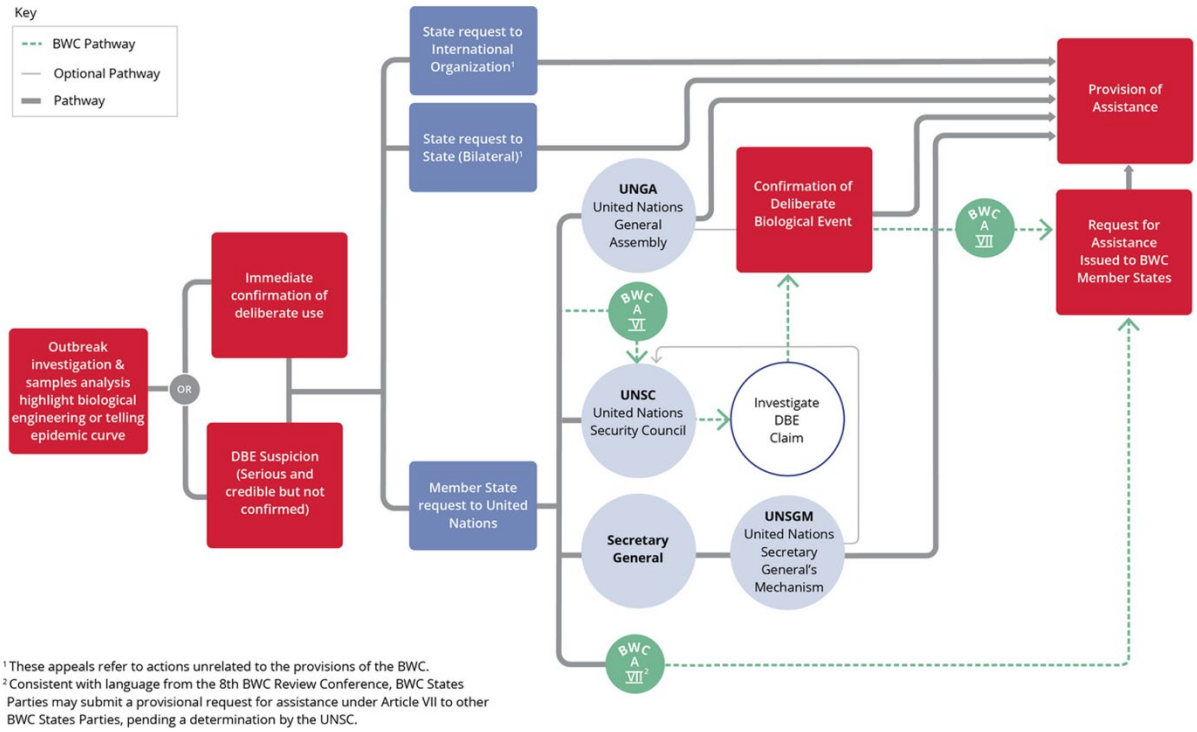


Figure 4. Pathways for assistance request during a suspect deliberate use event (Center for Global Health Science and Security, 2018).

Framework for Outbreak Assessment

To effectively determine the origin of outbreaks, outbreak assessment teams require a comprehensive framework that incorporates the necessary expertise, technologies, and methodologies. This framework should promote multidisciplinary approaches, collaboration, and stakeholder information sharing. As a Member State organization, the WHO has the moral authority to lead investigations into the origin of outbreaks, which can only be triggered by way of a resolution.

The following components are essential for a robust outbreak assessment framework.

Expertise and Training

Establishing specialized teams comprising epidemiologists, virologists, microbiologists, law enforcement, counterterrorism, criminology, intelligence, hazardous material specialists, environmental scientists, public health, veterinary and agricultural experts, and security professionals is vital. Countries must provide ongoing training and capacity-building programs to ensure team members possess the necessary skills to assess outbreaks of varying origins. Collaborating with international organizations, research institutions, and subject matter experts is critical to leveraging their expertise and enhancing the knowledge base.

Technological Infrastructure

Investments in state-of-the-art laboratory facilities equipped with advanced diagnostic technologies, including high-throughput sequencing, rapid pathogen detection systems, and bioinformatics capabilities, are critical. Countries must develop and deploy surveillance systems that utilize real-time data collection, analysis, and reporting mechanisms. They must continually explore the potential of emerging technologies, such as artificial intelligence, machine learning, and predictive modeling, to

enhance outbreak assessment capabilities and adapt biosecurity measures at vulnerable infrastructures. Countries lacking the resources for these technologies should develop partnerships with others in the region or with donor entities to ensure coverage.

Methodologies and Protocols

Countries should standardize outbreak assessment methodologies, including case definition criteria, data collection tools, and analytical frameworks. Additionally, they should develop joint risk assessment models that integrate epidemiological, criminological, intelligence, environmental, and social factors to determine the likelihood and impact of outbreaks. They should establish and update protocols for rapid response and deployment of assessment teams, ensuring timely arrival at outbreak sites for accurate data collection and assessment.

Multidisciplinary Approaches and Collaboration

Using a One Health strategy, countries should foster collaboration and information sharing among national and regional public health agencies, research institutions, academia, veterinary, agricultural, and environmental services, and international partners. They should facilitate joint investigations and data sharing to enable comprehensive outbreak assessments using multiple perspectives and expertise. Finally, they should continually establish communication channels and platforms for real-time exchange of information, best practices, and lessons learned.

Integration of Intelligence and Security

Countries should strengthen collaboration among public health agencies and intelligence and security entities to detect and respond to deliberate outbreaks. They should establish mechanisms for intelligence gathering, risk analysis, and threat assessment to identify potential deliberate outbreaks and minimize their impact. Finally, they should promote information sharing, and joint training and exercises among public health, veterinary, agricultural, and environmental services, and security agencies to enhance preparedness and response capabilities. These principles are enshrined in the efforts under the Global Health Security Agenda and the IHR's Linking Public Health and Law Enforcement.

The World Organization for Animal Health proposes various indicators in epidemiology, laboratory, and law enforcement that could suggest the presence of a disease outbreak or biothreat. (WOAH, 2021). In epidemiology, the indicators include cases of eradicated, emerging, or exotic diseases, changes in disease characteristics, decreased susceptibility to countermeasures, and unusual disease patterns. In the laboratory, indicators involve missing pathogens or toxins, security breaches, and testing results changes. Indicators in law enforcement include credible threats, online discussions about biothreats, accidental findings, suspicious behavior, whistleblowers, and cybersecurity breaches.

The US CDC field epidemiology manual (CDC, 2018) provides trigger questions for notifying law enforcement. These triggers include positive test results for biological or toxic agents, unexplained symptoms, illnesses, or deaths, unusual disease presentations, increased incidence of endemic diseases, unexpected morbidity and mortality rates, and unexplained illness or death in animals related to zoonotic agents.

The Joint Criminal and Epidemiological Investigations Handbook (US CDC, 2016) proposes public health and law enforcement triggers. Public health triggers include positive test results for potential biological threat-related agents, large numbers of patients with similar symptoms or diseases, unexplained symptoms, diseases, or deaths, unusual disease presentations, increased incidence of endemic diseases, and unexplained illness or death in animals related to zoonotic agents. Law

enforcement triggers involve indications of unlawful possession of biological agents, seizure of bio-processing equipment or dissemination devices, the discovery of literature related to biological agents, assessments indicating a credible biological threat, and Hazardous Materials Emergency responses involving biological agents.

These guidance documents show that having a set of criteria or factors is vital to recognize and assess a potential public health or biosecurity threat, as is using them as a basis for SOPs and reporting mechanisms.

Implementation and Capacity Building

By implementing this framework, outbreak assessment teams will have the necessary expertise, technologies, and methodologies to assess outbreaks and comprehensively determine their nature. The multidisciplinary approach, collaboration, and information sharing among stakeholders will ensure a holistic understanding of outbreaks and enable effective response strategies tailored to the specific origin of the outbreak.

1. 1.Training and Capacity Building
   The importance of training programs and other capacity-building initiatives for outbreak assessment teams cannot be overstated. Countries must provide specialized training on outbreak assessment methodologies, criminology, intelligence analysis, advanced technologies, and interdisciplinary collaboration for accidental and deliberate events. In addition, they should provide awareness raising resources and campaigns for non-specialized units. Finally, governments should develop standardized training modules, workshops, and simulation exercises to enhance the preparedness of outbreak assessment teams.

2. Collaboration with Regional and International Partners
   Collaboration with regional and international partners is vital to strengthen capacities and share best practices, as many of the activities mentioned above are highly technical and specialized. Establishing networks and platforms for information exchange, joint exercises, and mutual support is essential during outbreak assessments. Working with other countries, creation of regional or continental centers of excellence for outbreak assessment will foster collaboration and knowledge sharing.

3. Technology and Data Management Systems
   Advanced data management systems are needed to collect, analyze, and share real-time outbreak-related information. Countries need to leverage the potential of artificial intelligence, machine learning, and data visualization tools in improving outbreak assessment capabilities and decision-making processes.

4. Early Warning Mechanisms
   Early warning mechanisms are vital to detecting outbreaks and initiating timely response measures. Countries should explore the potential use of predictive modeling, syndromic surveillance, and event-based surveillance systems to enhance early detection capabilities. Finally, governments should work towards establishing robust communication channels and reporting mechanisms to facilitate the sharing of outbreak-related information across different stakeholders.

Early warning systems, such as the Tripartite Global Early Warning System (GLEWS), have been developed at the international level but these systems are not built to detect accidental or deliberate events. INTERPOL is launching BioTracker, a law enforcement-dedicated platform to facilitate the exchange of information between countries and the assessment of biological incidents. While aiming to enhance the analytical and intelligence capabilities of the global law enforcement community on biological threats and incidents, BioTracker has a built-in early warning system and visual interface that will increase timely preparedness and response of its membership to the deliberate release of biological agents.

5. Resource Mobilization and Sustainability
   Adequate resources, including funding, equipment, and personnel, are needed to support the implementation of the framework. Countries should adopt multi-pronged strategies for resource mobilization, including domestic funding, partnerships with development agencies, donor organizations, and private sector entities. Finally, sustainability should be explored by integrating outbreak assessment and consequence management into existing public health systems and structures.

6. Monitoring, Evaluation, and Adaptation
   Countries should establish, adopt, and adapt monitoring and evaluation mechanisms to assess the framework's effectiveness and identify areas for improvement. Continuous learning, adaptation, and refinement of outbreak assessment strategies are paramount and vital based on lessons from previous outbreaks. Finally, countries need regular reviews, feedback mechanisms, and knowledge-sharing platforms to facilitate ongoing improvement and innovation.

7. Support the Development of Diagnostics and Medical Countermeasures
   Vaccines, drugs, biologicals, and diagnostics useful in outbreak response by biothreat agents are dangerously lacking. The mandate of national or regional high-containment laboratories should be expanded to include collaborating on the development of diagnostics and medical countermeasures for the pathogens labs are actively studying.

African governments, with input from the Africa CDC, should encourage the expansion of the Coalition for Epidemic Preparedness Initiative's (CEPI) portfolio of priority known diseases beyond its current list of six pathogens: MERS, Lassa Fever. Nipah, Rift Valley Fever, Chikungunya, and Ebola. The additional targets should be selected from the US CDC's list biothreat agents based on perceived risk to Africa. The national or regional high-containment labs would partner with CEPI in the development of new vaccines.

High containment labs could be encouraged to develop animal models of pathogens of interest that can be used to support product licensure under a process similar to the US FDA Animal Rule. The regulations commonly known as the Animal Rule (21 CFR 314.600-650 for drugs; 21 CFR 601.90-95 for biologics; effective July 1, 2002) allow for the approval of drugs and licensure of biological products when human efficacy studies are not ethical and field trials to study the effectiveness of drugs or biological products are not feasible. The use of the Animal Rule is intended for drugs and biological products developed to reduce or prevent serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic chemical, biological, radiological, or nuclear substances. The use of such products could be earmarked for professions at high risk for exposure to the pathogen, e.g.,

researchers, epidemiologists, medical and veterinary personnel involved in outbreak assessment, and the public in the event of an outbreak.

To facilitate the development and approval of medical countermeasures for diseases of importance to Africa, regulations/legislation should be encouraged to develop creating an Animal Rule and emergency use authorization.

The proposed framework can be effectively implemented by prioritizing training and capacity building, fostering collaboration, leveraging technology, and implementing robust early warning mechanisms. Strengthening outbreak assessment capabilities will enhance Africa's ability to respond to outbreaks of all origins, ensuring early detection, accurate assessment, and appropriate consequence management.

Conclusion

Establishing a comprehensive outbreak assessment and consequence management framework is vital to African public health. Through this brief, we can better understand the associated risks and implement targeted response measures by addressing the nature of outbreaks and their potential origins.

The brief emphasized the importance of early detection, accurate assessment, and appropriate response to outbreaks, considering the potential variations in their origins. It outlined a proposed framework encompassing the expertise, technologies, and methodologies required for comprehensive outbreak assessment. The framework promotes multidisciplinary approaches, collaboration, and information sharing among stakeholders to enhance outbreak response capabilities.

The brief further discussed the consequence management pathways for natural, accidental, and deliberate outbreaks. It detailed specific strategies for surveillance, rapid response, containment, investigation, and mitigation, tailored to each type of outbreak. Additionally, it highlighted the challenges and complexities associated with identifying deliberate attacks and emphasized the need for law enforcement coordination, public communication strategies, and the strengthening of biosecurity measures.

In addition, the brief stressed the importance of training and capacity building for outbreak assessment teams, collaboration with regional and international partners, leveraging technology and data management systems, and establishing early warning mechanisms. These elements will enhance Africa's outbreak assessment capabilities, enable proactive measures, timely response, and continuous improvement to ensure successful implementation.

By adopting the proposed framework and implementing the recommended strategies, Africa will be better equipped to detect and assess outbreaks swiftly, determine their origins accurately, and implement appropriate consequence management pathways. Proactive measures, timely response, and continuous improvement in outbreak assessment capabilities will strengthen Africa's - and indeed all countries adopting the guidelines - resilience against disease outbreaks.

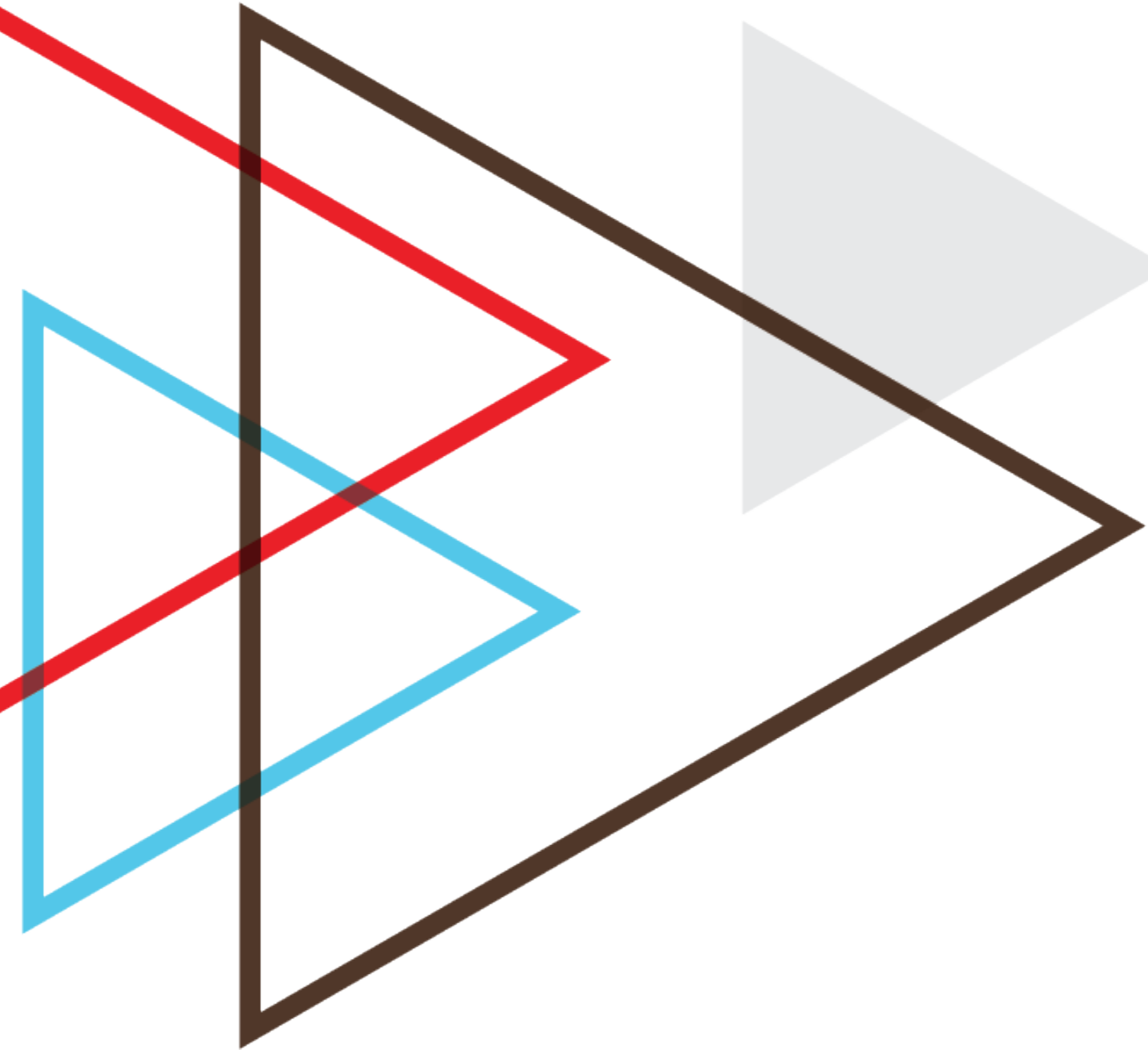
The increasing threat of accidental and deliberate release of biological agents constitutes a new species of trouble in global health. Governments, public health agencies, and relevant stakeholders must prioritize establishing this framework, allocating necessary resources, and collaborating effectively to ensure its successful implementation. By doing so, countries will be better prepared to address outbreaks and protect its population from the devastating impacts of infectious diseases.

Works Cited

1. Africa CDC. "Advocacy and Communication Strategy for the Biosafety and Biosecurity Legal Framework – Africa CDC." *Africa CDC*, 31 May 2021, https://africacdc.org/download/advocacy-and-communication-strategy-for-the-biosafety-and-biosecurity-legal-framework/. Accessed 30 May 2023.
2. Africa CDC. "Africa CDC Event-based Surveillance Resources – Africa CDC." *Africa CDC*, 28 March 2023, https://africacdc.org/download/africa-cdc-event-based-surveillance-framework-2/. Accessed 30 May 2023.
3. Africa CDC. "Africa CDC Guidance for Assessment, Monitoring, and Movement Restrictions of People at Risk for COVID-19 in Africa – Africa CDC." *Africa CDC*, 5 March 2020, https://africacdc.org/download/africa-cdc-guidance-for-assessment-monitoring-and-movement-restrictions-of-people-at-risk-for-covid-19-in-africa/. Accessed 30 May 2023.
4. Africa CDC. "Africa CDC Strategic Plan 2022-2026 – Africa CDC." *Africa CDC*, 18 March 2023, https://africacdc.org/download/africa-cdc-strategic-plan-2022-2026/. Accessed 30 May 2023.
5. Africa CDC. "Africa Centres for Diseases Control and Prevention launches new networks to fight health threats in Africa – Africa CDC." *Africa CDC*, 9 October 2017, https://africacdc.org/news-item/africa-centres-for-diseases-control-and-prevention-launches-new-networks-to-fight-health-threats-in-africa/. Accessed 30 May 2023.
6. Africa CDC. "African Union establishes One Health Coordination Group on Zoonotic Diseases – Africa CDC." *Africa CDC*, 4 July 2022, https://africacdc.org/news-item/african-union-establishes-one-health-coordination-group-on-zoonotic-diseases/. Accessed 30 May 2023.
7. Africa CDC. "African Union Health Information Exchange Guidelines and Standards – Africa CDC." *Africa CDC*, 28 March 2023, https://africacdc.org/download/african-union-health-information-exchange-guidelines-and-standards/. Accessed 30 May 2023.
8. Africa CDC. "Biosafety and Biosecurity Initiative 2021 - 2025 Strategic Plan – Africa CDC." *Africa CDC*, 7 July 2021, https://africacdc.org/download/biosafety-and-biosecurity-initiative-2021-2025-strategic-plan/. Accessed 30 May 2023.
9. Africa CDC. "COVID-19 guidance for educational settings – Africa CDC." *Africa CDC*, 26 May 2020, https://africacdc.org/download/covid-19-guidance-for-educational-settings/. Accessed 30 May 2023.
10. Africa CDC. "Development of a National Biosafety and Biosecurity Strategy – Africa CDC." *Africa CDC*, 13 June 2022, https://africacdc.org/download/development-of-a-national-biosafety-and-biosecurity-strategy/. Accessed 30 May 2023.
11. Africa CDC. "Framework for Development of National Public Health Institutes in Africa – Africa CDC." *Africa CDC*, 9 September 2019, https://africacdc.org/download/framework-for-development-of-national-public-health-institutes-in-africa/. Accessed 30 May 2023.
12. Africa CDC. "Framework for One Health Practice in National Public Health Institutes – Africa CDC." *Africa CDC*, 26 October 2020, https://africacdc.org/download/framework-for-one-health-practice-in-national-public-health-institutes/. Accessed 30 May 2023.
13. Africa CDC. "Framework for Public Health Workforce Development, 2020-2025 – Africa CDC." *Africa CDC*, 10 March 2020, https://africacdc.org/download/framework-for-public-health-workforce-development-2020-2025/. Accessed 30 May 2023.
14. Africa CDC. "Handbook for Public Health Emergency Operations Center Operations and Management – Africa CDC." *Africa CDC*, 16 June 2021, https://africacdc.org/download/handbook-for-public-health-emergency-operations-center-operations-and-management/. Accessed 30 May 2023.
15. Africa CDC. "One Health Programme – Africa CDC." *Africa CDC*, 2018, https://africacdc.org/programme/surveillance-disease-intelligence/one-health/. Accessed 30 May 2023.
16. Africa CDC. "Press Release on Africa CDC Strategic Plan 2022-2026 – Africa CDC." *Africa CDC*, 18 March 2023, https://africacdc.org/news-item/press-release-on-africa-cdc-strategic-plan-2022-2026/.
17. Africa CDC. "The regulatory and certification framework for institutions handling high-risk pathogens in the Africa Region – Africa CDC." *Africa CDC*, 9 August 2022, https://africacdc.org/download/the-regulatory-and-certification-framework-for-institutions-handling-high-risk-pathogens-in-the-africa-region/. Accessed 30 May 2023.
18. Africa CDC. "Statute of the Africa Centers for Disease Control and Prevention (Africa CDC) – Africa CDC." *Africa CDC*, 31 January 2017, https://africacdc.org/download/statute-of-the-africa-centers-for-disease-control-and-prevention-africa-cdc/. Accessed 30 May 2023.
19. African Union. "African Union Health Information Exchange Guidelines and Standards – Africa CDC." *Africa CDC*, 28 March 2023, https://africacdc.org/download/african-union-health-information-exchange-guidelines-and-standards/. Accessed 30 May 2023.

20. African Union. “The African Union launches Africa CDC, a Continent-wide Public Health Agency.” *African Union*, 2 February 2017, https://au.int/en/pressreleases/20170202/african-union-launches-africa-cdc-continent-wide-public-health-agency. Accessed 30 May 2023.
21. Bloom, David E., et al. “The Economic Risks and Impacts of Epidemics - IMF F&D Magazine - June 2018 | Volume 55 | Number 2.” *International Monetary Fund*, June 2018, https://www.imf.org/en/Publications/fandd/issues/2018/06/economic-risks-and-impacts-of-epidemics-bloom. Accessed 30 May 2023.
22. Brough, Richard. “Systemic capacity building: a hierarchy of needs.” *PubMed*, 1 September 2004, https://pubmed.ncbi.nlm.nih.gov/15310668/. Accessed 30 May 2023.
23. US CDC. “Suspected Intentional Use Of Biologic And Toxic Agents | Epidemic Intelligence Service | CDC.” *Centers for Disease Control and Prevention*, 13 December 2018, https://www.cdc.gov/eis/field-epi-manual/chapters/Biologic-Toxic-Agents.html. Accessed 30 May 2023.
24. Center for Global Health Science and Security. “Deliberate Biological Event Stakeholders Tool.” *Biological Event Stakeholders*, 31 July 2018, https://dbe.talusanalytics.com/#pathways. Accessed 30 May 2023.
25. US CDC, *The CDC Field Epidemiology Manual*. Edited by Richard A. Goodman and Sonja A. Rasmussen, Oxford University Press, 2019.
26. Donachie, D., et al. Animal Agrocrime: An Overlooked Biological Threat. Health Security. Ahead of print. http://doi.org/10.1089/hs.2022.0144
27. EAC. “East African Integrated Disease Surveillance Network.” *East African Community*, 2000, https://www.eac.int/health/disease-prevention/east-african-integrated-disease-surveillance-network. Accessed 30 May 2023.
28. Ihekweazu, Chikwe. “Strategies for coping with the health and economic effects of the COVID-19 pandemic in Africa.” *Brookings Institution*, 18 March 2020, https://www.brookings.edu/blog/africa-in-focus/2020/03/18/strategies-for-coping-with-the-health-and-economic-effects-of-the-covid-19-pandemic-in-africa/. Accessed 30 May 2023.
29. INTERPOL. “Bioterrorism”. https://www.interpol.int/Crimes/Terrorism/Bioterrorism. Accessed 12 Aug 2023.
30. Madhav, Nita. “Pandemics: Risks, Impacts, and Mitigation - Disease Control Priorities: Improving Health and Reducing Poverty.” *NCBI*, 17 November 2017, https://www.ncbi.nlm.nih.gov/books/NBK525302/. Accessed 30 May 2023.
31. Nardi, Marco De. “Implementation of a Regional Training Program on African Swine Fever As Part of the Cooperative Biological Engagement Program across the Caucasus Region.” *NCBI*, 26 October 2017, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5662547/. Accessed 30 May 2023.
32. “Responding to the Consequences of Chemical and Biological Terrorism.” *The Climate Change and Public Health Law Site*, 2006, https://biotech.law.lsu.edu/blaw/FEMA/Proceedings.pdf. Accessed 30 May 2023.
33. Staempfli, Sabina. “Unintended Consequences of Pandemic Management Strategies on Residents and Family in One Long-term Care Home in British Columbia: A Patient-Supported Qualitative Study.” *PubMed*, 2 July 2022, https://pubmed.ncbi.nlm.nih.gov/35812793/. Accessed 30 May 2023.
34. UNIPH. "Improvement in reporting and monitoring of Public Health Events following the introduction of electronic-based surveillance systems." *Uganda National Institute of Public Health*, 26 November 2021, https://uniph.go.ug/improvement-in-reporting-and-monitoring-of-public-health-events-following-introduction-of-electronic-based-surveillance-systems/. Accessed 30 May 2023.
35. Vasconcelos Gioia, G., et al. Informing resilience building: FAO’s Surveillance Evaluation Tool (SET) Biothreat Detection Module will help assess national capacities to detect agro-terrorism and agro-crime. One Health Outlook 3, 14 (2021). https://doi.org/10.1186/s42522-021-00045-8
36. WHO AFRO. “Integrated disease surveillance in the African region: a regional strategy for communicable diseases 1999-2003.” *WHO Afro*, 2 September 1998, https://www.afro.who.int/sites/default/files/2017-06/ids-strat-99-03.pdf. Accessed 30 May 2023.
37. WHO AFRO. “Strengthening public health laboratories in the WHO African Region: A critical need for disease control.” *WHO Africa*, 1 June 2010, https://www.afro.who.int/publications/strengthening-public-health-laboratories-who-african-region-critical-need-disease. Accessed 30 May 2023.
38. WOAH. "Guidelines for the investigation of suspicious biological events - WOAH Bulletin." *OIE Bulletin*, 23 February 2021, https://bulletin.woah.org/?panorama=05-1-0-2020-1-suspicious-events. Accessed 30 May 2023.
39. Pinet, Paula. “Tripartite and UNEP Support OHHLEP’s Definition of ‘One Health.’” *WOAH - World Organisation for Animal Health*, Dec. 2021, www.woah.org/en/tripartite-and-unep-support-ohhleps-definition-of-one-health.
40. WHO. “Epidemic Intelligence from Open Sources (EIOS).” *EIOS*. www.who.int/initiatives/eios.
41. Maruta, Talkmore. “The Evolution of SARS CoV 2 Testing in Africa.” *ResearchGate*, May 2021, www.researchgate.net/publication/351625477_The_evolution_of_SARS_CoV_2_testing_in_Africa.

42. Africa Centres for Disease Control and Prevention. “The Regional Training and Certification Program for Biosafety and Biosecurity Professionals &Ndash; Africa CDC.” *Africa CDC*, 24 Aug. 2022, africacdc.org/download/the-regional-training-and-certification-program-for-biosafety-and-biosecurity-professionals.
43. Africa Centres for Disease Control and Prevention. “Certified African Regional Professionals: Level 1 Biorisk Management; Africa CDC.” *Africa CDC*, 13 June 2023, africacdc.org/download/certified-african-regional-professionals-level-1-biorisk-management.
44. WHO. “Ebola Outbreak 2022 - Uganda.” *WHO*, 3 Nov. 2022, www.who.int/emergencies/situations/ebola-uganda-2022.
45. Australian Disaster Resilience. “Lessons Management Handbook | Australian Disaster Resilience Knowledge Hub.” *Australian Disaster Resilience - Knowledge Hub*, knowledge.aidr.org.au/resources/lessons-management-handbook.
46. Wenham, Clare. “Clare Wenham: Let’s Recognise All Women Who Have Been Caregivers During This Last Year.” *The BMJ*, Mar. 2021, blogs.bmj.com/bmj/2021/03/08/clare-wenham-lets-recognise-all-women-who-have-been-caregivers-during-this-last-year.
47. Harper, David, et al. “The Chatham House Sustainable Laboratories Initiative Prior Assessment Tool.” *Biosecurity Central*, biosecuritycentral.org/resource/core-guidance-and-recommendations/prior-assessment-tool.
48. Blacksell, Stuart D., et al. “The Biosafety Research Road Map: The Search for Evidence to Support Practices in Human and Veterinary Laboratories.” *Applied Biosafety*, SAGE Publishing, May 2023, doi:10.1089/apb.2022.0040.
49. Wurtz, Nathalie, et al. “Survey of Laboratory-acquired Infections Around the World in Biosafety Level 3 and 4 Laboratories.” *European Journal of Clinical Microbiology & Infectious Diseases*, vol. 35, no. 8, Springer Science+Business Media, May 2016, pp. 1247–58, doi:10.1007/s10096-016-2657-1.
50. WOAH. “Responding to the COVID-19 Crisis: The Contribution of the Veterinary Profession.” *WOAH - World Organisation for Animal Health*, July 2022, www.woah.org/en/responding-to-the-covid-19-crisis-the-contribution-of-the-veterinary-profession. Accessed 3 Nov. 2022.
51. WOAH. “Guidelines for Simulation Exercises.” *WOAH - World Organization for Animal Health*. ISBN: 978-92-95115-83-5.
52. WHO. “Tripartite Zoonosis Guide.” *WHO*, 21 Sept. 2022, www.who.int/initiatives/tripartite-zoonosis-guide. Accessed 23 Aug. 2023.
53. CEPI. “Priority Diseases; CEPI.” *CEPI*, 12 Dec. 2018, cepi.net/research_dev/priority-diseases. Accessed 23 Aug. 2023.
54. US CDC. “Emergency Preparedness and Response - Bioterrorism Agents/Diseases.” *Centers for Disease Control and Prevention*, emergency.cdc.gov/agent/agentlist-category.asp. Accessed 23 Aug. 2023.



THEPANDEMICCENTER