NATIONAL LABORATORY PLANNING: DEVELOPING SUSTAINABLE BIOCONTAINMENT LABORATORIES IN LIMITED RESOURCE AREAS

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Strategic laboratory planning in limited resource areas is essential for addressing global health security issues. Establishing a national reference laboratory, especially one with BSL-3 or -4 biocontainment facilities, requires a heavy investment of resources, a multisectoral approach, and commitments from multiple stakeholders. We make the case for donor organizations and recipient partners to develop a comprehensive laboratory operations roadmap that addresses factors such as mission and roles, engaging national and political support, securing financial support, defining stakeholder involvement, fostering partnerships, and building trust. Successful development occurred with projects in African countries and in Azerbaijan, where strong leadership and a clear management framework have been key to success. A clearly identified and agreed management framework facilitate identifying the responsibility for developing laboratory capabilities and support services, including biosafety and biosecurity, quality assurance, equipment maintenance, supply chain establishment, staff certification and training, retention of human resources, and sustainable operating revenue. These capabilities and support services pose rate-limiting yet necessary challenges. Laboratory capabilities depend on mission and role, as determined by all stakeholders, and demonstrate the need for relevant metrics to monitor the success of the laboratory, including support for internal and external audits. Our analysis concludes that alternative frameworks for success exist for developing and implementing capabilities at regional and national levels in limited resource areas. Thus, achieving a balance for standardizing practices between local procedures and accepted international standards is a prerequisite for integrating new facilities into a country's existing public health infrastructure and into the overall international scientific community.

THE EBOLA OUTBREAK OF 2014-15 required global mobilization of resources and material in order to respond to and mitigate the epidemic, and it demonstrated the need for coordinated local and international resources. As of April 2016, there were more than 28,000 cases of

Ebola, resulting in more than 11,000 deaths.¹ This outbreak emphasized the need for functioning public health systems, with specially trained laboratory workers who can support timely and accurate laboratory diagnostic testing and reporting, as well as access to biocontainment facilities.

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In Africa, the lack of reliable and quality laboratory diagnostic testing compromises patient care, particularly when there is a local perception that laboratory diagnostic testing is not helpful.² Therefore, consideration needs to be given to developing integrated national laboratory plans and strategies that include a comprehensive phased approach for implementing laboratory quality management systems.³ This applies to national and regional laboratories responsible for health and security and includes infectious disease surveillance for the detection of outbreaks. The Ebola outbreak developed into a public health emergency of international concern (PHEIC), allowing the principles of the US government's Global Health Security Agenda (GHSA) effort to be put into practice in a real scenario and resulting in system-strengthening efforts to further the linking of health and security sectors.^{4,5}

Although some consensus documents and standards point to plans, no international standards exist. However, the World Health Organization's (WHO) *Guidance for Development of National Laboratory Strategic Plans* document⁶ (hereafter referred to as the WHO *Guidance* document) is generally recognized as a useful tool. This is the closest approximation to guidelines for developing a "roadmap" that national leaders can use to develop a consensus plan; it is focused on enhancing quality laboratory diagnostic testing for endemic diseases such as HIV/AIDS, TB, and malaria. The WHO *Guidance* document was developed by the international community, including stakeholders who contributed to the Maputo Declaration, a consensus meeting held January 22-24, 2008, to develop recommendations on laboratory standardization and harmonization. Several countries, such as Ethiopia, Nigeria, and South Africa, supported by the US President's Emergency Plan for AIDS Relief (PEPFAR), which has become a model for treating other diseases such as Ebola, have developed national strategic laboratory plans to enhance their health systems. Under PEPFAR, the WHO *Guidance* document has been used to engage and advise national laboratory strategic plans in more than 20 countries (mostly in Africa) worldwide.

The number of biosafety level (BSL) -3 and BSL-4 laboratories continues to increase, although the exact number of high-biocontainment laboratories worldwide is difficult to determine, as there is no central tracking authority and no enforced standard definition of what capabilities constitute a BSL-3 or BSL-4 laboratory. The motivations for building high-containment laboratories include basic scientific and diagnostic needs, promoting national growth in biotechnology and related fields, and the need for specialized facilities and infrastructure-augmenting capabilities to enhance disease surveillance.⁷ The need to attract external funding and a desire for national prestige complicate the reality of the handling of potential biological threats and the importance of geographic proximity to other regional and local laboratories.⁷

Extrapolating recent experience with an analytical review of the literature, we discuss examples of national and regional

biocontainment laboratories worldwide with reference to their planning and establishment, function, and future prospects. Highlighting important elements in the development of sustainable health security laboratories in limited resource areas, we include low, lower-middle, and upper-middle income countries based on their gross national income (GNI) per capita, according to the World Bank. Laboratories from the former Soviet Union (FSU), Africa, India, and those funded under PEPFAR were examined for the appropriateness of their initial laboratory planning by assessing: (1) stated mission and role, (2) setting of laboratory objectives, (3) membership of core planning groups, (4) assessment of national laboratory capability through gap analysis, and (5) capabilities to be provided. As a rule, donors and stakeholders influence the development of a laboratory's mission, role, and capabilities.

PLANNING AND ROADMAP

Comparing national laboratory planning in our selected laboratories included efforts funded by the US government, other national governments, and commercial entities. Since 2003, PEPFAR has been engaged in the potential establishment of national laboratory strategic plans in 26 countries. To date, plans have been developed in 12 countries and implemented in 2, Ethiopia and Rwanda. PEPFAR funding has also involved laboratory construction and renovation that has included BSL-3 and enhanced BSL-2 facilities (complementary use of BSL-3 practices and procedures in the BSL-2 environment). Owing to limited resources, one of the key elements in PEPFAR is to integrate national laboratory diagnostic testing capabilities to ensure efficiency and sustainability of those services. Without close coordination, donor funding may set up laboratory services that simply parallel existing laboratory systems, needlessly straining sustainability resources.⁸

Forming close and productive working relationships between funding agencies and recipient partners to develop a national plan for integration of new resources is essential but presents challenges. Both recipient and stakeholders must have input to ensure that expectations and development of plans are aligned and that there is a path for the recipient to sustain activity after the initial investment.⁷ To better coordinate and emphasize leadership of the transfer of support to the recipient country, the logical approach is for the recipient country to take ownership of the plan and its development and fully engage with the donor country.⁹ While various limited resource area recipients may have similar general needs (ie, improved biocontainment capabilities, modern equipment and maintenance support, training, and sustainability), the programs must also be matched to the specific needs and capabilities of the partner country. PEPFAR employs a collaborative governance mechanism at the headquarters and the country level to ensure stakeholders engage and work together.¹⁰ Such an

approach, developed for HIV/AIDS, can be applied to enhancing overall laboratory systems for other endemic and emerging diseases.¹¹

Not all of the laboratories we highlight here were planned to have a primary mission and role relating to laboratory diagnostic testing, unlike the focus of the WHO *Guidance* document. For example, the purpose of developing national and regional laboratories by the US Defense Threat Reduction Agency (DTRA) Cooperative Biological Engagement Program (CBEP) in collaboration with the partner countries was increased oversight of especially dangerous pathogens. This included research work and diagnostic testing.¹² In the former Soviet Union, DTRA CBEP funded the design, construction, or renovation of dozens of BSL-2 zonal diagnostic laboratories (ZDLs) and regional laboratories in Azerbaijan, Georgia, Kazakhstan, Ukraine, and Uzbekistan,¹³ as well as national central reference laboratories (CRLs) in Georgia, Ukraine, Kazakhstan, and Azerbaijan. DTRA, in concert with national stakeholders in their partner countries, helped develop the laboratories' missions, roles, and capabilities.

The DTRA CBEP program objectives included consolidation of national collections of especially dangerous pathogens into a minimal number of secure repositories, as well as ensuring that internationally recognized biosafety and biosecurity measures for the handling and transport of samples were in place for research and training activities. The CBEP research strategy uses a collaborative approach that tasks national, US, and other international partners to develop research engagements; these form the basis for reinforcing internationally recognized biosafety and biosecurity standards, related mentorship, and training on topics such as biological risk management.¹² The DTRA-funded central reference laboratories have defined missions that include: (1) maintaining a repository of especially dangerous pathogens; (2) establishing reference laboratory capability that can be used by regional and local diagnostic laboratories; (3) coordinating the national laboratory networks, including zonal diagnostic laboratories and regional laboratories; and (4) enhancing clinical and diagnostic research activities.

The laboratories built and renovated in the former Soviet Union by DTRA CBEP have similar core national leadership, defined stakeholders, and capabilities consistent with their missions and roles. The national leadership included those ministries and their subordinate institutes (delegated by provincial and district responsibilities) in their national public health structures. The international stakeholders included government and nongovernment organizations and collaborators. Similar to the WHO *Guidance* document and PEPFAR national laboratory strategic plans, the DTRA CBEP-funded laboratories are structured in a tiered network headed by a central reference laboratory, followed by subordinate regional and local laboratories. The laboratory capabilities are based on national, regional, or local responsibilities, which include

enhancing availability and performance of diagnostics and biosafety and biosecurity and the ability to permit samples of interest to be efficiently prioritized and elevated to more specialized secure laboratories.

In Africa, 2 BSL-3 and BSL-4 biocontainment labs that were built and commissioned with a short timeline are the Mycobacteriology Laboratory at the Makerere University Teaching Hospital, Uganda, and the Centre International des Recherches Medicales de Franceville (CIRMF), Gabon. In addition, the National TB and Leprosy Training Center (NTBLTC) has a modular BSL-3 laboratory in Zaria, Nigeria.

The Mycobacteriology Laboratory at Makerere University is a BSL-3 laboratory established in 2008-09 with funding for construction and equipment provided by the Aeras Global TB Vaccine foundation. The mission is to participate in tuberculosis-related clinical research, to collaborate with the National TB Reference Laboratory (NTRL), and to train healthcare workers. Following an initial validation phase for procedures and equipment with NTRL, the Mycobacteriology Laboratory started full operations in 2009. Soon a 3-year performance indicators guide with programs leading to the full implementation of external quality assessment (EQA) registrations was established that included a functional quality management system (QMS).¹⁴

CIRMF was funded by both national and international stakeholders that included the Gabon government (20%), the TOTAL-GABON oil company (65%), the French Ministry of Foreign and European Affairs (10%), and various international institutions (5%). CIRMF's mission and role are to serve as the national reference laboratory and provide capabilities for diagnosis of suspected cases of viral hemorrhagic fevers (VHF). In addition, CIRMF is charged with developing new diagnostic methods, conducting animal surveillance, and performing investigations of outbreaks of unknown etiology.¹⁵

The NTBLTC in Nigeria was funded by the US CDC, PEPFAR, and the government of Nigeria and was established in 2004 by a joint partnership between the Institute of Human Virology (IHV) of the University of Maryland's School of Medicine in Baltimore and the Institute of Human Virology-Nigeria. PEPFAR supports AIDS Care Treatment in Nigeria (ACTION), which is a network of laboratories that includes the NTBLTC.¹⁶ CIRMF, Gabon, the Mycobacteriology Laboratory in Uganda, and the NTBLTC in Nigeria are well-established and functioning institutes that set good examples of the benefits of national laboratory planning.

In Pune, India, the National Institute of Virology (NIV) is one of the major institutes of the Indian Council of Medical Research (ICMR). The ICMR is the principal government body in India for the coordination and promotion of biomedical research; it is funded by the government of India through the Ministry of Health and Family Welfare. The NIV was established in 1952 as the

Virus Research Centre (VRC) under the sponsorships of the ICMR and the Rockefeller Foundation USA. The Rockefeller Foundation withdrew its support in 1967, and since then the institute has been entirely funded by the ICMR. The NIV has been designated as one of the “collaborating laboratories” of the WHO and acts as the WHO regional center in Southeast Asia for arbovirus studies, hemorrhagic fever reference and research, and rapid laboratory diagnosis. NIV is also the national monitoring center responsible for monitoring influenza, Japanese encephalitis, rotavirus disease, measles, hepatitis, and other viral diseases that may become important. Other major activities of NIV include outbreak response; diagnostics development and kit supply; viral surveillance of humans, mosquitoes, birds, and poultry; and basic and applied research and supply of laboratory animals. The institute also works with local hospitals and collects clinical samples for confirmation of diagnoses.¹⁷ In addition to its ongoing support of NIV, in 2013 the government of India launched a broader national program on emerging pathogens involving specific support to key virology research laboratories.¹⁸

PEPFAR and its implementing agencies worked with each partner country to apply a stepwise process for addressing each category of the WHO *Guidance* document. For example, laboratory capabilities such as quality management systems, equipment maintenance/supply chain, and training and retention of human resources were identified as core elements (laboratory capabilities or systems) that are applicable to all diseases of interest under a national laboratory strategic plan.¹⁹ Laboratories should consider their core elements when determining which services they will provide. Likewise, DTRA CBEP and its biological threat reduction integrating contractor worked with their partner country stakeholders to develop foundational documents as part of laboratory set up, with, for example, the central reference laboratories in Azerbaijan, Georgia, and Kazakhstan. The foundational documents address WHO *Guidance* categories in the areas of organization, implementation, and transition plans and also referenced the NIH *Design Requirements Manual*²⁰ relevant to laboratory and animal research requirements.

LABORATORY, INSTITUTIONAL, AND MANAGEMENT FRAMEWORK

Strong leadership, administration, and political support are key to facility success, as demonstrated by our examples—especially those in Africa, where the laboratories had strong external collaborations and funding. The NIV and extended ICMR plans in India are supported by an administration department that is multifaceted and includes material, financial, and personnel management.

In Azerbaijan, a clear framework underpins both new and renovated facilities’ roles in the national laboratory system, including the management structure and the link-

ages between national and regional laboratories, the ministry of health, and other government groups, as well as outside funders and collaborators. Both the regional laboratories and central reference laboratories were upgrades (replacements) for existing ministry of health facilities and not new entities. If facilities are being upgraded, a framework exists but needs to be reviewed to ensure it still fits the purpose of the new laboratory. If a facility is entirely new, then careful consideration is required to properly fit the new capabilities into the current public health architecture of the country.

The government of Kazakhstan will take ownership and operate the central reference laboratory in Almaty, which is planned to be shared by 3 ministries: agriculture, education and science, and health. Thus far, the cooperation of these 3 ministries, DTRA CBEP, and other collaborators and stakeholders has addressed the 7 categories from the WHO *Guidance* document through separate foundational documents. The framework encompasses an early stage development that includes the handoff of the central reference laboratory to the government of Kazakhstan, followed by a later stage that will include investment from other donors and funders. In addition, DTRA CBEP funds research and training to address specific needs—for example, developing a framework and related details pertaining to enhancing the synergy among different Kazakh institutes.

LABORATORY SERVICES PLAN

Based on laboratory mission and objectives, several operational and policy components are needed to define the laboratory services that will be provided. The NTBLTC in Nigeria, partnered with the IHV-UMD, provides a good model for organizing and implementing a laboratory services plan that includes training, renovating infrastructure, establishing maintenance and service of equipment, and establishing quality assurance and quality control.¹⁶ The NTBLTC’s close collaboration with their hospital and facility management teams ensured that each new laboratory service item had adequate maintenance and sustainability planning. Similarly, the NIV has developed capability with advice from various institutes in India using experts who have a history of postgraduate training abroad.

A major challenge for developing an effective laboratory services plan or research program is establishing a framework of biosafety and biosecurity guidelines that align with national legislation, as well as meeting internationally recognized regulatory standards. Achieving a suitable legislative framework for biosafety and biosecurity guidelines requires an appropriate ministerial-level lead to adopt and enact legal guidelines. To varying extents, these already exist and are practiced by peer countries, creating suitable starting points or models and providing relevant subject matter expertise available for technical input and support.²¹ Not only are biosafety and biosecurity important in the context of

laboratory containment, but they also affect training of personnel and maintenance of infrastructure and equipment. For example, the Indian NIV has an institutional biosafety committee that includes a maintenance group in which staff members work with apprentice students to perform routine preventive maintenance tasks. Regular equipment maintenance, servicing, and overhauling is undertaken to successfully extend the life of laboratory facilities.

The importance and limitations of, as well as the need for, risk-based assessments, particularly in training local experts to conduct and guide their personnel, were in evidence during the Ebola outbreak. Since biosafety and biosecurity are part of DTRA CBEP's key pillars, they have adopted the use of biological risk management planning, based on an all-hazards approach.²² This includes a system-wide analysis, taking into account mitigation and prevention, as determined by a comprehensive assessment that aligns the laboratory mission with biosafety and biosecurity. An important emphasis is on mentoring biosafety officers in partner countries and ensuring that biosafety officers feel ownership of these activities. Similarly, the Association of Public Health Laboratories (APHL) provides a tool for laboratories conducting TB diagnostics.²³ In addition, RAND has developed a measure for the performance of CBEP activities, by defining metrics related to capability and sustainability for biosafety and biosecurity, biosurveillance, and cooperative research activities.²⁴ Applying these metrics has been important for early development of strategic laboratory planning of CBEP's central reference laboratories.

Equally important as institutional review, the policies are applied to the processes at the working level by administering periodic review of the diagnostic testing algorithms. In Azerbaijan, diagnostic algorithms were revised to include new techniques, and the sample flow was adjusted and documented to provide a single point of reference for laboratories, in the form of printed guidelines issued by the ministry of health. Supply chain issues continue, and, as with any limited resource environment, reagents for the newest gold standard test may be unavailable (issues include cost, long delivery time, storage/transportation temperature requirement, centralized procurement, and shelf life). Thus, acceptable alternative tests should be included during the planning. Improving existing test algorithms also negates some supply chain issues, as these reagents and supplies are largely already being provided. Another key area to be addressed at the working level is waste management, and care must be taken here to conform with international as well as local standards and practices.

HUMAN RESOURCES SYSTEMS

It is obviously very important to encourage retention of staff (eg, avoid migration of trained individuals to the private sector or other agencies or countries) and to check for biosecurity

issues when hiring (eg, background checks and personnel reliability programs). Staffing plans should be prepared to ensure there are sufficient personnel in the correct roles to allow the facility to function optimally and that, to the extent possible, compensation is comparable to what workers might receive from other employers for similar activities. Provision of job descriptions and preservice training plans, as well as continued training and education opportunities, are essential. When the Soviet Union dissolved, state salary support for laboratory scientists was drastically reduced, and scientists in need of income could be swayed to divulge knowledge and material to higher bidders; one scientist was arrested for attempted theft of pathogens in Almaty, Kazakhstan, in 2002.²⁵ Hence, personnel reliability is a vital issue.

In Azerbaijan, the staffing plans for regional sites were clear, but for the new central reference laboratory, the existing anti-plague system staffing plan was modified to reduce down time and increase efficiency in a more technique-focused setting. Technique-based job descriptions and training plans were jointly developed to replace disease-based versions, with initial training provided by DTRA, assisted by ministry of health training personnel, to provide an opportunity to gain experience and be prepared to take over training delivery in the future.²⁶ This approach seems to have worked well.

LABORATORY SUPPORT SYSTEMS

Laboratory planning can often focus on science and diagnostics and ignore supply chain, IT, maintenance, and other support system needs. This can become a serious issue in low resource environments and will result in service interruptions if key reagents go out of stock or critical equipment such as biosafety cabinets, autoclaves, and air handling equipment cannot be serviced or repaired without bringing engineers from overseas. This is especially critical at a BSL-3 or higher containment level laboratory. Standardization of equipment and tests across a public health system in a given country through the national laboratory planning process described here makes a system more sustainable, as solutions become more cost-effective due to economies of scale. Especially problematic in many countries is the issue of biosafety cabinet certification. While this is recognized as something required by international biosafety standards, it is usually difficult to find qualified and certified technicians and calibrated test equipment in-country. Often no national legislation exists to enforce the annual certification requirement. This lack of ongoing certification of biosafety cabinets can affect future operations of laboratories, as this gap can hinder access to international collaborations and research funding because of safety concerns.

In Azerbaijan, ministry of health engineers were provided with training in maintenance of laboratory equipment to support scientific operations. In addition, the suppliers of facilities and infrastructure equipment for heating, ventilation, and air conditioning (HVAC) and boilers were made

responsible for providing specific training on these systems. It was necessary to supply engineers with tool kits and, in the case of US-sourced equipment, to provide imperial-sized tools such as hex keys and socket sets rather than the metric tools found in Azerbaijan, a compatibility issue that is easily overlooked. Biosafety cabinet certification training was also provided, and while the engineers are not certified by industry standards, they do have the skills and equipment to verify that a biosafety cabinet is operating within normal parameters; this was considered an acceptable solution by the government of Azerbaijan. ACTION's supported laboratories in Nigeria tracked routine preventive maintenance through regular logs that equipment vendors augmented with periodic training.¹⁶

LABORATORY QUALITY SYSTEMS

Quality systems and quality assurance can support ISO accreditation, which is often held by governments as the ultimate goal for diagnostic facilities. Reliable documentation of activities strengthens the overall lab performance and has biosecurity implications (eg, strain inventories). A quality management system documents lab SOPs, risk assessments, and corrective actions, thus better equipping a lab for international collaborations, as a written record of all of these processes can easily be shared.

In Africa, the WHO has produced guidance on a Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA). This is a framework for improving the quality of public health laboratories in the African Region to eventually reach ISO 15189:2012 standards. It is based on the principles of affordability, scalability, measurability, and accessibility and could easily be applied outside of the African Region to aid laboratories in the development of their quality systems.²⁷ This process often requires a significant cultural shift and adopting a “no-blame” culture. This is important to foster the openness necessary for solid quality management systems, but can require a significant investment of time and training. By considering such quality management and its associated challenges early in the planning process for a new laboratory, the key stakeholders have the opportunity to clearly display their commitment to a quality management system.

MONITORING AND EVALUATING LABORATORY SERVICES

Internal and external audits work to support a quality management system by ensuring quality of results and verifying that protocols and processes are being followed and properly documented. Monitoring and evaluation is usually a critical part of obtaining lab accreditations (whether national or international) that support laboratory use and collaborations and can also lead to WHO collaborating lab status. The SLIPTA program includes a standardized audit template aligned to ISO standards, which can be used as a guide for initial audits by

laboratories. Though designed as an audit tool, careful review of this template during the planning and stand up of new laboratories can inform the process and ensure consideration is given to improving critical areas. This same document can later be used by quality and biosafety officers to monitor processes and progress in the laboratory, based on scores during the baseline and exit assessments.²⁸ SLIPTA examines the systems and documentation in use but does not evaluate the results of laboratory work. To this end, proficiency testing of laboratory assays—for example, processing of mock samples either through intralaboratory result comparisons or internationally accredited proficiency testing programs—can identify areas for process modification or additional training.

POLICY, LEGAL, AND REGULATORY FRAMEWORK

Strengthening the legal and regulatory framework is another important step in supporting implementation of national laboratory policy. If plans are not properly supported via a regulatory framework, they may not be valid or they may be disregarded. Thus, once all of the above plans have been developed, they must finally be considered in the light of legal and regulatory requirements to allow them to be fully deployed and enforced.

As an example, in Azerbaijan, updated diagnostic algorithms were not initially supported by signed ministry of health regulations. This meant that PCR assays were not considered valid tests and that only Soviet-era methodologies were legally able to be used to test for pathogens. Once this was rectified, the new techniques began to gain traction. Less is known about our other example laboratories, but it is likely that situations similar to the above exist or existed in other low resource countries. Thus, governance and regulatory policy is another laboratory core element that is important in determining which laboratory services can be provided.

DISCUSSION

Laboratories described in our review have either already been constructed or the construction is currently in progress. However, even in many established (or soon to be established) facilities, local sustainment and long-term engagement may be limited, and the maturity of laboratory capabilities varies. Contributing to some uncertainty in this area, information pertaining to specific laboratories is often partial, unpublished, or not publicly available.

Developing strategic laboratory plans requires a strong basic framework; this should include a metric-based approach and should specify operational capabilities, as well as defined commitments by the donor(s) and recipient. Where no formal guidance exists, examples from laboratories already developed under health and security missions should be used, as these may offer tested applications for

future development of laboratories where issues will occur on a case-by-case basis. Importantly, the donor(s) and recipient need to agree on expectations at an early stage of discussions, if they are to avoid duplicating existing laboratory capabilities and national program efforts and provide a best path for sustainment.

PEPFAR exemplifies the model for effective international donor funding to enable partner countries to develop strategic laboratory plans in a stepwise fashion, taking into account capabilities in low resource areas. The US government typically uses cooperative agreements, direct contracts, and grants to fund their activities. Agencies such as CDC, PEPFAR, and USAID often contract work through the use of cooperative agreements that actively involve the agency, contractor, and recipient, which can allow the activity to be more effectively coordinated. DTRA CBEP has also achieved its mission through government-to-government cooperative agreements and has implemented work mainly through direct funding to contractors to build and renovate laboratories. In this context, DTRA CBEP has funded construction and renovation of laboratories, training on biosafety and biosecurity, infectious disease surveillance, and related research. Many laboratories, especially those in low resource areas funded by PEPFAR, focus on developing diagnostic capabilities, and, while BSL-3 standards such as Class II A1, A2 biosafety cabinets are recommended for TB diagnostics, only laboratories such as NTBLTC in Nigeria and the Mycobacteriology Lab in Uganda have true BSL-3 facilities. Often, work on HIV/AIDS is routinely performed in BSL-2 facilities, which is the minimum requirement. Risk-based assessments such as biosafety and biosecurity and working level documents, such as those referenced for TB diagnostics and program metrics, are useful in developing “as is” and “to be” type capabilities.

One of the most difficult issues in establishing health security laboratories is public opinion, which greatly influences successful engagement. Even after the facility is planned and built, it may take years to clear all the official and unofficial hurdles to full operation. Securing a positive public attitude is an essential part of successful planning and implementation of BSL-3 and BSL-4 laboratory construction and operation in both resource-limited and resource-rich settings.

Cataloging the progress of laboratory capability and operations development can be a difficult but necessary task. Identifying and tracking metrics while developing successful ways to ensure long-term sustainability is clearly important. Designing a framework that is a matrix of laboratory capabilities and laboratory services—such as Nkengasong et al reported;¹⁹ the WHO *Guidance* document, which presents a checklist for planning strategic objectives over a 5-year period;⁶ and the metric performance that Young et al described²⁴—are good examples of complementary references that can aid in a capability maturity analysis. These authors state, with some justification, that capacities and sustainability enablers are the building blocks that inform and maintain the capabilities of a

partner country. In addition to discussing this type of analysis, our review has also listed additional references that are excellent tools for determining and assessing capabilities.

The use of any such framework at the outset of a project to develop a national reference laboratory with biocontainment facilities is essential to harmonize the expectations of the recipient (ultimately the end user) and the donor (domestic and/or international). Throughout this review, we have sought to remind both recipients and donors of the importance of strategic plans to determine milestones and timelines. We have also drawn attention to examples in which a holistic approach to planning has assisted in project success. The WHO *Guidance* document, on which we focused, has a national laboratory strategic plan development checklist and plan containing tables that describe each element (with important objectives and useful timelines).

However, as our analysis shows, alternative frameworks with relevant lessons learned also exist. While a single global standard is ideal and would certainly benefit progress, it is important to recognize that a balance of best practices among accepted international standards and local procedures is the most practical approach. Through the use of published references as a starting point, with the agreement of all parties, a project-specific framework should be produced as the first activity in any laboratory development project.

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